VIEWPOINT

The Department of Ophthalmology Columbia University
at The Edward S. Harkness Eye Institute

Fall 1999

Scientists Dig for AMD's Roots

Family Links to AMD

It's become an all-out race, and scientists are rapidly approaching their goal. The Human Genome Project--arguably one of the most ambitious biomedical quests ever pursued--is actually ahead of schedule. By next spring, the project is expected to produce a "rough draft," or what some scientists are calling the "Book of Life," locating each of the three billion base pairs of genes that make up human existence. Scientists hope that the information gleaned from mapping the human genome will ultimately make it possible to correct the genetic "mistakes," or mutations,

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Is AMD Inherited?

Olympic Gold Medalist, skater Dick Button and his brother, Jack, have joined a Columbia study examining the genetics of macular degeneration.

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Views from the Chair

Dear Friends,

Columbia's Department of Ophthalmology has a remarkable history of leadership in vision research, and I am proud to say that we are maintaining that role today as we continue adding to our record of achievement. Three years ago for example, latanaprost, a revolutionary glaucoma drug developed at Columbia by Dr. Laszlo Bito, received F.D.A. approval for patient treatment. Although it remains under scrutiny for any unforeseen side effects (see page 4), latanaprost is regarded as one of the safest, most convenient and most effective glaucoma drugs. The kind of diligent and creative enterprise that led to the discovery of this successful treatment is still being applied to developing further innovations in glaucoma prevention and care. Our deep appreciation goes especially to Mr. Homer McK. Rees and to many other friends who have so generously helped to make our efforts successful.

I'm also pleased to bring you news of a major clinical research initiative to identify genetic and environmental links to age-related macular degeneration (AMD) that is being led by Drs. R. Theodore Smith, Gaetano Barile and Rando Allikmets. Another important study under the direction of Dr. Janet Sparrow seeks to demonstrate the relationship between AMD, sunlight, and a Vitamin A derivative that accumulates in the retina. Such promising research projects in this area of inquiry offer us hope of one day eliminating AMD's threat to our vision.

Finally, a major gift from the Gladys Brooks Foundation to the Harkness Eye Institute's John M. Wheeler Library gave us the idea of showcasing the highlights of this collection in *Viewpoint*. It is a delight to be able to share this extraordinary resource with you through some evocative photographs and a brief description of the library and its special history.

As we approach the excitement of a new millennium, it is my wish that the future will bring new progress in vision-saving care. I wish you all a very happy holiday season and hope that you and your loved ones will enjoy good health and joy throughout the new year.

Sincerely,

Stanley Chang, M.D.
Edward S. Harkness Professor
Department of Ophthalmology Chairman

Expanding Frontiers in Glaucoma Research

Rees Glaucoma Scholar's Program Established

Struck by the fact that no one really understands how glaucoma develops, Homer McK. Rees, a retired businessman and former chairman of Prudential Capital Corporation, decided to invest in Columbia's efforts to find long-needed answers. "I have personal reasons for helping," explains Mr. Rees, referring to his own battle with glaucoma. "It's obvious that we need to learn more about the disease."

Not long ago, Mr. Rees, wishing to make the type of investment that yields a greater return than mere dollars and cents, pledged $300,000, over a three-year period, to create the Rees Glaucoma Scholar's Program at Columbia. The Rees Glaucoma Scholar will be selected from among top researchers in the field and will work toward developing new insights into glaucoma prevention and treatment.

Glaucoma is the leading cause of preventable blindness in the United States, affecting an estimated three million Americans. It is a silent villain that, with little or no warning, robs its victims of their ability to see. Once destroyed, vision lost to glaucoma cannot be restored. But there are a number of effective drug therapies, as well as surgical options, that can prevent glaucoma-related damage from taking its devastating toll on sight.

The key to glaucoma control, say doctors, is early detection. The disease occurs when, for as yet poorly understood reasons, the eye's nerve fiber layer, which transmits visual images to

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"I have personal reasons for helping... It's obvious that we need to learn more about the disease."

Homer McK. Rees

Glaucoma from page 3

the brain, begins to erode. Often, the condition is tied to an increase in the eye's internal pressure, but glaucoma can also affect vision without elevated intraocular pressure. And, just as mysteriously, patients may have excess pressure without associated damage from disease.

