“Fluorescent” Cells Give Early Warning for Eye Disease

A device that measures metabolic stress could help eye doctors diagnose disease before symptoms appear.

Kellogg researchers have shown that their new metabolic imaging instrument can accurately detect eye disease at a very early stage. Such a device would be vision-saving because many severe eye diseases do not exhibit early warning signals before they begin to diminish vision. The testing is non-invasive and takes less than 6 minutes to administer to a patient.

In a recent study, this instrument was used to measure the degree to which a subtle visual condition affected six women. Victor M. Elner, M.D., Ph.D., and Howard R. Petty, Ph.D., report their findings in the February issue of Archives of Ophthalmology.

The women in the study were newly diagnosed with pseudotumor cerebri and had not yet received treatment. According to standard tests they had good visual acuity, and their visual field tests indicated only normal, mimicking a brain tumor.

Usually the first symptoms a patient with PTC notices are headaches, brief visual blackouts (2-30 seconds), and blurred or double vision. Patients with headaches frequently see their primary doctor, and patients with visual complaints see the eye doctor. When the physician observes swelling of the optic nerve, called papilledema, he or she will suspect PTC—or a real tumor—and will refer the patient to a specialist in neuro-ophthalmology.

When this patient comes to Kellogg’s Neuro-ophthalmology Clinic, we run a series of tests, including an MRI and lumbar puncture, to look for the primary characteristics of PTC: normal MRI and elevated intracranial pressure without infection that is creating pressure on the optic nerve.

My primary concern is to make sure the patient does not suffer vision loss as a result of damage to the optic nerve. In most cases, medication will relieve the pressure and its effect on vision along with the other symptoms. Perhaps 5% or fewer will need surgery.

For most patients the condition resolves within 6 months with treatment. A small number will have a second occurrence. Fortunately, they will recognize the symptoms and know they need to return for further treatment.

We don’t know the precise cause of PTC. The condition is not common, but at a referral facility like Kellogg, we see about two patients a month with PTC.
FROM THE CHAIR
Looking inside the Expansion

A few weeks ago, the construction crew for the Eye Center Expansion led several of us on a tour of the new building. With a little imagination we could begin to see the contours of our new clinics and laboratories, and it won’t be long before the inner framework and walls will be in place. We have come a long way, even since November, when we held a “Topping Out” ceremony to celebrate the completion of the steel framework.

Several friends and colleagues joined us for the Topping Out celebration, and you will see their photos on page 4. We cannot thank them often enough for helping us realize our vision to build one of the nation’s best facilities for eye care, education, and research.

You will also read about some longtime friends in this issue. In the early 1980s, when plans were on the table for the new Kellogg Research Tower, the late Dr. Harry Towsley encouraged us to dream big. And so we did. Now, the Towsley Foundation, named for Dr. Towsley and his wife, Margaret, has provided funding for a new Ophthalmic Imaging Center. We cannot adequately thank the Towsley family for its support over the years, and for its generous support today.

TOWSLEY FOUNDATION GIFT WILL ENHANCE PATIENT CARE

When plans for building a comprehensive eye center at the University of Michigan began to take shape in the early ’80s, pediatrician and philanthropist Harry A. Towsley was pleased to help. He offered advice and encouraged faculty members to reach out to the community. “Dr. Towsley said that when we thought our vision was enough, we should double it,” says Dr. Paul Lichter, F. Bruce Fralick Professor and Chair of the Department of Ophthalmology and Visual Sciences. “His support and guidance were critical to our success.”

In keeping with Dr. Towsley’s advice to always reach for new heights, the University is again asking the community to support a building project designed to enhance patient care, vision research, and the education of future ophthalmologists. The addition to the Kellogg Eye Center that is now under construction will increase by 50 percent the space devoted to these goals at U-M.

Meanwhile our clinical and research efforts continue, albeit in tight quarters. In a small room in our current ophthalmic photography center, Dr. Victor Elner and Dr. Howard Petty have constructed a prototype for an imaging instrument that could one day become indispensable for ophthalmologists. In Archives of Ophthalmology—and in this newsletter—they report on their progress creating an instrument capable of detecting eye disease at an exceptionally early stage.

