

Koret Vision Institute + Beckman Vision Center + Department of Ophthalmology

Summer 2008

University of California, San Francisco + That Man May See

Focal Point



Dear Friends,

The impact of UCSF Ophthalmology around the world is made evident in stories throughout this issue of Visions. Addressing world blindness is a hands-on effort of dedication, compassion, and teamwork. The sheer number of people suffering severe visual disabilities in Africa alone (84 million) makes it essential that we invest in this work.

One of our stories describes the ongoing accomplishments in Ethiopia and India of a remarkable team of researchers from UCSF's Francis I. Proctor Foundation. We also highlight the impact of our international fellowship programs on global medical practice and education. UCSF Ophthalmology mentors promising young medical doctors who serve on our campus for a year or two and then return to their countries, better equipped to handle the vision challenges they find there.

Every day I take great pride in our outstanding faculty. As you read, we wish to underscore the role your gifts play in our ability to do this work. When you support That Man May See, you help us envision a world without blindness. Thank you for making a difference for the vision impaired here in the Bay Area and for the many who benefit from our research in remote regions of the world.

Sincerely,



Envision the Future Helping the World to See

Widespread and tenacious causes of blindness in the developing world challenge the experts at UCSF Ophthalmology to find answers. Research, treatment, and education all come into play for Jack Whitcher, MD, MPH, Thomas Lietman, MD, and Nisha Acharya, MD, a formidable team working to prevent blindness and visual disability in Ethiopia and India. They proceed under the auspices of the International Programs Group of the Francis I. Proctor Foundation for Research in Ophthalmology and collaborate with other universities, international nongovernmental organizations (NGOs), and local partners.

UCSF's Proctor Foundation, an independent research unit directed by **Todd Margolis, MD, PhD,** is a vital part of UCSF Ophthalmology. The foundation emphasizes the development of long-term solutions – its goal is to identify causes and determine the most effective strategies for eradicating blinding conditions entirely. Established in 1947 and located on the Parnassus Heights campus, Proctor is dedicated to research and training in infectious and inflammatory ocular diseases and to the application of this research to the prevention of blindness worldwide.

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Ophthalmology Insight Think Global, Train Local



Stephen D. McLeod, MD Theresa M. and Wayne M. Caygill, MD, Endowed Chair Professor and Chairman



In 1966, an eager young doctor named **Francisco Contreras** arrived in San Francisco from Lima, Peru, with his wife and daughters in tow. He had been chosen from a highly competitive pool to receive a fellowship – a year of advanced training beyond his

three-year residency- with UCSF Ophthalmology's renowned faculty.

UCSF Ophthalmology's commitment to global ocular health shapes its provisions for advanced education of ophthalmologists from around the world. The Department of Ophthalmology began its fellowships with gifts from the William Randolph Hearst family and the Hearst Foundations. Dr. Contreras was the first recipient of this prestigious award. Today the *Continued on page 6*

A PEEK INSIDE:

Thailand: Saving AIDS Survivors from Blindness





Visionary Continues with International Research

Denmark to India: Team Builds Database for Sjögren's Syndrome



China and the Americas: Dr. Richard Abbott Honored

San Francisco: The Mettiers Envision the Future



A Tour de Force Leads the Way

Motivated by the blindness he saw in Nepal and India early in his career, Dr. Whitcher joined the Proctor Foundation full time in 1991 and began developing international research/treatment studies. He has been the driving force behind Proctor's international projects ever since. As Dr. Whitcher reaches "retirement age," he is passing leadership to his mentee Dr. Lietman, Director of the World Health Organization (WHO) Collaborating Center at Proctor. Dr. Whitcher continues as elder statesman – if someone who travels abroad at least five times per year and walks through the Gondar hills of Ethiopia to examine trachoma patients can be considered an elder of any kind (see "Visionary Continues with International Research," page 5).

"We're Aiming Higher"

Dr. Margolis expresses confidence and pride in the doctors working in Proctor's international programs. "We find the most productive, creative, intelligent people and turn them loose to do what they want within the mission of the foundation," he says. And he sums up the foundation's global influence with satisfaction: "If we just provided individual on-the-spot treatment, it would be valuable," he says. "But that approach has a limited impact. We're aiming higher, doing research on how to reduce the burden of blindness in entire populations."

> FFIf trachoma can be eliminated in Ethiopian communities where we are working, it can be eliminated anywhere."

UCSF Shares Bill and Melinda Gates Foundation Grant

The Bill and Melinda Gates Foundation recently awarded a \$10 million grant to three ophthalmology teams – including UCSF Proctor Foundation's international programs group – working together to eradicate trachoma worldwide. UCSF partners in the grant are Johns Hopkins University (grant administrator) and the London School of Hygiene and Tropical Medicine.

Blindness Reaps Devastation in Ethiopia

orldwide 84 million people are afflicted by trachoma. It flourishes where living conditions are poor and clean water hard to come by. Because this blinding disease is both chronic and highly contagious, areas with untreated cases are burdened with tremendous rates of blindness from infections that invariably begin in childhood. The consequences are parents who cannot work, families torn apart as disabled partners are left to fend for themselves, and children (especially girls) who leave school to take on caretaking roles.

The trachoma infection (caused by the *Chlamydia trachomatis* bacteria) is highly visible to the trained observer, with red, inflamed linings of the eyelids associated with follicles that cause scarring of the undersides of the eyelids as they heal. If left untreated, the infection eventually causes the eyelids to turn inward which causes the eyelashes to rub on the eyeball, resulting in intense pain and scarring of the front of the eye. This ultimately leads to irreversible blindness, typically at between 30 and 40 years of age, when most adults are most productive.

Relief vs. ERADICATION

Dr. Francis I. Proctor was particularly interested in trachoma – in 1927 he helped establish a research center at Fort Apache, New Mexico, where the disease was rampant among Native Americans. He served for many years as a trachoma consultant to the Bureau of Indian Affairs. By the 1970s the disease had been eradicated in the United States.

Many humanitarian groups, including the World Health Organization, work to control trachoma. Dr. Lietman distinguishes between these activities and the plan of the Proctor Foundation: ERADICATION. It's an audacious goal, primarily supported by funds from the National Institutes of Health, the Bill and Melinda Gates Foundation, and the Bernard Osher Foundation (see donor list on page 4). When eradication is complete, trachoma will be the first disease ever eliminated globally through the use of antibiotics. (Previous eradications, such as smallpox, have been accomplished through vaccinations.)