In explaining his desire to support Columbia's glaucoma investigations, Mr. Rees, a patient of Dr. Max Forbes, also noted, "There's no time like the present to invest in research. The stock market is high. It's an ideal time to give appreciated securities. I had every reason to help!"

Investigating a Miracle Drug's Possible Side Effects

Latanaprost is a revolutionary glaucoma treatment, which received F.D.A. approval in 1996. Developed at Columbia by Dr. Laszlo Bito, the drug works by increasing the eye's natural outflow of fluid, thereby reducing pressure within the eye. But a small number of patients have experienced problems that may have resulted from latanaprost use. Now, Columbia University is participating in an international, multicenter study to analyze possible complications associated with the drug, also known as Xalatan.

One of the leading therapies for glaucoma management, latanaprost is popular because the drug is both easy to tolerate and effective with just a single daily dose. But side effects that include macular swelling, corneal erosion and a darkening of the iris, may be associated with latanaprost use. Curiously, the drug may actually produce a desirable cosmetic result -- that of longer, thicker and darker eye lashes!

According to Principal Investigator Steven Odrich, M.D., who is assistant professor of Clinical Ophthalmology at Columbia, the latanaprost study will examine 6,000 patients worldwide over a five-year period to determine what, if any, side effects are associated with the drug, how many patients are affected, and to what degree. "This research," he adds, "will also help doctors make more accurate comparisons among the various glaucoma medications that are currently available. Unfortunately, they also have their own drawbacks."

Setting Standards for Laser Vision Correction

In another research project, Dr. Steven Odrich has teamed with Professor of Clinical Ophthalmology Stephen Trokel, M.D., and Assistant Professor of Clinical Ophthalmology

Marc Odrich, M.D., to define standards for the safe use of laser surgery in vision correction. Increasingly popular, laser surgery can treat nearsightedness, farsightedness and astigmatism, offering patients the opportunity to see clearly without glasses or contact lenses. However, the procedure, which is considered to be safe and effective for many patients, may not be advisable for people at risk for developing glaucoma, according to Dr. Steven Odrich. Among the risk factors associated with glaucoma are a family history of the disease, nearsightedness, diabetes, hypertension and being of African-American descent.

"Laser vision correction is a great innovation," Dr. Odrich says, "but, it may not be for everybody." The problem, he explains, "is that laser correction changes the cornea's thickness and elastic properties, making it difficult to accurately measure intraocular pressure." Early detection, frequent monitoring and appropriate treatment are critically important in preventing glaucoma-related damage to the eyes. Dr. Odrich, who is also trying to find better ways of detecting glaucoma in patients who have had laser vision correction, is nevertheless optimistic about the surgical procedure, as well as about new developments in glaucoma research. "The next decade," he suggests, "offers the promise of improved diagnosis and new treatment modalities to help prevent this serious cause of blindness."

Breakthrough Technology Helps Keep Glaucoma In Check

A welcome advancement in glaucoma detection and management is a new type of technology, Optical Coherence Tomography (OCT). The technology provides doctors with computerized measurements and an analysis of the nerve fiber layer that can determine if and when glaucoma treatment should be recommended to avert vision loss. The Department's purchase of the technology was made possible by a generous gift from Homer McK. Rees, who also endowed the Rees Glaucoma Scholar's Program at Columbia.

Dr. Liselotte Pieroth, now a resident in Ophthalmology at Columbia, was one of a team of researchers at Tufts University, who helped to design computer software for OCT.

Genetic Links from page 1

associated with a wide range of afflictions as seemingly different from one another as cancer and schizophrenia or diabetes and hypertension.

Among the disorders certain to be linked to specific genetic flaws is age-related macular degeneration (AMD). In fact, whether we are--or are not--stricken with AMD, is largely determined by heredity, although the condition's development and progression are also connected with environmental factors, including smoking, exposure to sun and the effects of diet.

The leading cause of blindness in older Americans, AMD strips away central vision from an estimated 400,000 new patients each year, hampering their mobility, destroying their independence and restricting their lifestyle. Which specific gene sequences are linked to macular function? What genetic mutations lead to AMD? To what degree do individual habits such as smoking and sunbathing affect AMD progression? These are among the questions researchers at Columbia have begun to investigate as part of their multifaceted “Genetics of Macular Degeneration” study to learn more about AMD's causes and to identify the disorder's genetic origins.

Dr. Smith examining a patient.