Finally, a word about the global presence of the U-M Medical School and of this Department. Recently Dean Woolliscroft launched a new program, Global REACH. It underlines the role a medical institution like ours can play in research, education, and collaboration throughout the world. For years, our faculty have given generously of their time, through visiting professor exchanges, participation in international conferences, and programs to provide eye care and physician training where it is needed most. We look forward to finding new ways to contribute to the University’s global outreach.

Read about our outreach efforts in this issue, and stay in touch as we work around the world and at home to provide people everywhere with the finest eye care possible.

Paul R. Lichter, M.D.
F. Bruce Fralick Professor and Chair
Department of Ophthalmology and Visual Sciences
Director, W.K. Kellogg Eye Center

“It is a family tradition to be involved with the Kellogg Eye Center, but more importantly we are thrilled and excited about the work they are doing today.”

—Margaret Ann Riecker

And the Towsley family has once again responded with generous support. Though Dr. Towsley passed away in 1993, the Harry A. and Margaret D. Towsley Foundation has pledged $1.5 million to build and name a state-of-the-art Ophthalmic Imaging Center within the new Kellogg building.

“It is a family tradition to be involved with the Kellogg Eye Center, but more importantly we are thrilled and excited about the work they are doing today,” says Margaret Ann Riecker, Chairperson of the Foundation and one of Dr. and Mrs. Towsley’s daughters. “We are so glad to be a part of the Eye Center’s growth.”

The Ophthalmic Imaging Center will play a key role in all aspects of the Eye Center’s mission. Photographers use special equipment to take photos of the retina, cornea, and other parts of the interior of the eye as well as perform dye- and laser-based testing. Images of the eye are essential to diagnosing and treating disease, and they are the main tool educators have for increasing residents’ understanding of disease processes. Such images are also at the heart of the Eye Center’s efforts to find new treatments for such diseases as age-related macular degeneration, diabetic retinopathy, and glaucoma.

“The whole idea of good science and research is so important to health care, and the University of Michigan is certainly the place for that,” says Mrs. Riecker. Both Harry and Margaret Towsley were graduates of the University of Michigan. Dr. Towsley served as a U-M professor of pediatrics and Chairman of the post-graduate medicine department. Since its inception in 1959, the Towsley Foundation has supported a wide range of University and community initiatives in education, health care, and medical education.
Cardiologists have long used blood.

activity is a very good indicator of eye

important. This study suggests that FA

detection of subtle distinctions is significant.

Dr. Elner, who is an ophthalmologist

healthy eyes.

difference in FA values between their

administered, the researchers measured

subtle abnormalities or none at all.

After the standard vision tests were

FA values for the six women and an age-

pressure testing and control to ward off heart disease and stroke. We believe that FA testing will likewise be a helpful diagnostic tool for eye doctors looking to prevent blindness.”

Drs. Elner and Petty have filed for a patent and are investigating the instrument’s use as a screening device in other major eye diseases.

This study was supported by grants from the National Eye Institute. Dr. Elner is a Research to Prevent Blindness Senior Scientific Investigator.

A new study is in press. Upon publication, you will find news at our web site on the technology’s use in screening for diabetes-related eye disease.

continued from page 1

So many of our patients struggle with more than one eye disease. The physical layout of the new facility will be much better for those who go to several clinics during each visit. One patient may need to see a glaucoma and a retina specialist, and then will want to visit our Low Vision Clinic. Our goal of providing excellent clinical care will not change in the new building. But it will be easier and less stressful for patients and their families to move through their scheduled appointments.

The new space will also allow our researchers to work in new ways. Twenty-first century science is not one scientist working in an individual lab. It requires a team approach—perhaps with each laboratory contributing a very focused area of expertise—and then several coming together to yield a greater result.

To cite one example, collaborative research between a clinician and a scientist at Kellogg has led to the development of a new instrument for detecting eye disease. I can imagine using the system both to diagnose glaucoma and to track progression of the disease. We might collect clinical information to help identify genetic markers that distinguish patients whose condition progresses at a fast rate vs. a slow rate. As we gain a greater understanding of the disease process, we’ll be able to provide treatment tailored to the individual.