Immensity of Trachoma Challenge

"I think that trachoma will be eliminated in the next 20 years or so," says Dr. Lietman. "If it can be eliminated in Ethiopian communities where we are working, it can be eliminated anywhere." Ethiopia has the highest

Eradicating Trachoma with Antibiotics







prevalence of infection on the planet. "It may take an intensive effort in some hot spots, with strategies such as those we're now developing."

Proctor's international team started trachoma studies in Ethiopia in 2001 and is now beginning its third largescale project. This invaluable research is, in sheer numbers of patients, by far one of the largest trachoma studies ever undertaken. The result is a huge pool of data that demonstrates conclusively the effect of treatment variation on the elimination of the disease. The antibiotic azithromycin, donated by Pfizer, Inc., is given to all the study subjects; the scientists have varied the frequency and number of treatments in order to determine the treatment protocol needed to prevent re-infection within communities.

"Being blind in a rural village in the developing world leaves a person in darkness and dependence, often unable to earn a living or assist in the duties of their household," says Mr. Gates. Two principles guide the work of the Bill and Melinda Gates Foundation:

- All lives, no matter where they are lived, have equal value, and
- To whom much is given, much is expected.

This major gift will carry forward the work of Drs. Thomas Lietman, Jack Whitcher, and others who have been seeking solutions to trachoma for years, developing and testing treatment strategies to end this blinding epidemic.



More than 50% of the children tested in Ethiopia had trachoma. Doctors track the number of reinfections for each of three treatment plans (single, annual, and biannual antibiotics). Dr. Lietman then mathematically determines how often and over what period of time antibiotics must be administered to stop reinfection. The blue line shows the treatment plan necessary to get to 0% reinfection.







Dr. Lietman has been the primary author of dozens of published papers on the topic over the past eight years, many written in partnership with Dr. Whitcher and international researchers. The accumulated data has allowed Dr. Lietman to develop a mathematical model for a treatment strategy effective enough to stop the spread of the disease, with the goal of eventually eradicating it. Biannual treatment for a period of four years seems to be effective in the Ethiopian environment, with its high infection rates (see graph, previous page). Eventually Dr. Lietman hopes to develop an algorithm that can define the optimal treatment plan for any given area in the world, based on its infection rate.

Proctor's Ethiopian studies all follow a similar protocol. The researchers, joined by fellows and support staff, examine a representative subgroup of the 100,000 to 200,000 Ethiopian children and adults in as many as 48 to 80 villages three times per year. They are accompanied by local counterparts from the Carter Center, Orbis International, or Ethiopia's Gondar University, partners who provide the antibiotics to the villagers according to a precise timetable. The UCSF team then assesses the effectiveness of the treatment strategy by two methods.

Ulcers and Infections: Finding Answers in India

In India, Proctor researchers study the effectiveness of treatments for corneal ulcers and tuberculosis-related uveitis. Dr. Lietman serves as a mentor for Dr. Acharya, and they travel to Madurai, India, at least twice a year to oversee studies carried out at Aravind Eye Hospital, the largest eye hospital in the world. Dr. Acharya also directs the Ocular Inflammatory Disease and Uveitis Clinic at UCSF. Study patients for the corneal ulcer trials are enrolled at UCSF and at the Dartmouth-Hitchcock Medical Center in New Hampshire, but most of the patients are in India. "We couldn't do these trials in the United States because there aren't enough cases," explains Dr. Margolis. "The rate of corneal ulcers in India is much higher, so we can study enough people at one center to get usable results in two years instead of ten."

The patients for the studies in India are selected from among those who come to Aravind Hospital's cornea and uveitis clinics. Both the ulcers and uveitis are potentially debilitating conditions, and many of the study subjects have vision loss substantial enough to prevent them from working. The ulcers cause severe pain – patients sometimes can't even keep their eyes open – and blurred vision. Uveitis, while less painful, causes blurred vision, too, and may cause light sensitivity and "floaters" as well.

Corneal Ulcers: Testing Treatment Options

The NIH-funded Steroid for Corneal Ulcers Trial, begun in 2006, is designed to determine the effect of topical corticosteroid drops on bacterial corneal ulcers and to optimize treatment based on type of bacteria. "Hopefully, the data generated will help us determine if corticosteroid drops are an effective treatment for bacterial ulcers, used in addition to antibiotics," says Dr. Acharya. Right now, no one knows the best way to treat corneal ulcers or whether the steroids are useful or even harmful. This randomized control trial will help determine the best way to treat patients with bacterial corneal ulcers.

Fungal corneal ulcers need their own treatments. The Mycotic Ulcer Treatment Pilot Trial has enrolled 120 patients with fungal ulcers in order to 1) compare the effectiveness of two antifungal medications and 2) to

Drs. Nisha Acharya, Thomas Lietman, and Jack Whitcher pursue long-term solutions to blinding diseases in the developing world Seeing the magnitude of the vision problems in India reminds me how important our international research is." – Dr. Nisha Acharya

gauge the effectiveness of repeated scraping of the ulcers, a process that utilizes a tool called the Kimura spatula. The initial study, funded by That Man May See, is being completed this summer. Drs. Acharya and Lietman hope that its results will attract support for a larger-scale clinical trial in the near future.

Diagnosing TB Uveitis

Dr. Acharya is in charge of a study of tuberculosisrelated uveitis (TB uveitis) that is just beginning. "Managing TB uveitis remains a challenge because there's no gold standard for determining when TB is causing the uveitis," she says. Uveitis can have many causes and, while TB can exist in the eye, tests for its presence are also imperfect.

To establish a better diagnostic paradigm, the team will examine suspected TB uveitis patients and perform all the available tests for determining its causes and whether TB is present. Then, all the patients will receive the full anti-TB chemotherapy course of treatment, with the assumption that, if the uveitis responds, it is likely linked to TB. Finally, the team will do statistical analyses to find out which diagnostic test or tests best predict that chemotherapy will be effective.

Dr. Acharya's experience in India helps refresh her commitment to the field. "I've been to Aravind Hospital more than ten times now," she says. "I'm always inspired by the dedication of the Indian doctors there. Just seeing the magnitude of the problems they deal with and collaborating with them on these difficult, widespread vision problems reminds me how important our international research is." •

To make a financial contribution for the Proctor Foundation's international work, contact Kathleen Rydar, president of That Man May See, at rydark@vision.ucsf.edu or 415.476.4016.