Led by Columbia Drs. R. Theodore Smith and Gaetano Barile, both assistant professors of Clinical Ophthalmology, and Dr. Rando Allikmets, assistant professor of Ophthalmic Science, the study will include several hundred patients with AMD, as well as a control group of people 60 years of age or older without AMD-related vision loss. Study participants, referred by ophthalmologists and eye care centers throughout the New York area, will be screened for AMD in order to diagnose the disease or analyze its progression. Participants will also be asked to complete a simple medical history and lifestyle questionnaire and to provide blood samples for Dr. Allikmets's DNA research.

Two years ago, Dr. Allikmets, who was appointed Louis V. Gerstner, Jr., Scholar at Columbia in 1999, discovered a genetic abnormality linked to the juvenile form of macular degeneration called Stargardt's disease. Since that time, Dr. Allikmets's multicenter investigation in the United States as well as in seven European countries has shown possible links between the Stargardt's gene, known as ABCR, and AMD. Researchers hope that finding the genes responsible for AMD will help them to develop innovative ways of preventing its destructive results. Genetically engineered treatments could eventually make it possible to replace the defective genes, or the proteins these genes normally produce that are related to AMD.

If you are 60 years of age or older and would like to join this important study, please speak to your ophthalmologist or call Columbia's Department of Ophthalmology at 212-305-0653 for details. All records and information will remain confidential.

ABCR was the first and is so far the only gene proven to be linked to AMD. "We know ABCR is a player in the condition's development," notes Dr. Allikmets, "but we have yet to determine the importance of its role and to identify other genes that may be involved."

"Finding the gene that causes Stargardt's was an enormous breakthrough," says Dr. Smith, but, he adds, "unlike Stargardt's, which is caused by a single genetic defect, AMD has multiple causes. This new research gives us a great opportunity to find specific genetic and environmental explanations for one of the most prevalent and perplexing threats to aging eyes."

Dick and Jack Button Join Study on AMD

Brothers Dick and Jack Button, patients of Dr. Smith, are among those who have volunteered to participate in Columbia's AMD study. Dick Button, an Olympic Gold Medal figure skating champion and television sportscaster, enjoys the good fortune of having excellent vision. His brother, Jack, a businessman and former pilot, has been grappling with sight loss from macular degeneration for the past two decades. Their mother, say the Buttons, was also a victim of the disorder.

Siblings like Dick and Jack Button are of special interest to researchers, according to Dr. Allikmets, because their genetic similarities and differences could help to identify variant genes related to AMD. "If, for example," he says, "several members of a family have AMD and also have the same genetic abnormality, we're onto something. If, on the other hand, one or more older relatives don't have the disorder, their genetic and lifestyle differences may help to explain the disparity."

Does AMD run in families? Dick and Jack Button with their brother, George (l-r), as adults and as children. Columbia doctors are investigating AMD's genetic and environmental causes. A childhood eye injury precludes George Button from participating in the study.

Does A2E+Sun=AMD?