This entire building is designed specifically to enhance collaboration which, in the end, will benefit patients now and in the years to come.

Grant M. Comer, M.D., has joined the faculty of the Retina, Uveitis, and Ocular Oncology Service. He will see patients in Ann Arbor as well as at Kellogg’s Brighton office. Dr. Comer earned his M.D. and completed his ophthalmology residency at Indiana University. He then completed a retina fellowship at the University of Michigan Kellogg Eye Center.

Carlton J. Foster, O.D., has joined the Pediatric Ophthalmology and Adult Strabismus Service. He will provide eye examinations for Kellogg’s pediatric patients in Ann Arbor in collaboration with our pediatric ophthalmologists. Dr. Foster received his O.D. from the Illinois College of Optometry.

Alon Kahana, M.D., Ph.D., is an Assistant Professor on the Eye Plastic, Orbital and Facial Cosmetic Surgery Service and will see patients in Ann Arbor. Dr. Kahana earned both his Ph.D. in Molecular Genetics and Cell Biology and his M.D. from the University of Chicago. He then completed a residency and two fellowships—Oculofacial Plastic and Reconstructive Surgery and Facial Cosmetic Surgery—at the University of Wisconsin.

Joshua D. Stein, M.D., M.S., has joined the Glaucoma Service as an Assistant Professor and will see patients in Ann Arbor. Dr. Stein received a master’s degree in Evaluative Clinical Sciences from Dartmouth Medical College and then earned his M.D. from Thomas Jefferson University. He completed his ophthalmology residency at New York University and a glaucoma fellowship at Duke University.
LEARNING WITH THE BEST
One-on-one fellowship to study retina disorders

For three months last fall, ophthalmologist Henry A. Ferreyra, M.D., came to the Kellogg Eye Center for a concentrated fellowship with one of the world authorities on inherited retinal dystrophies. He studied with Kellogg’s Dr. John R. Heckenlively, reviewing case studies, learning how to perform and interpret specialized diagnostic testing, and seeing retinal dystrophy patients with Dr. Heckenlively, so that when he returned to the University of California, San Diego he could set up his own retinal dystrophy clinic.

Dr. Ferreyra requested the fellowship on the advice of faculty at UCSD’s Shiley Eye Center. “There are so few retina specialists with expertise in retinal dystrophies,” he said. “Among them, Dr. Heckenlively is a leader in the field with both a strong clinical practice and an active research program. Coming to Kellogg to work with Dr. Heckenlively was an obvious choice.”

The Eye Center’s position as a major referral center allowed Dr. Ferreyra to observe patients with a wide range of rare retinal conditions. Working with Dr. Heckenlively further allowed him to delve into one of the most puzzling retinal diseases, autoimmune retinopathy (AIR). The disease causes progressive vision loss, and often, blindness; it is poorly understood and many assume there are no treatments for AIR.

Dr. Heckenlively has proven otherwise, according to Dr. Ferreyra. He was first to publish on the role of the autoimmune system in this disease. After describing AIR as having distinct features from other retinal degenerations, Dr. Heckenlively went on to show that treatment with autoimmune medications could help many of his patients.

Using Dr. Heckenlively’s rich collection of case histories, Dr. Ferreyra reviewed the course of treatment for patients with AIR since 1989. He found that 65% of them had responded to one of several treatment options, most achieving at least modest gains. The challenge now, he says, is to build on the data and design prospective studies to discover who is most likely to respond to treatment.

The fellowship was rewarding for Dr. Heckenlively, as well. “It was a pleasure to work with someone as knowledgeable as Henry Ferreyra. We could quickly move to discussions of nuance rather than focusing on the basics,” he said.

Dr. Ferreyra returned to UCSD knowing that he will be able to offer treatment to at least some of his patients. Like his mentor Dr. Heckenlively, Dr. Ferreyra has his eye on another goal: creating a reliable diagnostic test to make sure no one overlooks the patients who could benefit most from treatment.