High Standards for Research

Like other trachoma research groups, Proctor research physicians perform visual exams on subjects, looking for inflamed eyelid linings. But Drs. Lietman and Whitcher, with the help of **Dr. Bruce Gaynor**, a research associate, are working smarter than most, applying a new gold standard for diagnosis as well as statistical sampling methods to determine how many adults and children need to be examined on each trip. The statistical sampling allows them to track the eye health of an entire community, rather than that of individuals.

Their new gold standard for trachoma diagnosis – DNA sampling of smears from the patients' conjunctiva – is a step that few in the field have taken. This sampling

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Commitment to Vision in **Developing Countries**

UCSF's Francis I. Proctor Foundation and That Man May See thank all the donors who support research/treatment programs in Ethiopia, India, and Thailand. Major contributors include:

National Institutes of Health/National Eye Institute International Trachoma Initiative The Bill and Melinda Gates Foundation The Bernard Osher Foundation Research to Prevent Blindness The Bodhri Foundation The Harper/Inglis Trust The South Asia **Research Fund** World Health Organization **ORBIS** International

Carter Center Harper/Inglis Trust The Peierls Foundation Alta California Eye Research Foundation Annie Henry JaMel and Tom Perkins Family Foundation of the **Chicago Community Trust** Charles W. Leiter, PharmD, and Susan Leiter Morton R. Leiter, RPH Thomas R. and Johanna K. Baruch **Müller Family Trust** Laurence and Sue Spitters

Ethiopia Continued from page 3

allows them to accurately assess what percentage of each village population has trachomatous bacterial infection, as opposed to eve infections due to other causes. By applying this standard, they effectively avoid overdiagnosis, which leads to unnecessary medication efforts as well as skewed mathematical models and algorithms.

Overcoming Challenges

These Ethiopian studies bring with them a host of logistical issues, many of which fall to the Ethiopia Project Coordinator Jenafir House, who holds master's degrees in public health and social work. Simply reaching the patients' villages can be a challenge. "Often there are no roads so, after driving for an hour, the medical team might face a three-hour walk," she says. "We use a global positioning system, but we also rely on our local team members." Locating the villages is just one reason

it's essential to have relationships with local health workers.

Ms. House also coordinates the "cold chain" for the samples taken in the villages. These must be preserved at low temperatures until they can be analyzed for DNA by polymerase chain reaction back at the Proctor Foundation. Since the villages lack electricity, the researchers use coolers for initial storage, and then Ms. House is accountable for keeping them frozen as they are moved to Addis Ababa and flown to California.

Communications with Ethiopian coordinators and institutions can be daunting. "The idea of a research study can be a very Western concept," Ms. House says. "We need to be clearer in communicating the longer-term benefits of our work - how ending trachoma will change the face of rural life in Ethiopia."

Thailand **Telemedicine Targets Blindness from AIDS**

he good news is that effective AIDS drugs are making their way into sub-Saharan Africa, India, and Southeast Asia, and survival rates are rising. In Thailand, where 580,000 people are afflicted with AIDS, the Thai government subsidizes the antiretroviral treatment that has transformed outcomes in the West.

The bad news is this: these survivors are likely to go blind. Because people in developing countries tend to delay treatment until their immune systems are seriously depressed, they are at high risk for a viral infection called cytomegalovirus (CMV) retinitis. CMV, a herpes virus common throughout the world, is held in check by a healthy immune system. Unrestrained it can cause blindness and even death, but it is largely neglected in the developing world.

Alison Skalet, MD, PhD, a young doctor beginning her residency at UCSF Ophthalmology, is developing a telemedicine pilot study that could revolutionize diagnosis of this retinal disease. Todd Margolis, MD, PhD, director of UCSF's Francis

I. Proctor Foundation, and Dr. Somsanguan Ausayakhun, chairman of ophthalmology at Chiang Mai University, are the lead scientists working with Dr. Skalet.

Emerging technologies have the potential to greatly reduce the burden of blindness that threatens to overwhelm survivors of the HIV/AIDS pandemic."

- Dr. Alison Skalet

The herpesvirus family is of special interest to Dr. Margolis - he studied and treated AIDS patients with CMV retinitis in San Francisco early in the AIDS epidemic, before treatment with antiretroviral drugs was available.

High-Tech Strategy

Telemedicine utilizes the Internet to transmit medical image files and text from medically underserved locations to specialized health centers such as UCSF. Highly trained ophthalmologists can review the data and send

> back a diagnosis to health workers in the field, who then prescribe treatment. Combined with newly affordable oral medication, telemedicine may make CMV retinitis treatable at primary care clinics – a huge advantage in a ountry with few ophthalmologists.





Dr. Skalet is implementing a study on a blinding viral infection at Chiang Mai University in Thailand (top).

AIDS patients in Thailand need to be screened for cytomega/ovirus retinitis.

The pilot study, based in Chiang Mai, Thailand (a city of 700,000), will do two things: 1) determine the prevalence of this viral infection in AIDS patients seen at Chiang Mai University Hospital and 2) compare the reliability of remote diagnosis via the Internet with expert in-person diagnosis.



Dr. Skalet explains: "This has the potential to greatly reduce the burden of blindness that threatens to overwhelm survivors of the HIV/AIDS pandemic."

Preparing for Phase Two

If remote diagnosis proves reliable, the next step will be to screen HIV patients with retinal photos during their usual primary care appointments. A newly developed digital camera will be used at each site. The pilot study is currently getting underway, and the Thailand team seeks support for the next phase of this important project.

Drs. Alison Skalet and Todd Margolis

PERSPECTIVE

Dr. Jack Whitcher "Retires" Visionary Continues with International Research



Dr. Whitcher with a village elder in Ethiopia.

Uack Whitcher, MD, MPH, has devoted much of his career to preventing blindness in developing countries. It's a passion he developed as a young man, and it has never waned over a career split between UCSF's Francis I. Proctor Foundation for Research in Ophthalmology and his years of private practice.

