

# MACULAR DEGENERATION CENTER



# INSIGHT

## Wet AMD: Today's Treatments and Tomorrow's Possibilities

If you are getting injections for wet age-related macular degeneration (AMD), you are not alone. The treatment has now surpassed cataract surgery as the most frequently reimbursed procedure in Medicare.

This remarkable statistic is due to a number of factors: The prevalence of wet AMD in our aging population, the availability of effective medications and the need to give these treatments about every month indefinitely to stabilize the condition.

Although the wet form is less common than dry AMD, it can be more severe and is considered an advanced stage of AMD. It happens when abnormal blood vessels grow under the macula and leak blood and fluid, called choroidal neovascularization. Damage to the macula can occur quickly and cause irreversible loss of central vision.

After decades of research and testing, three medications are now available that target vascular endothelial growth factor (VEGF), a chemical signal in the eye that triggers uncontrolled growth of these fragile blood vessels. Injected into the vitreous of the eye, these drugs slow the disease and help avoid more vision loss. Some patients even experience better vision.

However, researchers at Casey Eye Institute and elsewhere continue to compare and refine these therapies and test more long-lasting alternatives that are less invasive and more cost effective.

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## AMD: A Look at Today's Treatments and Tomorrow's Possibilities *(Continued from page 1)*

### Lucentis and Avastin — Is There a Difference?

Most patients being treated for wet AMD receive injections of Lucentis (ranibizumab) or Avastin (bevacizumab), both developed by Genentech and similar in makeup. Lucentis was specifically formulated for wet AMD and approved for that purpose by the Food and Drug Administration. Avastin, on the other hand, is a cancer drug used off-label for wet AMD and is much less expensive than Lucentis. Some ophthalmologists began using small amounts of Avastin in their patients before Lucentis became available and found it to be beneficial. A single dose of Lucentis costs approximately \$2,000 while a single dose of Avastin is approximately \$50.

Studies are being conducted throughout the world to compare the safety and effectiveness of these two popular drugs.

Casey Eye Institute was one of several research centers involved in the Comparison of Age-Related Macular Degeneration Treatments (CATT) Trial, sponsored by the U.S. National Eye Institute.

In the study more than 1,000 participants received one or the other drug. Their vision was tracked throughout the trial

and was nearly identical for both groups of patients at the end of two years.

The findings, published last May in the medical journal *Ophthalmology*, also showed that Lucentis and Avastin had similar effects on vision when the dosing schedules were the same; patients who received monthly injections with either drug had slightly better vision and there was no difference in side effects normally expected with these drugs, such as stroke, heart attack or death.

One-year results from a comparison study in the United Kingdom, also announced in May, found that Lucentis and Avastin were equally effective in treating wet AMD. In this clinical trial, known as IVAN, researchers also learned that patients given the drug as needed instead of monthly experienced almost identical levels of vision. The study is continuing to follow participants to two years, when a more detailed analysis will be presented.

### Eylea: The Newest Option

Approved by the Food and Drug Administration in late 2011, Eylea (aflibercept) is the newest treatment option for patients with wet AMD. "Although it acts in the same way as Avastin and Lucentis, it

is made up of a different molecule," says Casey retina specialist Steven Bailey, M.D. Not only does Eylea block VEGF, but it also traps a second growth factor that may also hinder blood vessel growth, according to Regeneron, the company that developed the drug.

One possible advantage of Eylea is that its dosing schedule calls for fewer injections than its counterparts and costs slightly less than Lucentis, though significantly more expensive than Avastin. Patients receive injections monthly for the first three months and then every eight weeks after that.

Based on that dosing schedule, clinical trials of Eylea after one year produced results similar to those in Lucentis studies, notes Dr. Bailey. "There are now three drugs available with equal effectiveness and similar safety profiles," he says. Dr. Bailey recommends that patients talk to their ophthalmologist to determine the most beneficial treatment and dosing schedule.

### An Eye to the Future

While anti-VEGF drugs have helped preserve the vision of millions of patients, researchers at the Macular Degeneration Center and elsewhere are exploring ways to extend their benefit.

Some experimental approaches involve supplementing Lucentis with other treatments, such as anti-inflammatory agents, nutritional supplements, low-level laser or infrared radiation. These additional therapies may tackle other factors that contribute to the disease and consequently lengthen the time between injections.