On November 6, 2007, faculty, staff, students, trainees, and friends of the Eye Center gathered outside to celebrate “Topping Out,” the ceremony held when the major structural steel of a construction project is complete.

Among those who signed the last beam and watched as it was hoisted up to the top and set in place were Helmut Stern, Larry Miller, Carolyn Lichter, Marian Poling, Harold “Red” Poling, Paul Lichter, M.D., and Douglas Strong.
RESCUING RODS AND CONES—AND VISION
Kellogg finds clues to other diseases in its study of retinal detachment

Over the course of a year, physicians at the Kellogg Eye Center will treat hundreds of patients with retinal detachments. Specialists like David N. Zacks, M.D., Ph.D., respond quickly with a number of techniques, largely surgical, to repair the retina.

But Dr. Zacks believes there may be an additional way to help his patients. In two recent papers he reports on a phenomenon that is common to retinal detachment and many retinal diseases. His research concerns the biological chain of events that results in the death of photoreceptors, the rods and cones that enable us to perceive light and color. When photoreceptors die, vision is compromised.

Within hours of a retinal detachment, photoreceptors begin an orderly process toward death. It is a genetically programmed process that scientists refer to as apoptosis. Once launched, the process is difficult to stop, even if the underlying cause of the detachment has been successfully treated.

If the cellular events along this pathway can be understood, it may eventually be possible to intervene with therapies to rescue the dying photoreceptors—and restore lost vision. The knowledge could apply to such diseases as diabetic retinopathy and age-related macular degeneration as well as to other causes of retinal detachments, like injury, infection, surgery, and disease.

In his two most recent studies, Dr. Zacks has gained considerable insight into events that contribute to the demise of photoreceptors. In 2004, he reported that retinal detachments activate a protein known as Fas, and that this protein then initiates apoptosis.

Then, in the November 2007 issue of Archives of Ophthalmology, Dr. Zacks posed the next logical question: could photoreceptors be saved by “turning off” the protein that signals the start of the deathward march? As Dr. Zacks had hoped, he found several signs of increased photoreceptor survival when Fas was inhibited. There were fewer damaged cells immediately following the detachment as well as strong evidence of viability as long as two months after the retinal separation. He also observed an increase in the number and thickness of cells in the outer nuclear layer of the retina.

“Many eye diseases include a retinal detachment as part of the larger clinical picture,” says Dr. Zacks. “Our findings suggest that suppressing Fas signaling could well become a useful part of the treatment, not only for retinal detachment but for many other diseases that arise from the death of photoreceptors.”
Monte A. Del Monte, M.D., and alumnus Keith D. Carter, M.D., will be among the ophthalmologists traveling to Vietnam as part of an ORBIS outreach project. Many Kellogg physicians have participated in ORBIS programs to train local eye health workers and perform surgery. Finding an ophthalmologist in Vietnam is not easy. ORBIS estimates there are 13.5 ophthalmologists per million Vietnamese, compared to 10 ophthalmologists per 100,000 in the U.S. Dr. Del Monte will spend a week in Vietnam as part of a 5-week program to train 200 local ophthalmologists and 40 nurses and perform surgery on 120 patients.

Bartley R. Frueh, M.D., returned to Guatemala, Nicaragua, and El Salvador in October to train ophthalmologists in eye plastic surgical procedures and treat patients. During his visit, he performed nearly 30 surgeries, treating patients with conditions from ptosis (droopy upper eyelid) to chronic dacryocystitis, an infection in a blocked tear drainage sac. As a board member of the World Eye Mission, Dr. Frueh invites Kellogg colleagues to participate in similar missions throughout Central America. Just this past January, Kellogg retina specialist Stephen J. Saxe, M.D., spent a week in Guatemala City lecturing to residents and staff, holding clinics each morning, and performing surgery in the afternoon. After treating a woman with a retinal detachment, he noted, “The opportunity to help patients like this made the entire experience extremely gratifying and inspirational.”

Dr. Del Monte’s visit to Vietnam will be featured in an upcoming television special. Check our website for date and time.