The Face of Blindness

When Dr. Whitcher began his career in the early '60s, he planned to go into obstetrics. But that changed when he joined the Peace Corps and was sent to Nepal. (He and his wife Marilyn, a trained public health nurse, were married there by a Jesuit priest.) "Walking around the bazaar in Kathmandu at 25," he recalls, "I was struck by how many children were blind or had one eye that was white from scarring. They accepted it as their *dharma* – their fate," he says. Work in India cemented Dr. Whitcher's dedication to preventing blindness. "It changed my attitude about how I should live my life," he says.

A Lifetime Commitment

Back in the States, Dr. Whitcher did his residency at UCSF's Department of Ophthalmology and then his fellowship at the Proctor Foundation. The fellowship included a year in Tunisia working on trachoma. His mentor, **Chan Dawson**, **MD**, taught him the nuts and bolts of epidemiologic research and how to examine children in the field. After his fellowship, with grants hard to come by and a young family to provide for, he went into private practice.

Aching to help abroad, Dr. Whitcher returned to Nepal in 1985. By that time he knew that corneal ulcers were responsible for much of the blindness and scarring he had seen on his first trip. Paying his own way and working with **Gil Smolin, MD,** Dr. Whitcher helped set up a microbiology lab at the university in Kathmandu and launched a study to find the cause.

The lab traced the ulcers to the bacterium *Streptococcus pneumoniae*. Common agricultural injuries of the cornea, usually caused by rice paddy stalks, were allowing the bacteria to enter the corneal tissue and cause a blinding infection. The same process was taking place in children's eyes, caused by dirt, rocks, and other culprits. Armed with this knowledge, doctors in Nepal were able to more effectively treat the ulcers, and ultimately Dr. Whitcher and his colleagues were able to develop a village-based, grassroots public health strategy that would prevent 96 percent of the ulcers from occurring.

> Sparing people from preventable blindness is his cherished mission.

In the United States, corneal ulcers occur at the rate of 11 per 100,000 people. In Nepal, Dr. Whitcher demonstrated a rate of 799 per 100,000. After his experience in Nepal, with the help of the World Health Organization and his Nepali and Indian colleagues, he demonstrated in Bhutan, Burma, and India that corneal ulcers could be prevented to a large extent by a simple public health intervention.

Achievements at UCSF

In 1991, the Proctor Foundation had an opening for a senior Professor of Ophthalmology and Epidemiology;

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Sjögren's Syndrome Causes Visual Disability Genetic Database Improves Outlook

Tot all of UCSF Ophthalmology's \mathbf{N} international work takes place in developing countries. Sjögren's syndrome, an autoimmune disorder that results in intense visual discomfort and progressive blurring, exists in many countries. Key glands can stop producing moisture, such as tears and saliva, wreaking havoc on organs. Women comprise 93 percent of known cases. "Considering the misery this disease causes, it hasn't gotten the attention it deserves," says Jack Whitcher, MD. Dr. Whitcher and Nancy McNamara, MD, both pursue research to find longterm solutions.

and Troy Daniels in the School of Dentistry, Dr. Whitcher serves as one of the lead investigators for the research, which is funded by the National Institutes of Health and run by UCSF's interdepartmental Sjögren's Syndrome Clinic.

Genes May Flag Those at Risk The alliance is compiling a genetic database for the disease by acquiring DNA samples from diverse patient



These specialists are participants in a five-year investigation – along with more than 100 other Sjögren's syndrome researchers and clinicians in China, Japan, Argentina, Denmark, the United Kingdom, and India. This alliance is developing new tools to benefit those affected now and those who may be susceptible to the disease in the future. Working with **Drs. John Greenspan** populations. Researchers send samples of blood, tears, mucous membrane, and RNA from the ocular surface to UCSF for processing and data entry. If the database reveals a distinct genetic profile for the disease, then ophthalmologists may be able to identify high-risk disease "suspects" before their eyes are damaged. Early treatment offers the best hope for delaying, reducing, and even preventing eye damage.

"All I could do before was help patients cope with the problem," explains Dr. Whitcher. "Now I can offer the hope of a cure." •

> Many parts of the body can be affected when this autoimmune disorder causes glands to stop producing moisture.

Think Global, Train Local Continued from page 1

More than 200 international fellows have now taken UCSF Ophthalmology training home to their countries.

The impact of their dedication as professors, clinicians, surgeons, and innovators includes:

- Increased access to ophthalmologists trained in specialized disciplines
- Introduction of new technologies and procedures
- Local expertise in research techniques and methodology
- Research that adds to global knowledge about eye disease

department invests in the training of several international fellows each year. UCSF's Francis I. Proctor Foundation has trained at least one international fellow every year since the late 1950s, with the total now at more than 75.

Expertise and inspiration gained at UCSF Ophthalmology are reflected in the paths taken by these international ophthalmologists. Dr. Contreras's story provides a striking example.

Dr. Contreras: Giving Back

Still energetic and working at the age of 82, Dr. Contreras feels that he owes a great deal to his early training in San Francisco. "My UCSF mentors inspired me to serve my community," he recalls fondly. "So much of the knowledge they shared has changed, but their spiritual legacy remains constant. It's a feeling in my heart."

His commitment to the welfare of the Peruvian population, matched by initiative and expertise, has significantly improved ocular medicine in Peru and beyond. Originally trained as an ocular pathologist (assessing diseases by examining tissue samples) he soon expanded his work. In 1987 he founded the Peruvian National Eye Institute in Lima and served as its director for ten years. He notes that doctors in developing nations must adapt Western innovations to medical systems with fewer resources.

In Peru, cataracts account for 60 percent of blindness, and only about 10 percent of the population has the resources for medical services. As a result, cataracts are generally left untreated. As a member of the Pan-American Ophthalmology Association (PAOA), Dr. Contreras helped to create "cataract free zones" in Peru and Brazil. He led the association in the early 1990s and today serves as chairman of its Prevention of Blindness committee.

This visionary ophthalmologist's work in blindness prevention and ocular health has led to numerous honors. Three he prizes most are the Leslie Dana Gold Medal Award from the St. Louis Society for the Blind and Visually Impaired; the Honor Award from the International Agency for the Prevention of Blindness; and the A. Edward Maumenee Distinguished Services Medal from the Pan-American Ophthalmology Association (PAOA).



Dr. Francisco Contreras came from Peru for the opportunity to train as a fellow at UCSF Ophthalmology in 1966. He returned to UCSF earlier this year to deliver the annual Hearst Lecture, "Ocular Aspects of Infectious Diseases in Latin America." He reminded the audience of the distinct set of conditions that Latin American ophthalmologists are concerned with.