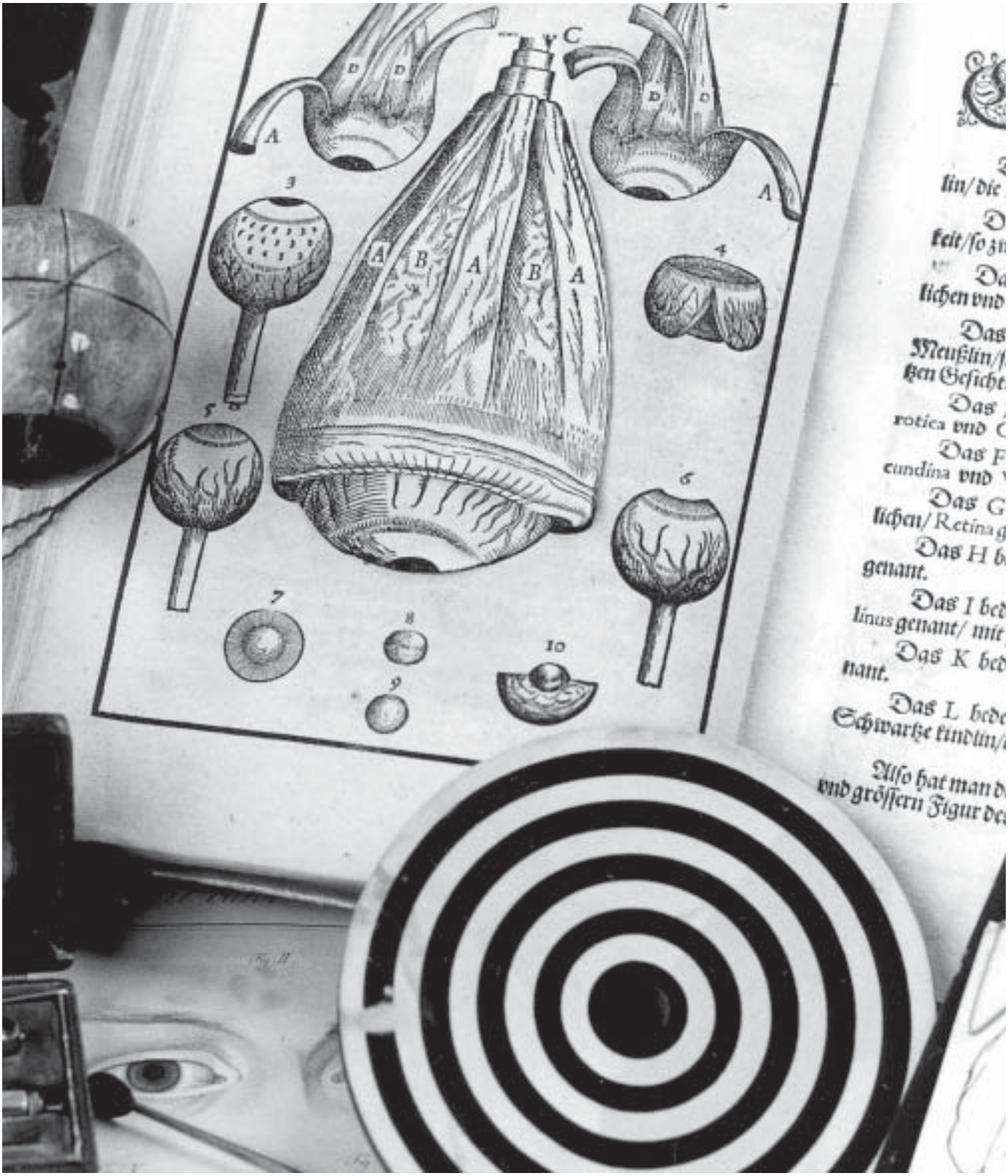
Thinking about vacationing on a sunny beach? Sounds delightful, especially as we approach winter's cold, dreary months. But, just in case you haven't already heard, the sunshine we treasure has a darker side, not only because of its potential to harm your skin, but also because it can cause serious damage to your eyes.

Dr. Sparrow, conducting her research with the highly specialized Zeiss flourescence microscope, purchased with the Schering-Plough Foundation's support.

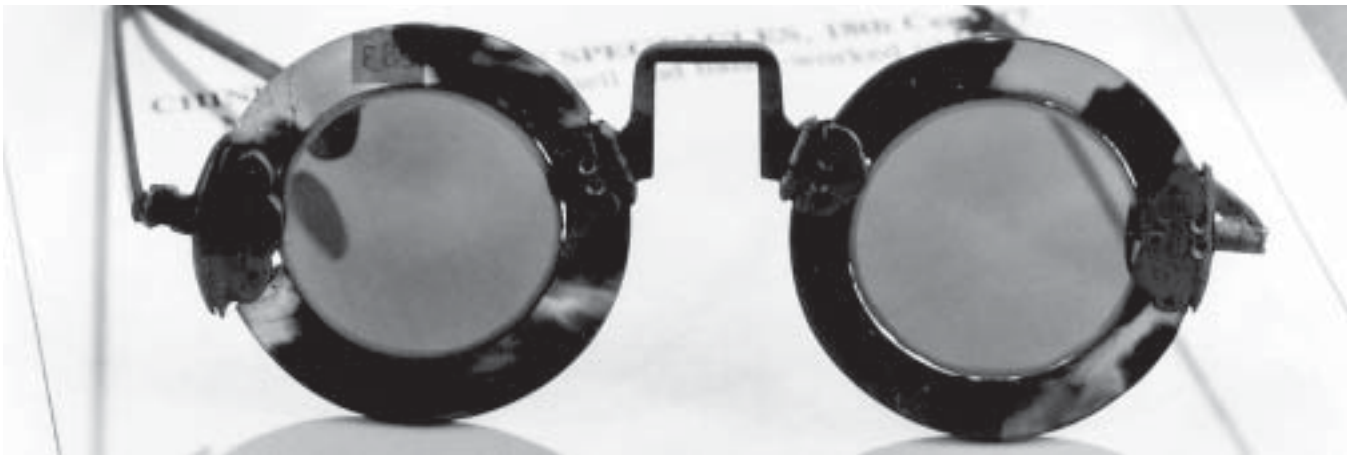
How do the sun's soothing rays destroy vision? Recently, Dr. Janet Sparrow, associate professor of Ophthalmology, conducted a laboratory experiment to explain how light from the sun may accelerate the progression of AMD. Key to her research was the ready availability of A2E, a Vitamin A derivative normally found in aging eyes, which Dr. Sparrow's colleagues in the Department of Chemistry at Columbia have synthesized. To understand how sunlight causes its damage, Dr. Sparrow added A2E to a test tube containing retinal pigment epithelium (RPE) cells normally found in the retina. When RPE cells containing A2E were exposed to blue light similar to rays from the sun, the cells died. But when RPE cells that did not contain A2E were exposed to the same type of light, they remained healthy.