5,000 MILES TO KELLOGG
A young boy from Ghana finds help and compassion at Michigan

Ocularist Gregory Dootz works with children from around the world, adding a compassionate touch to reflect the global reach of the Kellogg Eye Center.

In his 29 years at Kellogg, Mr. Dootz has fitted many children — and adults — with eye prostheses. He has created nearly 800 eyes for his pediatric patients and, during this time, he has developed close relationships with them.

Last summer a nine-year-old boy from West Africa proved to be a special patient.

In a remote village in the northern region of Ghana, Yakubu Sulemana is one of 30 children in a family that lives in grass huts with dirt floors. There is no heat or electricity, and certainly no medical care. After Yakubu injured his left eye in a fall from a tree, missionary Emmanuel Mohammed Tijani of Children’s Medical Missions Ghana found him while traveling through the village.

Emmanuel worked closely with Tami Shobe from Children’s Medical Missions West in Ohio to find medical care for Yakubu. In seeking the best eye care for Yakubu, Ms. Shobe turned to Kellogg and the youngster soon began a journey to the United States. After a one-hour walk from his village to a car and a two-hour ride to an airport in Ghana, Yakubu began a nine-hour flight to New York City and then continued on to the home of Elaine Sheehan — his “host mom” in Toledo, Ohio.

Yakubu came to Kellogg in May 2007 to have his injured eye removed and, after eight weeks of healing, Mr. Dootz worked with the young patient, creating a new prosthetic eye. Because Yakubu spoke no English, Ms. Sheehan says she struggled to communicate with him about what was happening, but Mr. Dootz quickly reassured them noting, “Little boys are little boys no matter where they come from.”

Ms. Sheehan says Yakubu, indeed, was confused and scared in the beginning, but Mr. Dootz and the rest of the staff at Kellogg did their best to make him comfortable, and they succeeded. After a few follow-up visits to complete the fitting, Yakubu returned home in late August with his new eye.

“I was stunned that, in such a large place like the University of Michigan, everyone is treated individually and with such respect.”

— Elaine Sheehan
Yakubu’s host mother

Gregory Dootz creates prosthetic eyes for adults and young patients like Yakubu Sulemana.
ASK THE EXPERT: CLINICAL TRIALS 101
by Susan G. Elner, M.D.

As part of a major research center, we receive many questions about clinical trials. Some patients ask whether a new treatment can provide improvement for a disease that has compromised their vision. Others want to contribute to medical research that could lead to new and better treatments for their children or grandchildren.

Whatever your reason, it is a good idea to understand why the trial is being conducted and what are the potential benefits and risks of participating.

A clinical trial is a research study designed either to determine if a specific treatment—a drug or medical device—is safe and effective or to compare more than one form of treatment with another. Clinical trials will recruit two or more groups of patient volunteers who are typically randomly assigned into the different arms of the study. Clinical trials one group of patients may receive the new treatment and the other group may receive either the standard treatment or a placebo (dummy) drug.

By the time a drug, device, or other treatment is used in a clinical trial, years of research have already taken place proving to scientists there is a good likelihood that patients will benefit from the new treatment and that the risks are low.

Several measures are in place to protect the safety of the patient and assure accuracy of results. Each trial has a specific set of criteria defining who is eligible to enroll so that the findings are valid. Participants are given an informed consent document that describes the trial in great detail, including potential risks and benefits. Clinical trials are run according to a carefully defined series of steps, called a protocol. Each person has ample time to ask questions before signing the consent.

Trials are funded by the National Institutes of Health, a funding agency, or a private company. They are governed by the Food and Drug Administration and may proceed through three phases:

- Phase I trials address safety only. These trials involve a small group of healthy people and determine how a drug should be given and what dose will be safe.
- Phase II trials continue monitoring safety but also begin to evaluate effectiveness of the drug, device, or procedure. These studies involve a larger group of people who have the disease or condition that is to be treated.
- Phase III trials, like the one below, usually compare a new drug, group of drugs, device, or procedure against the current standard treatment. These studies address effectiveness and require a large pool of volunteer subjects to assure the validity of the findings. To eliminate bias, each participant is randomly assigned either to the current standard treatment or to the alternative treatment by a coin toss or by computer. Many Phase III trials are conducted nationwide, each center following the same stringent protocol to test the new treatment over a large and diverse population.