Cysticercosis is the most common parasitic infestation of the central nervous system worldwide. Humans develop cysticercosis when they ingest tapeworm eggs or larvae in unclean drinking water or uncooked pork.

Leprosy, or Hansen's disease, is a chronic infectious disease caused by a bacterium. Left untreated, leprosy can be progressive, causing permanent damage to the eyes, skin, nerves, and limbs. Rhinosporidiosis is a fungal disease of the external mucous membranes (as of the eyes or nose) characterized by pinkish red polyps.

Dr. William Hoyt: Legacy of Fellows A renowned neuro-ophthalmologist and professor emeritus in the UCSF Department of Ophthalmology, William Hoyt, MD, has mentored more than 300 residents and 120 neuroophthalmology fellows over the course of his career. He always insisted on training only those international fellows assured of future university positions in their home countries. His policy ensured that the impact of his training would multiply, extending an understanding of neuro-ophthalmology to medical students around the world. Seventy of his students became professors.

The achievements of Dr. Hoyt's former students would easily fill a book. One of his remarkable students is **Klara Landau, MD,** who studied with him in the early 1990s. Only the second neuroophthalmologist in Switzerland, she began as the lone female ophthalmologist in the country. Following Dr. Hoyt's teaching methods, she upgraded Swiss resident education by insisting on knowledge of the published literature and on American-style open discussion and encouragement to challenge the professor. Today Dr. Landau serves as department chair at the University of Zurich.

A sampling of the achievements by Dr. Hoyt's international fellows provides evidence for the value of the training program.

- Rafael Muci-Mendoza, MD (Venezuela) provides scarce neuroophthalmology expertise at a public hospital in Caracas and teaches residents from Venezuela, Colombia, and Ecuador. Dr. Hoyt comments, "If I'd trained 40 people and sent them to Venezuela, they would not have equaled the impact of this man."
- **Tulay Kansu, MD** (Turkey), serves as Dean of Medicine, Department of Neurology, at Hacettepe University in Ankara.
- Jordi Arruga, MD (Barcelona), is a renowned cataract surgeon and serves as Chief of Ophthal-mology at Bellvitge University Hospital.

My UCSF mentors inspired me to serve my community."

– Dr. Francisco Contreras

Today Dr. Contreras focuses primarily on health policy, where he feels he can make the greatest difference. He serves on the World Health Organization's Expert Advisory Panel on Prevention of Blindness and administers two public health initiatives in Peru. One of these initiatives builds professional relationships with rural ophthalmologists ("retrain, recapacitate, refresh") and the other addresses getting eyeglasses onto public school children who need them. (These low-income children generally receive no medical care.) The project trains teachers to screen students' vision, containing costs, and then professionals give eye exams to children who need further attention.

Sphere of Influence

Each year UCSF Ophthalmology welcomes outstanding international ophthalmologists to pursue advanced study as Fellows, resulting in improved ocular health and education across the globe. Hundreds of fellows have journeyed from dozens of countries, including the following:

Argentina
Armenia
Austria
Canada
Chile
Denmark
Egypt
Finland
France

6

Germany Great Britain Hong Kong India Indonesia Ireland Israel Italy Japan Korea Lebanon Mexico New Zealand Peru Singapore Spain Sweden Switzerland Taiwan Thailand Turkey United Kingdom United States Tanzania Venezuela



Dr. William Hoyt treasures the relationships he built with the international fellows he trained. He stays in touch through international meetings and email. The wall in Dr. Hoyt's office is covered with photos and notes on many of his protégés.

- Michael Sanders, MD (London), became one of the top neuro-ophthalmologists in Great Britain.
- Eeva Nikoskelainen, MD, PhD (Finland), is now Chief of Ophthalmology at the Department of Genetic Medicine, University of Turku. She has made substantial contributions to the understanding of a rare inherited form of retinal degeneration.
- Irina Rubtsova, MD (Russia), has pioneered neuro-ophthalmology in St. Petersburg after her training with Dr. Hoyt.

Surgical Expertise for the Developing World In countries with the least developed medical

systems, the impact of international fellows is most dramatic. The visionsaving surgical procedures they learn at UCSF and perform at home are one way they transform patients' lives. These surgeries are all the more impressive because international fellows, who are not board-certified in the United States, cannot perform any surgeries or even touch patients during their training at UCSF. They learn the procedures through observation and dialogue alone. Dr. Koanglu Wang came from Beijing, China, in 1982 to work with Alexander Irvine, MD, a pioneer in the surgical procedure called vitrectomy. The expertise Dr. Wang gained meant the difference between blindness and sight for Chinese patients with detached retinas. In Beijing he has performed hundreds of vitrectomies and thousands of laser surgeries. He has also trained the next generation of Chinese surgeons.

surgical techniques so he could help more patients with detached retinas. Twenty-seven years after his UCSF fellowship, his son Dr. Ajay Singh, was chosen for a Hearst Fellowship with Daniel Schwartz, MD, a UCSF retinal specialist.

The Internet Extends UCSF's Reach

Through its fellows program, UCSF Ophthalmology has forged ties with eye hospitals and vision institutions around the globe. These connections support ophthalmology efforts abroad and encourage multinational dialogue on issues of blindness and visual disability. The immediacy of Internet communication strengthens relationships forged at UCSF; most graduated fellows can stay better in touch with their mentors.

In countries with the least developed medical systems, the impact of international fellows is dramatic.

The Proctor Foundation has recently been using email to help its first international fellows from Ethiopia, Drs. Menin and Yared. These doctors are applying their UCSF training to perform the first corneal transplants ever in that nation. The foundation supported their efforts by sending **Doug**

Holsclaw, MD, to help them gear up to provide this surgery. The Ethiopian pioneers continue to email questions about particularly challenging or unclear cases, and Proctor provides consultation from its offices on the UCSF campus.

China and the Americas Dr. Richard Abbott **Impacts Practice**

or more than 25 years Richard Abbott, MD, a corneal specialist, has been involved with ophthalmology education and surgical patient care in China. His education efforts provide a foundation for improving and standardizing vision care in that rapidly changing country.

