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A SEMI-ANNUAL NEWSLETTER

Photo courtesy of Jeffrey Farrell

Myopia on the rise, especially among children

Myopia, also known as nearsightedness, is on the rise in the U.S. and around the world—particularly among children. The World Health Organization predicts that, if the current trend continues, half of the world's population will be nearsighted by 2050 — with up to one-fifth at an increased risk of blindness due to complications of severe myopia. Casey clinicians and researchers are exploring several potential solutions to preventing and slowing this troubling trend.

Why is it happening?

There is a growing scientific consensus that at least one contributor to the epidemic is an increase in the amount of time we spend indoors on phones and computers (known as 'near work') versus time outdoors, in natural light.

How does that happen?

When children spend time looking up close, a significant part of the image is not focused properly on the edges of the retina, the light-sensing part of the eye. This blurred image causes the eye to grow longer, which leads to increased levels of myopia. Researchers are investigating what chemical or physical process is controlling this eye growth, as understanding why it is happening may allow us to control the process in the future.

Another factor that may be contributing to myopia is the growing amount of time children spend indoors. Studies have shown that children who spend more time outside are less likely to develop myopia than those who spend more time indoors. While we don't yet understand exactly why, most pediatricians would agree that spending more time outdoors is good for everyone's physical and mental well-being.

Genes also play an important role in myopia. Children with one or both nearsighted parents are more likely to become myopic. But something else is happening — genes take many centuries to change, yet the prevalence of myopia in the U.S. increased from 25 percent in the early 1970s to nearly 42 percent just three decades later. It's clear that something in the environment is driving the current uptick in myopia.

(continued inside)

The problem goes beyond fitting more children with glasses. Children with higher degrees of myopia are more likely to develop sight-threatening complications later in life like cataracts, glaucoma, macular degeneration and retinal detachment.

(continued from cover)

"We see it more in countries where there's a more formal education system, where young children spend more time doing near work, either on printed material or a screen. Kids who spend more time outdoors seem to develop myopia at a lower rate. It's not just a function of researchers keeping better records, or an increase in screening," said Dr. Douglas Fredrick, Elks of Oregon Pediatric Ophthalmology Professor of Ophthalmology and director of the Elks Children's Eye Clinic at OHSU Casey Eye Institute. "The trend is indisputable."

What's at stake?

Myopia affects a child's academic success. Large studies have shown that children who have myopia, but don't have corrective glasses, fall behind in school, because they can't see the white board or Smart board at the front of a classroom, among other challenges.

The problem goes beyond fitting more children with glasses. Children with higher degrees of myopia are more likely to develop sight-threatening complications later in life like cataracts, glaucoma, macular degeneration and retinal detachment.

"Small or moderate degrees of myopia really don't worry us. The problem is that, of the total number of people who develop myopia, five to 15 percent will become very nearsighted, in the high myopia category. That's a problem when you're looking at millions of people around the world at risk of vision loss," said Fredrick. "If we can do something now to slow myopia development in children, we have the chance to prevent irreversible visual loss down the road," said Fredrick.

Casey researchers pursue solutions

Casey is participating in a national, multi-center clinical trial that involves using a medication called atropine to delay and slow the progression of myopia in children. The medication takes the form of nightly eyedrops. It is widely used to slow myopia in adults, but it's still not clear which dose is effective for slowing the rapid progression in children. The research is in early days, but the preliminary results are promising and further studies will help determine the ideal dose and timing.

Right now, the only FDA-approved treatment for myopia progression is the use of specially-made soft contact lenses. Children as young as six can start wearing them, and research shows they slow myopia's progression. One drawback is that the lenses are costly, and not yet covered by health insurance.

Fredrick predicts that, once FDA approved for children, the atropine eyedrops may be even more effective than contact lenses. While drops are less expenses than contacts, they are not currently covered by health insurance, either.

Early screening is key

Thanks to a grant from the Oregon State Elks Association, the Elks Children's Eye Clinic provides free vision screenings for preschoolers all over the state through its Preschool Vision Screening Program. The program collaborates with Head Start programs and public libraries to prevent vision loss in children by screening over 8,000 kids annually, referring over 700 kids every year to an eye doctor to be checked for a potential vision problem, like myopia.

Educating parents and pediatricians

Now that the research connecting myopia to time indoors and near work has become so clear, Casey clinicians are talking to parents and pediatricians about the importance of spending time outdoors. "That could end up being the most important prevention measure we have," said Fredrick.

Casey researchers bring new insights, new options for age-related macular degeneration

One hundred years ago, average life expectancy in the U.S. was about 60, and the most common cause of vision loss was cataracts. No one was particularly worried about losing their sight from age-related macular degeneration (AMD), which tends to manifest itself in people over 50. Now that average life expectancy is roughly 76 and rising, it's more common for people to lose vision from AMD—and potentially live for 20 or more years. This phenomenon is not confined to the U.S. As the world population ages, and life-expectancy increases, AMD is expected to become even more common, with the number of estimated cases worldwide predicted to reach 288 million by 2040.