Also on the drawing board are less invasive methods of delivering the medication over the long term. Several companies are

developing devices implanted beneath the sclera (white part of the eye) that continually release the anti-angiogenic drug.

### Helpful Genes to Treat Wet AMD

Gene therapy is also earning attention as a promising weapon against wet AMD, with Casey joining the RetinoStat Phase I GEM Study sponsored by Oxford Biomedica (see page 7). In this study, a single injection of two genes is delivered directly to the retina, where they express anti-angiogenic proteins. "The aim is

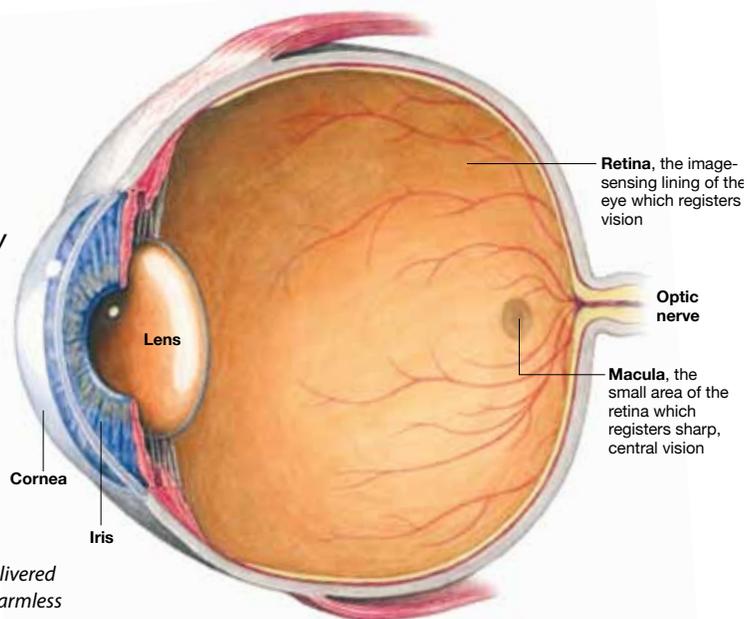
to preserve vision by blocking in a sustained fashion the growth of harmful and sight-threatening abnormal new blood vessels," says retina specialist Andreas Lauer, M.D., principal investigator of the Casey study. The treatment, called RetinoStat, was found to be safe in an earlier group of study patients. Casey is testing a final group in the clinical trial, with the first patient undergoing the procedure at Casey this fall. "We are excited to be part of this innovative effort," says Dr. Lauer.

*(Continued on page 12)*

### Fighting Vision Loss With Gene Therapy

Doctors at OHSU Casey Eye Institute are conducting a clinical trial using gene therapy to treat wet age-related macular degeneration (AMD) and other eye diseases.

Although the wet form is less common than dry AMD, it can be more severe and is considered an advanced stage of AMD. Abnormal blood vessels grow under the macula and leak blood and fluid. Damage to the macula can occur quickly and cause irreversible loss of central vision.



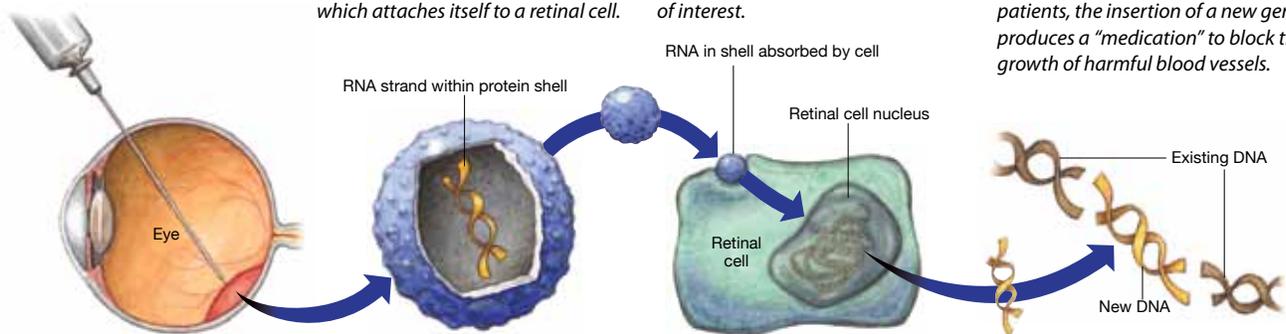
### The Gene Replacement Procedure

**1)** The gene therapy drug is injected into a specific location beneath the retina.

**2)** The gene therapy drug is delivered via a non-active virus that is harmless in humans. The virus contains a double strand of RNA that encodes the gene for transplantation. The virus is contained in a protein shell which attaches itself to a retinal cell.