Recently Dr. Abbott was awarded the prestigious International Distinguished Golden Service Award, cosponsored by the Chinese Academy of Ophthalmology and the Chinese Medical Association. This award is presented annually to an individual from outside China who has provided distinguished service to the Chinese medical profession through education, research, or patient care. In particular, the honor recognizes Dr. Abbott's leadership and organization of new evidence-based Chinese clinical practice guidelines. Past recipients of this award are Bruce Spivey, MD, President, International Council of Ophthalmology; Leon Elwein, PhD, of the National Eye Institute; and Stephen Ryan, MD, Dean, University of Southern California School of Medicine, and Former Chair, Doheney Eye Institute.

The clinical practice guidelines cover 18 medical conditions deemed to have the highest morbidity and prevalence in China. Introduced into practice about two years ago, the guidelines outline standards for clinical care and represent one phase in a strategic plan to improve outcomes for Chinese patients.

Dr. Abbott also will be involved in determining the impact of the guidelines on patient care and outcomes. Because glaucoma is the third leading cause of low vision in Beijing, doctors have designed a pilot project using the diagnosis and management of glaucoma in university-based hospitals in Beijing to assess impact. Because the levels of care in China are so diverse and the concept of evidencebased clinical guidelines is relatively new and foreign to practitioners, researchers expect to gain insight into some of the obstacles to implementation of the guidelines and then direct attention to those challenges.

On the other side of the globe, Dr. Abbott plays an important role in ophthalmic education and blindness prevention programs in Latin America. As president of the Pan-American Association of Ophthalmology, he helps lead and coordinate the sharing of medical breakthroughs and trends among ophthalmologists from two continents. UCSF clinical ophthalmologists participate in Latin American seminars, where productive ideas are exchanged and doctors can reach a better understanding of how to use new research and clinical concepts most effectively.

> Dr. Richard Abbott was recently awarded the International Distinguished Golden Service Award in China.

Dr. Rajbir Singh, from the city of Amritsar in the Indian state of Punjab, trained with Dr. Irvine in 1978. He returned to Amritsar to continue the family profession of ophthalmology in an eye hospital founded by his grandfather. His Hearst fellowship allowed him to learn the latest retinal

The web also creates opportunities for UCSF experts to share resources with the international community. For example, a free online library of Dr. William Hoyt's extensive collection of diagnostic photos makes it easy for neuro-ophthalmologists around the world to tap into his expertise. To view a few of his favorite images, go to http://ucsfeye.net/tmms.shtml.

UCSF Ophthalmology's sphere of influence extends farther than ever, thanks to this new technology.





Visionary Continues Continued from page 5

Drs. Jack Whitcher and Thomas Lietman

Dr. Whitcher came onboard. He began research projects on several debilitating vision disorders, and broadened his work on corneal ulcers. He and Dr. Smolin visited Aravind Eye Hospital in Madurai, India, and started a microbiology laboratory there, with the help of **Vicky Cevallos**. Aravind Eye Hospital subsequently started many similar laboratories and eye training programs around Southeast Asia. Also, Dr. Whitcher conducted a large-scale cataract prevention study in the 1990s with **Drs. Tom Lietman** and **David Gritz**.

Mentoring and Fundraising

Retired from patient care last summer, Dr. Whitcher mentors other Proctor researchers and continues with international studies. He works closely with Dr. Lietman and **Nisha Acharya, MD**, another gifted corneal specialist who shares his passion for blindness prevention. "As emeritus professor, I give Tom and Nisha advice, love, and encouragement, and work to raise money for them. India taught Marilyn and me that family is most important. We are grateful that we have been blessed with wonderful children and grandchildren, but the people doing this international work have become our extended family. We want to see them flourish."

Gratitude and The Big Picture Visionary funders have allowed Dr. Whitcher to make strides in preventing blindness around the world. He is currently stepping up his work with That Man May See, UCSF Ophthalmology's public charity, to keep funds flowing so that more people can be spared the disability of blindness.

His fondest hope is to see UCSF become the foremost center worldwide that addresses the problem of global blindness. "I want to see Proctor's international programs endowed and named. We're constantly running on handouts, and I want this work to thrive for many years to come," says Dr. Whitcher. Proctor, Johns Hopkins, and the London School of Tropical Medicine and Hygiene are the only major institutions focusing on global blindness. •

Remembering Friends of UCSF Ophthalmology

That Man May See honors the recent passing of special friends.

Contributions to That Man May See

Thank you for generous contributions and pledges for vision research, teaching, and patient care received in March, April, and May 2008.

Visionaries (\$100,000+)

The Estate of Jon Shastid William Randolph Hearst Foundation Don and Judy McCubbin The Bernard A. Newcomb Foundation at Silicon Valley Community Foundation The Bernard Osher Foundation Lela and Peter Moulthrop in memory of Theresa E. Allen

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Dream Makers (\$2,500+) Ms. Barbara Comer Harold and Annette Dobbs Family Supporting Foundation of the Jewish Community Endowment Fund Rajbir and Rita Singh

Innovators (\$1,000+)

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ANK YOU

• • •

George "Fritz" Jewett always brought a loving smile to the clinic and generously supported That Man May See, advancing research toward cures for macular degeneration and glaucoma.

Jon Shastid provided thoughtful leadership as a member of the honorary board and past member of the active board of directors of That Man May See. Jon included funds in a gift annuity that will support UCSF Ophthalmology research to preserve and restore sight.

Yvon Johnson, retired controller of That Man May See, oversaw financial functions with a wise and generous heart before retiring to Oregon to live closer to family. His son suggested gifts to That Man May See as memorial tributes.

Daniel Cook's appreciation for care was evidenced on each visit to the clinic, and he supported endowments as well as international research efforts fighting vision loss and blindness.

Bay Area figurative artist **Paul Wonner** helped launch an Eye on the Arts event at the de Young Museum in 2007, expressing his appreciation for the outstanding care that saved his vision.

Love at First Sight The Mettiers Leave a 20/20 Legacy

ancy and Stacy Mettier met walking down the aisle of a church in Carmel. She was the maid of honor and he the best man for the wedding of mutual friends in September of 1949. Call it love at first sight – they've been together ever since.

The Mettiers hold the history of That Man May See in their hearts. They've been involved with this public charity since 1971, when **Drs. Sam Kimura** and **Mike Hogan** founded the organization to help UCSF Ophthalmology raise funds for research, teaching, and patient care. The vision is to preserve and restore sight for present and future generations.