"A2E accumulates in our eyes gradually as we age," Dr. Sparrow noted. "To further our research, we now need to learn more about exactly how A2E damages retinal tissue and why some people accumulate more of this vitamin by-product in their eyes than others." But, she cautions, don't stop eating your carrots or other yellow vegetables to avoid A2E. "These Vitamin A containing foods are essential for night vision, healthy teeth and bones and other aspects of good health." Rather, she recommends, "Wear yellow-tinted sunglasses to block potentially dangerous levels of light and spare your eyes while enjoying the many rewarding pleasures of outdoor life!"

A Long Look at Ophthalmology's History



One of the first medical illustrations describing the anatomy of the eye, from Bartisch's "Das Ist Augendist," is shown with antique ophthalmologic instruments from the Wheeler Collection.



Eighteenth Century Chinese Mandarin spectacles.

The Wheeler Library

Hidden away on the Edward S. Harkness Eye Institute's eighth floor is a little-known treasure: the John M. Wheeler Library. Named for the Eye Institute's first director, the Wheeler Library gives visitors a fascinating glimpse into knowledge that has been accumulated on the ocular system and the development of the discipline of ophthalmology over several centuries and in many parts of the world. It houses a large and important collection of historic objects, journals and books--some of which are quite rare--all devoted to the study of vision.

The nucleus of the library came from the private collection of Dr. Henry D. Noyes (1832-1900), a prominent New York ophthalmologist. It eventually passed to Dr. Wheeler through his partner, a former Noyes associate, Dr. Dwight W. Hunter. Since coming under the guardianship of the Eye Institute, the library has expanded its holdings in European, North American and Asian ophthalmologic journals and historic books. Many works in the library's distinguished collection, which spans the sixteenth to the nineteenth centuries, are of great scholarly interest. One of them, an extremely rare and valuable title, is "Das Ist Augendist," the work of an itinerant German eye surgeon, named George Bartisch, that dates from 1583, making it the oldest text devoted exclusively to the eye. Another one, a well known book illustrating the structure of the eye, was published in Pavia in 1901 by Antonio Scarpa, one of the leading anatomists of his day.

An intriguing array of antique instruments and other types of technology used in eye care over a period of a hundred years or more complements