The Kellogg Eye Center routinely has between 10 and 20 clinical trials actively conducted and what are the potential benefits and risks of participating.

The Kellogg Eye Center routinely has between 10 and 20 clinical trials actively recruiting patient volunteers to assure the validity of the findings. Participants are given an informed consent document that describes the trial in great detail, including potential risks and benefits. Clinical trials are run according to a carefully defined series of steps, called a protocol. Each person has ample time to ask questions before signing the consent.

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The Kellogg Eye Center routinely has between 10 and 20 clinical trials actively recruiting patient volunteers. They are listed on our website www.kellogg.umich.edu/research/open_clinicaltrials.html.

MULTICENTER UVEITIS STEROID TREATMENT TRIAL PROTOCOL

The Multicenter Uveitis Steroid Treatment Trial is a clinical trial randomizing patients at multiple clinical centers, including the University of Michigan. This trial compares two FDA-approved treatments for severe uveitis (ocular inflammation in the back of the eye) to determine which of these two treatments may be better long-term. Patients with active uveitis who are eligible for this study will be randomly assigned by computer either to treatment with steroids or other immunosuppressive medicines or to have a very small slow-release steroid implant surgically placed in the eye. Patients will be followed over two years to monitor both the effectiveness of treatment and any side effects.

Principal Investigator: Susan G. Elner, M.D.
Study Sponsor: National Eye Institute of the National Institutes of Health

OUR MISSION

To solve the puzzles of blinding eye disease, to improve the quality of life for our patients, and to teach the next generation of vision scientists and clinicians.

Advances in Ophthalmology
Spring 2008

You can find many resources at our website: www.kellogg.umich.edu

Useful links from the front page:
- “Patient Care” for listings of our clinics
- “Find a Physician” for information about your physician
- “Eye Conditions” for information on specific eye diseases
- “LASIK” for complete information on refractive surgery
- “Expansion” for the latest on our building project

The Regents of the University of Michigan:
Julia Donovan Darlow, Ann Arbor
Laurence B. Deitch, Bingham Farms
Olivia P. Maynard, Goodrich
Rebecca McGowan, Ann Arbor
Andrew C. Richner, Grosse Pointe Park
S. Martin Taylor, Grosse Pointe Farms
Katherine E. White, Ann Arbor
Mary Sue Coleman, ex officio

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Joshua D. Stein, M.D., M.S., delivered a paper “Assessing the Safety of Trabeculectomy Among Elderly Americans” that was recognized as best among those presented at the Glaucoma Session of the 2007 AAO Annual Meeting. “Best Papers” is a new award given at the conclusion of each Free Paper session.

Peter F. Hitchcock, Ph.D., received a Senior Scientific Investigator Award from Research to Prevent Blindness for his work on the development and regeneration of photoreceptors in the vertebrate retina. Dr. Hitchcock investigates molecular mechanisms that regulate this event and, with graduate student Alexandra Calinescu, M.D., and postdoctoral fellow Sonya Craig, Ph.D., he has recently identified two unique signaling molecules involved in the regeneration of cone photoreceptors.

David C. Musch, Ph.D., has been appointed a member of the Clinical and Translational Scientific Review Committee, part of an NIH program that helps fund projects in the U-M Institute for Clinical and Health Research.

Roni M. Shtein, M.D., has been awarded a National Eye Institute K23 grant for her work on neovascularization patterns in corneal graft rejection.

In this issue: A New Screening Device for Eye Disease; Research for Rescuing Vision; A Visitor from Ghana; Perspectives on the Eye Center Expansion and more.

Faculty Briefs

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In this issue:

A new screening device for eye disease; research for rescuing vision; a visitor from Ghana; perspectives on the eye center expansion and more.


Lichter PR, Musch DC, Janz NK. The Investigators’ Perspective on the Collaborative Initial Glaucoma Treatment Study (CIGTS). Arch Ophthalmol 2008;126:122-124.