Stacy Mettier, Jr., MD, did his residency at UCSF, and both of his parents went to UCSF Medical School. His mother was a pediatrician, and his father became the head of hematology and rheumatology as well as a postgraduate medical division. Earlier, his father was part of a Nobel Prize-winning team from Harvard.

Nancy and Stacy have included That Man May See in their estate plans with a gift from their Individual Retirement Account (IRA). As members of the 20/20 Legacy, a visionary society of individuals who leave That Man May See in their wills, the Mettiers will make a lasting difference while meeting their own financial goals. By leaving personal wealth for vision research and education, these special friends have the satisfaction of helping vision scientists find cures for blinding diseases.

"This department has been good to me, so I want to give back," says Stacy. "With an inherited IRA, a large percent goes to taxes, so we prefer that it support a worthy cause instead."

Nancy and Stacy enjoy working closely with friends of That Man May See; Stacy served on the board for more than 30 years. Now an emeritus member, he remains closely involved. For Nancy, the most exciting visits to the Department of Ophthalmology are the ones arranged for friends of That Man May See, where she can go behind the scenes and see the scientists in action at the Koret Vision Research labs. "The electron microscope was a great introduction to our grandchildren," she says. "We love the science, and we enjoy the people," she continues. "The Kimuras, the Hogans, the Garrons, the Bells – we've had a wonderful time with all of them."

Both Mettiers treasure their vision, realizing that it's easy to take it for granted until eye disease strikes. Stacy, who treated many San Franciscans in his 32 years of private practice, says, "You don't have to tell anyone how important eyesight is. Think of where we would be without it."





THAT MAN MAY SEE

A Message from Kathleen L. Rydar President That Man May See is a 501(c)3 public charity. Its mission is to raise funds for the dedicated faculty of UCSF Ophthalmology to make possible breakthroughs in vision research, state-of-the-art patient care, and educational opportunities for residents and fellows.

What a Great Place to Be!

It's early Wednesday morning at the Koret Vision Research Center. In the corridor, **Dr. David Copenhagen** tells me about his work on how the retina extracts and encodes features of the visual scene such as local contrast, color information, and movement. He's modest as he tells me That Man May See can expect a gift from Alcon. He's just won the Alcon Prize, one of the most prestigious in the field of ophthalmology. Dr. Copenhagen will donate his personal award funds for vision research. (You'll be reading more about this award in the next issue of Visions.)

Then **Dr. Matt LaVail** comes beaming through the open door of his lab. "Did you know that our research on neuroprotection for visual cells (slowing down cell death) is currently in clinical trials?" he asks. This work can be beneficial in the treatment of glaucoma, diabetic retinopathy, macular degeneration, and other devastating eye diseases. That Man May See funded the research in its early stages, providing leverage for Dr. LaVail's team to receive \$1.9 million in National Institutes of Health grant funding. The phase II and III clinical trials are going on now, and UCSF is part of the multicenter effort to evaluate this promising new therapy on patients with retinitis pigmentosa, under the direction of **Dr. Jacque Duncan.** "Oh, and by the way – our Yorkshire Terrier just gave birth to seven puppies," Dr. LaVail announces with a grin.

I hurry down the corridor (or own a puppy) to meet with Dr. Duncan, who is celebrating the purchase of a state-of-the-art Heidelberg Spectralis HRA + OCT Laser Scanner Camera System. It's made possible with a gift of \$150,550 from Bernie Newcomb with funds at Silicon Valley Community Foundation. This wonderful machine scans the retina 100 times faster than is possible with current equipment and produces exceptionally detailed images. Five retinal faculty members are thrilled to use this new instrument for patient care, research, and teaching.

Gifts such as these to That Man May See make a real difference in our faculty's capability to effectively treat blinding eye diseases. We are grateful to special friends who contribute to our cause and to the dedicated team of clinicians and researchers who make breakthroughs possible. What a great place to be!

Faculty News

\$2.33 Million Advances Research

hat do vision researchers dream about? Gurus who help them master complex new technologies necessary for digging deeper. Engineers who help them develop tools for studying the visual system from fresh perspectives. Support services that facilitate vital progress in halting blindness.

A \$2.33 million Core grant from the National Institutes of Health (NIH), designed to fulfill these dreams, has just been renewed. Twenty-six UCSF scientists currently run vision-related projects that are funded by the National Institutes of Health. With NIH awards stretched further than ever, they breathed a collective sigh of relief. The five-year grant supports aspects of research that are best addressed jointly.

Senior researcher **Matt LaVail, PhD,** is thrilled with the renewal. "It really does make us more effective," he says. "Our individual grants go further, and we are able to focus on the job at hand – making progress toward breakthroughs that address blinding diseases." One of the five areas the grant supports is microscopy. The other areas are DNA sequencing and genotyping, digital imaging, computer and information technology, and an electrical and machine shop. This shop designs, fabricates, repairs, and maintains the specialized instruments and devices critical to each research project.

Dr. LaVail is an internationally known vision scientist whose work has been continuously funded by the National Eye Institute (the NIH's vision component) for 30 years. A vision pioneer who is well qualified to assess research needs and navigate federal requirements, he administers the core grant with the help of other faculty. The NIH has continuously renewed this Core grant to UCSF Ophthalmology since it was first awarded 31 years ago.

26 UCSF vision scientists will benefit from this five-year NIH Core grant.



Dr. Matt LaVail administers this grant, which encourages collaboration and shared resources.



Richard L. Abbott, MD

Appointment: Chair of Lasik Surgery Task Force for the American Academy of Ophthalmology

To learn more about the outcomes of LASIK surgeries and the impact the procedure has on patient quality of life, two ophthalmological professional organizations and two federal entities are joining forces to

fund and design a study. Dr. Abbott and his counterpart from the American Society of Cataract and Refractive Surgery will oversee the project, which will help physicians, researchers, and government regulators to understand the factors that most impact patient satisfaction and, ultimately, to improve the procedure and its results for patients.



Allan J. Flach, MD, PharmD

Publication: Hydroxychloroquine retinopathy: Improving the riskbenefit relationship and informed consent for patients. **Flach, AJ.** 2007. *Transactions of the American Ophthalmology Society*, December; 105: 191–197.

In this study Dr. Flach determined 1) the prevalence of high-risk factors for hydroxychloroquine-induced retinopathy in all patients using this drug at the Veterans Administration Medical Center in San Francisco and 2) compliance with the American Academy of Ophthalmology screening guidelines. Hydroxychloroquine (Plaquenil) is prescribed for immunological diseases. His results led to a redesigned medication information form that aims to improve each patient's risk-benefit relationship and avoid severe loss of vision that can include blindness.