"That's why it's so important to improve early detection and develop new treatments," said Dr. David Wilson, Paul H. Casey chair and director of Casey Eye Institute. "People are living with poor vision for many years, and it makes a big impact on their quality of life."

Casey has been at the forefront of AMD research and care for decades, creating increasingly better tools to diagnose and treat AMD. The new Wold Family Macular Degeneration Center is a central hub for the many research and clinical care efforts already underway, and a catalyst for further discovery and innovation by having research, clinical care and clinical trials all in one place. Indeed, Casey is involved in more macular degeneration clinical trials than almost anywhere in the world.

What we do and don't know about AMD

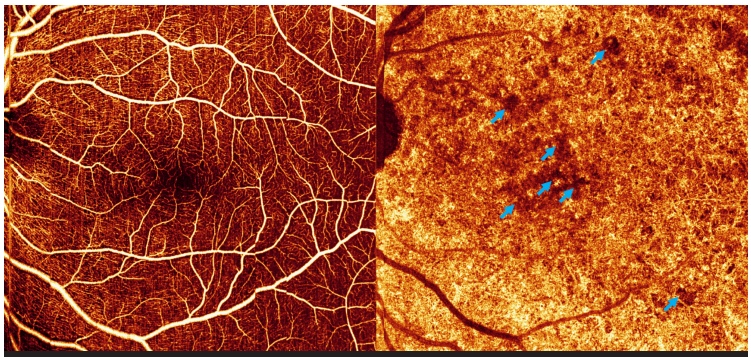
There are two kinds of AMD. Wet AMD is less common but a more immediate threat to vision. It's caused by the growth of abnormal blood vessels in the retina. The other, called dry AMD, develops when the cells in the retina start to atrophy. Dry AMD is more common and progresses more slowly.

There are effective treatments for wet AMD, but there is still no way to stop vision loss caused by dry AMD.

"We don't have a complete understanding of what causes AMD, but we do know some of the molecular mechanisms associated with disease progression. For wet AMD, a key molecule called vascular endothelial growth factor was identified and an effective treatment was developed by blocking its action. For dry AMD, we don't have the key to treatment yet, but an active search is underway," said David Huang, M.D., Ph.D., Peterson Professor of Ophthalmology and Professor of Biomedical Engineering and Associate Director of Casey Eye Institute.

Less time in the clinic for wet AMD patients

The Wold Family Macular Degeneration Center was a crucial clinical trial site for two promising treatments for wet AMD that gained FDA approval in the last year. As with all newly FDA-approved treatments, Casey will wait at least six months before offering the new treatments to patients.



A state-of-the-art imaging prototype using optical coherence tomography angiography reveals normal retinal capillaries and choriocapillaris defect (blue arrows) in an eye with dry AMD. The unprecedented capillary details captured with this imaging technology will be very useful to discover the role of choriocapillaris in AMD.

One treatment, now known as Suvismo™ (ranibizumab), takes the form of a permanent, **reusable drug reservoir** that allows wet AMD patients to forego monthly eye injections. The second, Vabysmo® (farcimab-svoa), is an **antibody drug** administered every four weeks for the first four doses, after which patients can potentially scale back to twice a year.

Both treatments have the potential to not only slow the progression of wet AMD, but to also improve patients' quality of life.

New hope for dry AMD patients

Historically, advanced dry AMD has been harder to treat than wet AMD, but new research could change that. One of the current clinical trials at the Wold Family Macular Degeneration Center is the Gallego study, which is testing a promising **new drug** designed to preserve retinal integrity and slow disease progression.

Another investigational treatment builds on Casey's experience as a national leader in gene therapy for retinal diseases. Casey is one of the sites conducting an international **gene therapy** study involving surgical treatment for dry AMD. The study entails a procedure in which surgeons replace or augment a gene associated with dry AMD.

Casey researchers bring new insights, new options for age-related macular degeneration *(cont.)*

In patients with AMD, the cells in the retina start to degenerate and disappear. A research team at Casey is exploring **cell-based therapy** to restore function, by transplanting cells back into the retina. The research is still in its early stages, but there is reason to be optimistic about this cutting-edge treatment.

Advanced imaging improves diagnosis and treatment

Long heralded as leaders in ophthalmic imaging, Casey is constantly improving its ability to visualize and track changes in areas of the eye affected by AMD. Today's primary tools for detecting AMD are optical coherence tomography (OCT) and OCT angiography, areas where Casey researchers are at the forefront of innovation.

"With OCT angiography, we can detect the onset and progression of wet AMD before fluid leakage occurs. For dry AMD we can visualize the degeneration of the layers in the retina, before vision is affected," said Dr. Huang. "Detecting changes in these layers is key to early diagnosis as well as assessing the effectiveness of potential new drugs to treat dry AMD."

Slow and steady progress

Progress can be slow and painstaking, but today's AMD patients have much better options than they did only 20 years ago.