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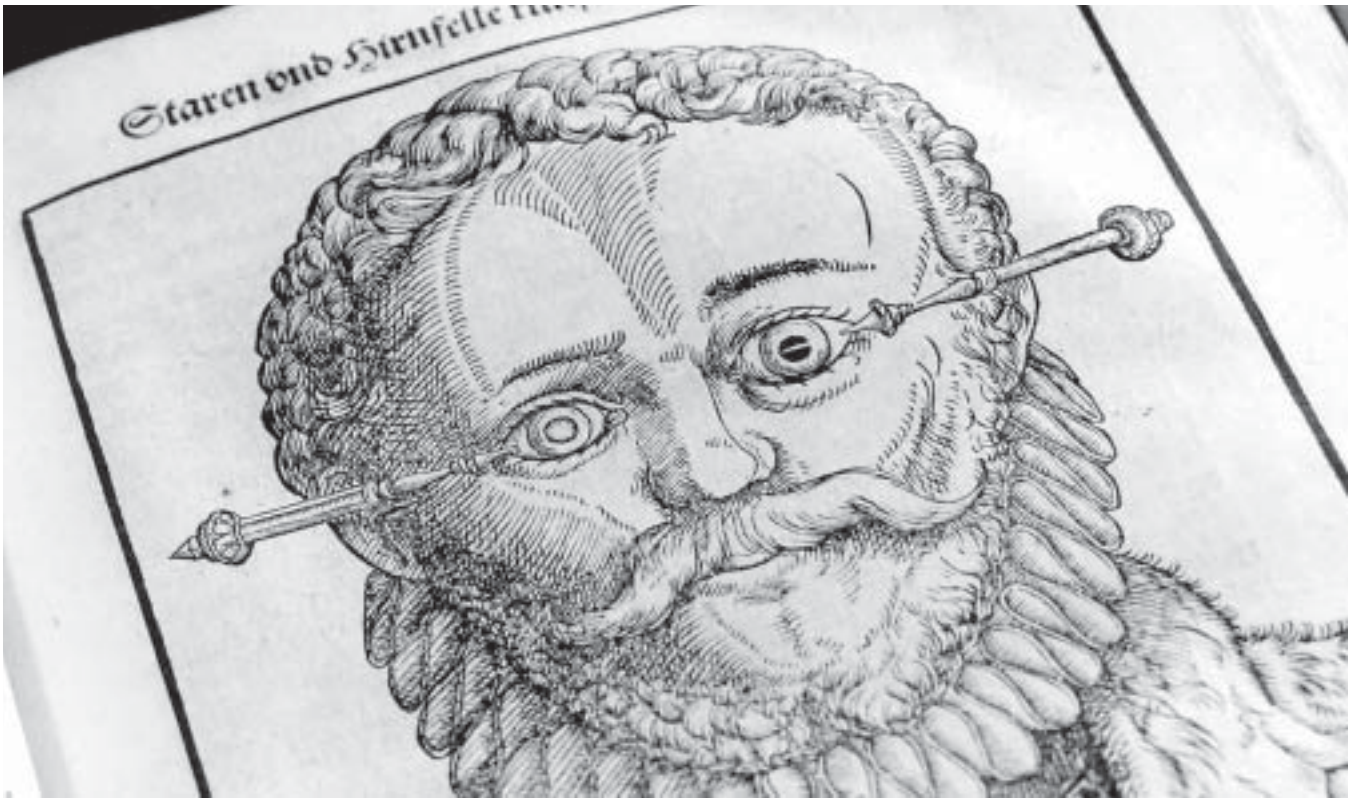
the Wheeler Library's literary offerings. Fascinating Chinese surgical tools and spectacles, nineteenth-century candle-illuminated implements for examining the external and internal eye, and a hand-held device called a "perimeter," dated 1889, for measuring a patient's visual field are among the antique scientific instruments that have been preserved in the collection. The library is also a repository for more than 2,000 medical illustrations, many by prolific Eye Institute artist-in-residence, Gus Bethke, who executed them before the advent of modern diagnostic imaging to document disorders of the eye.

Preserving the Past, With an Eye to Informing the Future

In 1931, Edward S. Harkness pledged $5 million to help construct and endow an eye institute at the newly-created Columbia-Presbyterian Medical Center. As the Institute's first director, Dr. Wheeler, made sure his collection of books and rare instruments would not only have a proper home, but would also grow to become a valuable resource to Columbia's Department of Ophthalmology students, residents and staff. Over time, many faculty members, realizing the significance of Dr. Wheeler's legacy, have contributed their own collections



This Sixteenth Century print from Bartisch's "Das Ist Augendist" illustrates the process of "couching" a cataract, or pushing the lens away from the patient's field of vision.

Researcher Dr. Aleksandra Iljin, Library Committee Director Dr. John Merriam, and librarian Dr. Lisa Tian, with a Nineteenth Century model made to explain the mechanisms of eye movement.

of antique spectacles, instruments and books to the library's resources.

"The library has been fortunate to receive support from a number of devoted patrons," notes Library Committee Director and Associate Clinical Professor John Merriam, M.D. The Dunlevy Milbank Foundation and Catherine and Henry Gaisman, for instance, deserve special mention for making critically needed funds available to ensure that the library's old and rare books were properly preserved and stored. Then, in 1997, the Gladys Brooks Foundation gave the library a generous $100,000 gift to create the Gladys Brooks Endowment for Acquisitions. "It's a great beginning," says a delighted Dr. Merriam, who nevertheless warns, "We still need a good deal of additional support to maintain this special resource."