Douglas B. Gould, PhD Invited Speaker: Gordon Research Conference on Basement Membranes

The Gordon Research Conferences, now in their 77th year, serve as an international forum for leading-edge research in the biological, chemical, and physical sciences. Dr. Gould studies the role of

basement membrane proteins in ocular development, glaucoma, and age-related macular degeneration. He uses genetic approaches to identify heritable factors that predispose individuals to eye diseases and to understand disease processes that can be targeted with novel therapeutics.



Todd P. Margolis, MD, PhD

Publication: Cytomegalovirus retinitis: the neglected disease of the AIDS pandemic. Heiden D, Ford N, Wilson D, Rodriguez WR,
Margolis T, Janssens B, Bedelu M, Tun N, Goemaere E, Saranchuk P, Sabapathy K, Smithuis F, Luyirika E, Drew WL. 2007. *Public Library of Science Medicine* 4(12):e334.

In this manuscript, Dr. Margolis and his colleagues review their data on the previously unrecognized magnitude of the epidemic of blinding eye disease caused by Cytomegalovirus retinitis, an AIDS-associated infection. In addition they propose cost-effective methods of screening for and treating this disorder, which affects millions of people worldwide.



Joan M. O'Brien, MD

Visiting Professorship: Dean McGee Eye Institute, Department of Ophthalmology, University of Oklahoma. Retinoblastoma: Clinical management and Retinoblastoma: Current research

Dr. O'Brien used this lecture to update the ophthalmology community on new developments and advances regarding retinoblastoma (a blinding pediatric cancer). She highlighted techniques in treatment and diagnosis, as well as the progression of research, including innovations through genetics.

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<u>GHTINGS</u> S

























That Man May See Chairman's Forum Luncheon

1 David Hwang, MD, greets Nancy Müller at Koret Vision Research Laboratories. Dr. Hwang shared information on his pioneering work in corneal disease and cataract surgery.

2 Dah Yu and Marjorie Cheng thank Dr. Hwang for his care at UCSF Ophthalmology.

That Man May See Eye on the Arts Event at Gap Inc.

3 UCSF Ophthalmology friends and faculty gathered for the second annual Eye on the Arts event, hosted by Doris

4 After viewing the works of art, guests were treated to presentations linking the biological basis of perception to the Fishers' collection. Jonathan Horton, MD, PhD, acts as moderator for the program and discusses visual processes.

5 Julie Schnapf, PhD, discusses light and color in relation to an Ellsworth Kelly painting.

6 TMMS board member **Angus MacLean** (left) and **Paul Bancroft** enjoy the event and the art.

7 TMMS staff members greet **Johanna Baruch** (left) and

8 The architecturally stunning headquarters of Gap Inc. features a walk-in sculpture by Richard Serra.

9 Todd Margolis, MD (right), welcomes friend of TMMS Michael Braude to the festivities.

¹⁰ **Doris and Robert Rivett** enjoy the impressive collection.

¹¹ TMMS board member **Paige Hutson** enjoys visiting with Wayne and Amy Sosnick, Marlene and Fred Levinson, and Martin Sosnick (left to right).

and Donald Fisher and sponsored by BNY Mellon. Marilynn and John Fulton relax before exploring the Fishers' contemporary art collection.

Torrie Groening as they arrive at Eye on the Arts.

12 Emely Weissman (left) and Béatrice Gomory celebrate Eye on the Arts.

That Man May See is a 501(c)3 public charity. Its mission is to raise funds for the dedicated faculty of UCSF Ophthalmology to make possible breakthroughs in vision research, state-of-the-art patient care, and educational opportunities for residents and fellows.

To make a gift of cash or securities, go to www.ucsfeye.net/tmms/shtml or contact Danielle Pickett at 415.476.4016 or pickettd@vision.ucsf.edu. Checks are payable to That Man May See.

That Man May See 10 Koret Way, Box 0352 San Francisco, CA 94143-0352 tmms@vision.ucsf.edu VISIONS is a publication of the Department of Ophthalmology at UCSF and is produced by That Man May See.

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Dr. Jonathan Horton Bressler Prize Honors Neuro-Ophthalmologist

Jonathan Horton, MD, PhD, has won the 2008 Bressler Prize from the Jewish Guild for the Blind. A committee of prominent ophthalmologists, optometrists, and vision scientists from the country's foremost universities and vision agencies chose Dr. Horton from a highly competitive field. "Support for our research promises to open new vistas in our understanding of the fundamental mechanisms of vision," says Dr. Horton.

Important Advancements

The prestigious award, with its \$40,000 prize, recognizes an American professional in the field of vision science whose leadership, research, and service have resulted in important advancements in the treatment of eye disease or rehabilitation of persons with vision loss. Dr. Horton, a professor in the UCSF departments of ophthalmology, neurology, and physiology, is respected both as an outstanding clinical neuroophthalmologist and as one of the leading neuroscientists in the country. All of Dr. Horton's contributions share a similar goal: to bring state-of-the-art neuroscience from the laboratory and apply it to important clinical problems.

Dr. Horton has made substantial contributions in clinical neuroophthalmology by elucidating the features, causes, and treatments of neurological disorders that cause visual loss in patients. He also devotes time to patients in the ophthalmology department's pediatric ophthalmology and strabismus division.

Amblyopia and Strabismus The study of amblyopia and strabismus (commonly referred to as "lazy eye" and "crossed eyes"), disorders that affect about two percent of children in the United States, is also a driving interest. He is the principal investigator of a study entitled "Structural Basis of Amblyopia and Strabismus," supported by the National Eye Institute. The goal of this research is to understand the alterations in the function of the visual cortex that occur in these conditions, in the hope of preventing or reversing them.

Visual Perception

Another area of Dr. Horton's research concerns the function of the visual cortex and how it mediates visual perception. The information gleaned from his studies will provide new insight into how visual areas in the brain are organized, their interconnections, and the impact of experience on their development.



The Jewish Guild for the Blind is one of the country's foremost vision healthcare agencies. Its mission is to bring dignity and independence to people who are blind or visually impaired. •

Dr. Horton is respected both as an outstanding clinical neuroophthalmologist and as one of the leading neuroscientists in the country.

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