**3)** The retinal cell engulfs the RNA, absorbing it into the cell. The RNA is converted to DNA, encoding the gene of interest.

**4)** The gene from the new DNA strand becomes part of the cell's existing DNA. In macular degeneration patients, the insertion of a new gene produces a "medication" to block the growth of harmful blood vessels.



Sources: The Casey Eye Institute, Oregon Health Sciences University

Eric Baker/ OHSU

# E-book Devices Expand Options for Reading with Vision Loss

Are e-book readers for you? In just the last few years, portable electronic devices like the Amazon Kindle, Barnes & Noble Nook and Apple iPad have surged in popularity, allowing readers instant access to countless books, newspapers and magazines.

Although many of their features, such as the ability to enlarge text, may appeal to older people with vision problems, you may wonder if these gadgets will enhance your ability to read or are best left to your adult children and grandchildren.

“Many people with age-related macular degeneration (AMD) or other eye conditions are good candidates for e-readers if they can read text about the size of a headline or find they read better with good lighting or contrast,” says John Boyer, O.D., director of Casey Eye Institute’s Vision Rehabilitation Center. “However, since there are a myriad of devices on the market and many features to consider they need to carefully weigh all the pros and cons to find the most suitable one,” he says. Some e-book readers, such as most Kindle and Nook models, use a spe-



*Dr. Grace Tran demonstrates the features of a tablet device.*

cial technology called e-ink that gives the appearance of a printed page. Tablet devices, such as the iPad, have LCD screens that produce bright, colorful images.

## How they work

With e-readers, content is downloaded onto your device from any number of online sources. Free digital material can be downloaded from your local library’s Web site or other public sites, such as Project Gutenberg

([www.gutenberg.org](http://www.gutenberg.org)). You can also purchase e-books and periodical subscriptions online from sites like Amazon, Barnes & Noble or iTunes.

If your vision loss significantly affects your ability to read standard print you may also qualify for Bookshare ([www.bookshare.org](http://www.bookshare.org)), which offers thousands of titles for a modest membership fee. However, its file format is not compatible with all devices, including the Kindle and Nook.

## Key Considerations

- **Ability to enlarge font size.** With an e-reader, you can enlarge the font size of any content you download. “This can make a big difference in the quality of reading and may make a magnifier unnecessary,” notes Grace Tran, O.D., F.A.A.O., a vision rehabilitation specialist at Casey. “Even if you still need a magnifier with an e-reader, you can use a lower power than you would use for printed books,” she adds, pointing out that the milder the magnifier, the bigger its diameter.

However, you may not be able to enlarge the menu portion of your e-book or the on-screen keyboard. If so, you may need to use magnification for those features or have someone help you.

- **Screen size.** E-readers come in a variety of screen sizes. Keep in mind that a smaller screen will display less text and the menu size will be smaller, says Dr. Boyer.
- **Audio Capability.** With e-readers, you can download audio books, or with the addition of text-to-speech software, have the material read to you through speakers in the

device or headphones.

The text-to-speech feature allows you to follow along or just listen while the material is read out loud.

- **Portability.** E-readers are much lighter and easier to hold than oversized large print books and magazines. It’s especially ideal for travel, since these devices can store the equivalent of hundreds of books at one time.
- **Light and contrast.** Many of these devices have built-in lighting, which adds that all-important contrast so crucial for readers with macular degeneration. You can heighten the contrast even more by shining an external light source onto your device.

However, some devices do better than others controlling glare, particularly when used in bright sunlight. “Glare can be very annoying, cause discomfort and worsen contrast,” says Dr. Tran.

- **Accessibility and Versatility.** While the variety of large print reading material is limited, the selection of digital books and periodicals seems almost infinite. Any book or magazine can easily be transformed into large print. E-readers also

allow you to take notes, save your place, highlight passages and even look up words. Tablets, such as the iPad, also let you browse the Internet, use e-mail and perform other interactive functions.