"I have patients who were in the original studies when I started here, close to 20 years ago, who are still able to see. So that's amazing progress. We have treatment options now that mean people don't have to worry about going completely blind, at least with the wet form of AMD. As long as they can get the injections and can come in, they are often able to maintain their vision, which is amazing," said Christina Flaxel, M.D., Bula Buck Arveson and Charles C. Arveson Professor of Macular Degeneration Research and director of the Wold Family Macular Degeneration Center.

This holds true for dozens of other eye conditions, and underlines the importance of basic science and clinical trials. One small research breakthrough leads to another and, eventually, a meaningful new option for patients.

A personal commitment

Philanthropist John Wold developed macular degeneration in his early 80s and lived with declining vision until his death at 100. "He had two decades in which his independence was quite limited. He knew first-hand how serious AMD could be," said Dr. Wilson. "His generosity, and that of The Wold Foundation, established the Wold Family Macular Degeneration Center that is making it possible for us to speed progress toward a cure."

Innovative diagnostic test catches rare eye cancers

The COVID pandemic, has posed particular challenges for research activities at Casey, and all of OHSU. Modified operations meant that on-site laboratory activities needed to be limited to the bare essentials. However, one laboratory at the Lanfrom Biomedical Research Building remained in operation without interruption, as it provides essential test results for patients around the world.

That laboratory is the Casey Eye Institute Ocular Immunology Laboratory, operated by Grazyna Adamus, Ph.D. For the past two decades, this CLIA certified laboratory has provided test results for specimens from around the world to support the diagnosis of cancer associated retinopathy (CAR), melanoma associated retinopathy (MAR) and autoimmune retinopathy (AR). These uncommon diseases are very challenging to diagnose, and Dr. Adamus' laboratory is in demand as the only location in the world offering a special antibody test that allows doctors to identify the cause for vision loss and to begin the search for the undiagnosed cancer.

Keen observation lead to problem solving

Dr. Adamus' career is a beautiful demonstration of basic science research leading to critical and ongoing improvements in medicine. Trained as a basic scientist working in the special area of immune responses in the eye, Dr. Adamus observed that various circulating antibodies can be the cause of severe vision loss. Many times, these antibodies develop in patients with an isolated and undiagnosed cancer and lead to the autoimmune destruction of retinal cells essential for vision. She then developed the antibody test that is now used exclusively in the Ocular Immunology Lab to diagnose these rare conditions and potentially save a patient's vision.

With specimens now flooding into Dr. Adamus' laboratory, she continues to demonstrate enormous commitment in providing this diagnostic test for patients, even through a pandemic.

Christina Flaxel, M.D.

FACULTY SPOTLIGHT

Dr. Julie Falardeau, Thelma and Gilbert Schnitzer Professor of Ophthalmology at the OHSU School of Medicine, Casey Eye Institute

Neuro ophthalmologist Dr. Julie Falardeau considers herself a bit of a detective.

"Patients will come in with symptoms, like vision loss or double vision, and the eye exam does not always give us answers. But, in the vast majority of these cases, a thorough history will lead us on the right path to arrive at a diagnosis. Sometimes it is a piece of information the patient thought insignificant or unrelated, and only provided the critical clue when asked. We're trying to put all the pieces together. Is it the brain? Is it a nerve problem? Or is it a problem with another part of the eye? It can be time-consuming but I find that extremely stimulating," said Dr. Falardeau.

Dr. Falardeau has been seeing patients and conducting research in neuro-ophthalmology at Casey since 2005. As the only full-time neuro-ophthalmologist in the state, she is in high demand and sees patients from across the region.

Falardeau is an active and sought-after clinical researcher, participating in a range of research projects that include specialists from across OHSU — and the world. For example, she's collaborating closely with colleagues from OHSU's multiple sclerosis clinic to explore novel treatments for optic neuritis, a condition that sometimes arises in MS patients and causes vision loss. She is also part of a multi-disciplinary team testing new approaches to treating idiopathic intracranial hypertension, a condition associated with elevated intracranial pressure that creates swelling of both optic nerves, putting patients at risk of permanent vision loss.

And sometimes there is no solution, only hard news. "I see a lot of patients who have conditions for which there's no treatment – such as vision loss after a stroke. Quite often they have been given that diagnosis already by their local eye care provider, but they come to me to confirm it. One of the most important roles I play is to take extra time to explain what happened and what needs to be done to reduce the risk of a similar event down the road and to maximize their overall health. Understandably, patients are often disappointed to hear that nothing can be done to improve their vision. However, they are very appreciative of the extra time we spent with them and despite the hard news, the interaction ends up being positive and rewarding," said Falardeau.

In addition, Dr. Falardeau has demonstrated a tremendous commitment to the profession of ophthalmology. For over a decade she has volunteered her time as an examiner for the American Board of Ophthalmology. Her dedication to Board activities recently led her to be selected to serve as a Director on the American Board of Ophthalmology. Selection for this important role is extraordinary and reflects the high esteem with which she is viewed by ophthalmologists across the nation.

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