If you would like to add your name to the list of those helping to preserve the library's valuable collection, please contact Susan Taylor, senior development officer for Columbia's Department of Ophthalmology at 212.304.7200. Or, you may send your contribution for the John M. Wheeler Library Fund to Ms. Taylor's attention at: Columbia University Health Sciences Development; 100 Haven Avenue; Suite 29D; New York, NY 10032.

Supportive Eye Institute Friends Make Exciting Research a Reality

William Acquavella, president of Acquavella Galleries and a member of the Eye Institute's Board of Advisors, has installed an exhibition of Cézanne watercolors at his gallery, running through December, to benefit the Department of Ophthalmology at Columbia. Eye Institute Board members were guests at a pre-opening reception held on October 18. Mr. Acquavella previously made a gift of $500,000 to the Department for establishing the Acquavella Scholarship in Retina Research. (above, left: detail from *Mount-Sainte-Victoire Seen from Les Lauves*. above, right: William Acquavella.)

Robert L. Burch, III, who gave the Department of Ophthalmology $500,000 last year to establish the Burch Scholarship in Retina Research, has made an additional gift of $100,000 to support gene therapy research for retinal disease. Lead investigators for the study are Professor of Ophthalmology Peter Gouras, Higgins Professor of Biochemistry and Molecular Biophysics Stephen Goff, Dr. Stephen Tsang, and Edward S. Harkness Professor of Ophthalmology Stanley Chang. Mr. Burch, a member of the Eye Institute's Board of Advisors, is chairman of Jonathan Manufacturing Corporation.

Joel Hoffman, a patient of Dr. Stanley Chang, gave the Department of Ophthalmology $100,000 in October to support retina research at Columbia. Inspired by *Viewpoint* articles describing the Department of Ophthalmology's research, as well as by conversations with Dr. Chang and his colleagues, Mr. Hoffman says he is interested in "developing a greater understanding of ophthalmology research at Columbia."

The Research to Prevent Blindness Foundation awarded Columbia's Department of Ophthalmology a grant of $180,000 this summer to support research by Dr. Rando Allikmets. The Foundation has been funding vision research at Columbia for more than 30 years, bringing more than $1.5 million in grants to the Department.

The Schering-Plough Foundation recently funded the purchase of a Zeiss fluorescence microscope used by Dr. Janet Sparrow to advance her research on age-related macular degeneration. (see page 12) Joseph C. Connors, executive vice-president for the foundation, is on the Department of Ophthalmology's Board of Advisors.

Creating a Bequest for Ophthalmology at Columbia

GIVING Well

- Support important vision research.
- Reduce estate taxes.
- Memorialize a loved one.

These are among the compelling reasons for making a bequest to Columbia's Department of Ophthalmology. Through a gift in your will, you can create a research or teaching endowment, fund a fellowship, or establish a named professorship. Typically, bequests reduce estate taxes without reducing the assets transferred to heirs. Your gift may also be designed to provide annual income to an heir.

Bequests to benefit ophthalmology at Columbia should specifically name "Columbia University in the City of New York," and be directed to the Department of Ophthalmology.

For example:

I give and bequeath to the Trustees of Columbia University in the City of New York, for its Department of Ophthalmology, the (amount of_____) (% of my estate or trust), to support (research) or (education) or (fellowships, etc.) in honor of _____.

Susan Taylor, our senior development officer, and Elia Desruisseaux, our director of Planned Giving, are available to work with you or your attorney to help plan your gift. They can be reached by phone at:
(212) 304-7200
or by e-mail at:
givingwell@columbia.edu

Columbia University in the City of New York
Edward S. Harkness Eye Institute
635 West 165th Street
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First Annual DeVoe Lecture

Dr. Arthur DeVoe, the first Edward S. Harkness Professor of Ophthalmology and a former chairman of the Department of Ophthalmology at Columbia, with Ms. Joan Gilson and Dr. Stanley Chang, current Edward S. Harkness Professor and chairman. Dr. Chang presented the first Annual DeVoe Lecture on October 14, 1999. The Lectureship was made possible by a generous gift from Ms. Gilson.