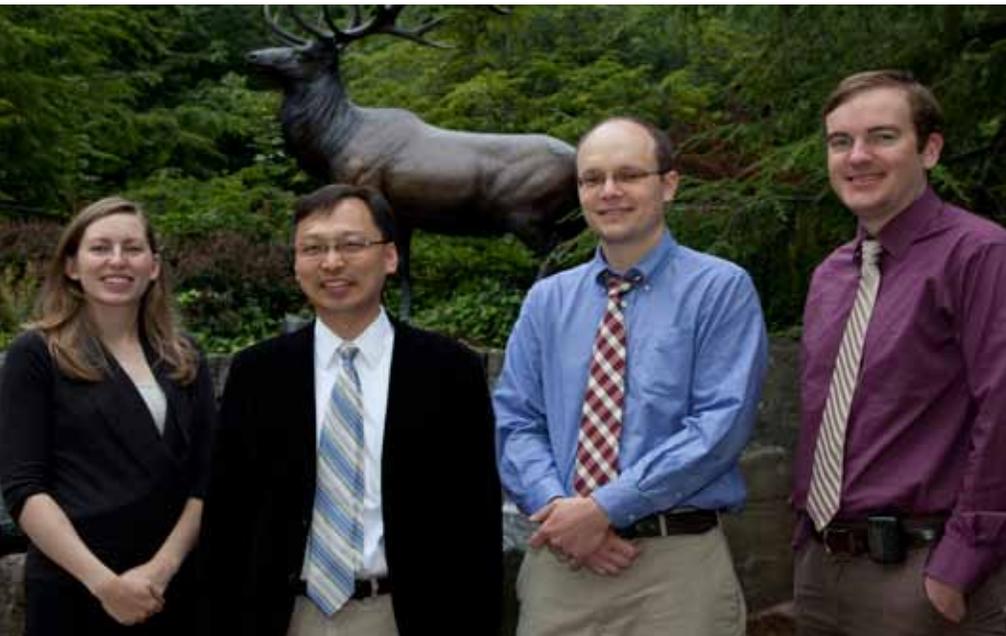
- **Navigation.** Some e-readers use a touch screen while others have small buttons for navigation. “These devices require good dexterity and comfort using electronic gadgets,” cautions Dr. Boyer.

Before making any purchase, be sure to spend time trying it out in the store. If you can, take it outside to check whether bright sunlight causes glare. Some public libraries will even allow you to check out a device to try at home.

“It’s exciting to see these products, originally intended for the mass market, become more and more capable of accommodating the needs of people with visual disabilities,” says Dr. Tran. “If you do purchase one, our vision rehabilitation department can help you use the features that enhance readability.”

**To reach Casey’s Vision Rehabilitation Center, call 503-494-3098. ●**

# Casey Offers Future Retina Specialists Top-Notch Training



*L to R: Elizabeth Verner-Cole, M.D., Thomas Hwang, M.D., Retina Fellowship Program director; Stephen Davis, M.D., and Peter Campbell, M.D.*

Macular degeneration patients throughout the Pacific Northwest choose Casey Eye Institute because of its wide array of clinical services, outstanding physicians and cutting-edge research. And it's those qualities that also attract the nation's top eye doctors, who come to Casey for advanced education in its well-regarded retina fellowship program.

Stephen Davis, M.D., Liz Verner-Cole, M.D., and Peter Campbell, M.D., Casey's current fellows, are spending two years intensively training in all aspects of medical and

surgical care of the retina. As part of their experience, the fellows see patients at weekly clinics, after hours and for urgent problems. They also accompany Casey's attending retina physicians during patient appointments.

"Our program is unique because it is one of the most comprehensive in the country. The fellows work with experts in all subspecialties of retina, such as eye tumors, ophthalmic genetics, pediatric retina and inflammatory eye disease," notes Thomas Hwang, M.D., director of the Retina Fellowship program.

The program's small size also is an advantage, allowing the fellows to work more closely with Casey's retina doctors, he adds.

The three fellows, selected from a pool of highly qualified candidates, have completed residencies in ophthalmology. All say they were drawn to Casey because of its stellar reputation and diverse opportunities in patient care.

"When I decided to do a fellowship in retina, I wanted to find a nationally recognized program with a wide assortment of patients and great faculty," says Dr. Davis, "It's been a great experience so far and everything I expected and more," he says, referring to the quality of training, welcoming staff and exposure to a full range of surgical procedures. A stint as an ophthalmic technician before medical school helped spark his interest in ophthalmology. "I like the visual nature of ophthalmology," he says, adding that he also finds it gratifying to be able to help preserve patients' vision.

Dr. Verner-Cole, who completed a fellowship in ophthalmic pathology before arriving at Casey last year, says the program had "all the points I wanted" and a location she found appealing. A "double

bonus," she says, is being able to work with Casey chairman David Wilson, M.D., who is a subspecialist in retina and ophthalmic pathology. She chose ophthalmology, she says, because she enjoys its hands-on approach and the opportunity to use the latest technology.

"Everyone from the administrative staff to the operating room personnel has been incredibly helpful," points out Dr. Campbell, who began his fellowship in July. "They like working here and share the same mission." Several factors contributed to his decision to specialize in retina. "I had great mentors in retina during medical school and my residency and always valued taking care of people with acute eye problems," he says.

"We look for candidates who are hard working, easy to teach, ethical and put patients and colleagues ahead of themselves. We also look at their capacity to grow," says Dr. Hwang. "Our current crop meets those expectations and more."

Not only do the fellows share an enthusiasm for learning and patient care, their outside lives have some similarities too. Within a one-month period last spring, all three became the parents of new babies. "It was pretty wild," chuckles Dr. Hwang. ●

## Ongoing Clinical Studies at the Macular Degeneration Center

### Age-Related Eye Disease Study (AREDS2)

**Purpose:** To evaluate the effects of lutein and zeaxanthin and omega-3 fatty acids on people at risk of progressing to advanced AMD and/or suffering moderate vision loss. The study is being carried out at Devers Eye Institute in Portland, one of the clinical centers sponsored by the National Eye Institute (NEI). Enrollment is completed and participants are being followed.

**Contact:** Devers Eye Institute, 503-413-8356

### Combination Ranibizumab and Pazopanib for Neovascular (Wet) AMD

**Purpose:** To demonstrate whether pazopanib eye drops are a safe and effective treatment for wet AMD in subjects whose disease is currently managed with anti-VEGF therapy. The study is evaluating whether daily doses of pazopanib eye drops can maintain or possibly improve vision, while reducing the continued need for anti-VEGF injections.

Enrollment is closed and patients are being followed.

### The GEM Study (Gene transfer of endostatin/angiostatin for Macular degeneration)

**Purpose:** To assess the safety and dosing levels of a gene-based treatment, RetinoStat®, for wet AMD. In this study, two corrective genes are delivered directly to the retina, with the aim of blocking the growth of abnormal blood vessels in a sustained fashion. Eligible patients must have established "wet" AMD with visual acuity equal or worse than 20/200 in the worse seeing eye. There must be some ongoing leakage associated with the "wet" AMD and scarring at the center of the macula ("evolving disciform scar").

**Contact:** Ann Lundquist, 503-494-6364

### Genetics of Age-Related Macular Degeneration Study

**Purpose:** To find genetic mechanisms associated with AMD. Families with at least four living affected members are being recruited and followed. Volunteers receive eye photography and DNA analysis at no cost. No travel is required.

**Contact:** Jennifer Maykoski, 503-494-3064

For more information about these studies, please contact the Macular Degeneration Center at 503-494-3537



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## AMD: A Look at Today's Treatments and Tomorrow's Possibilities *(Continued from page 3)*

Casey scientists are also focusing their efforts to better understand what causes angiogenesis in the eye and learn more about the genes involved. "There are dozens of genes that control blood vessel growth in the space beneath the retina," says Dr. Timothy Stout, M.D., Ph.D., M.B.A., a retina specialist and genetics expert at Casey. His research team is working to develop therapeutic genes that target AMD and other eye disorders. ●

## Connect with the Macular Degeneration Center!

Education and outreach is a top priority of Casey Eye Institute's Macular Degeneration Center, a national leader in research and patient care for age-related macular degeneration (AMD). If you'd like to be on our mailing list to receive the biannual *InSight* newsletter and other information — or have a speaker for your group, please call the center at 503-494-3537 or email us at [kahnj@ohsu.edu](mailto:kahnj@ohsu.edu).

Learn more about AMD and the work of the Macular Degeneration Center at [www.caseyamd.com](http://www.caseyamd.com)