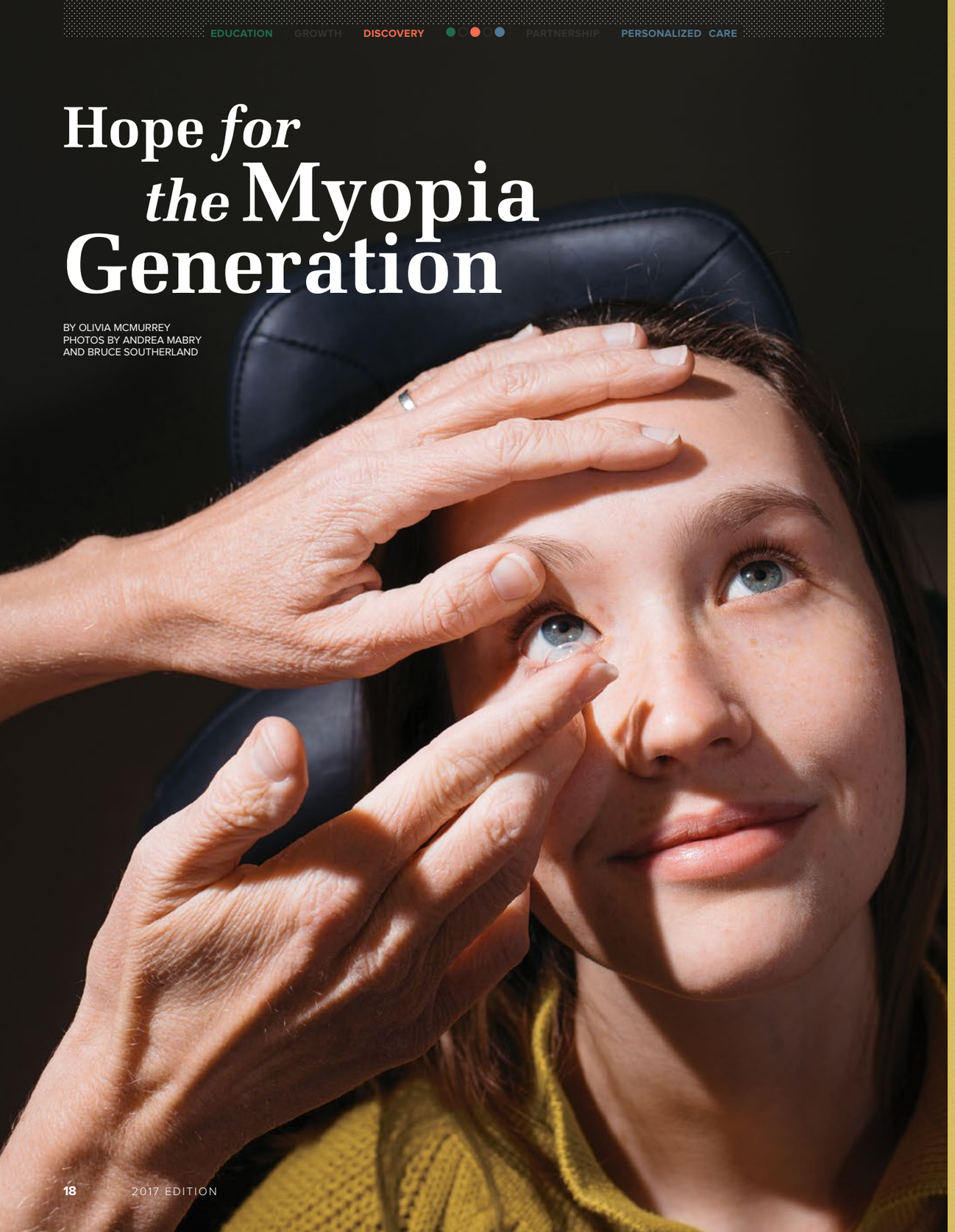
Hope *for the* Myopia Generation

BY OLIVIA MCMURREY
PHOTOS BY ANDREA MABRY AND BRUCE SOUTHERLAND



Pioneering research at the UAB School of Optometry leads to opening of the Myopia Control Clinic and helps fight impending public-health crisis

In Elena Chesnokova's fourth grade music class, the teacher often wrote song lyrics on the board for children to sing. One day the lyrics were too blurry for Elena to read. After a couple classes spent squinting at the board and worrying her teacher would notice she wasn't singing, Elena told her parents about the problem, and her father brought her to a UAB School of Optometry clinic, where she was diagnosed with myopia, or nearsightedness.

Elena is part of the "myopia generation," which has been described as a public-health time bomb. Myopia in American children increased approximately 66 percent between the 1970s and early 2000s, when 33 percent were found to be myopic.

In Asia, myopia has risen to epidemic levels, with 80 to 90 percent of children in some countries requiring vision correction. Once a child is diagnosed with myopia, his or her vision is likely to worsen at a steady rate for about nine years. Because people with myopia have higher risks for glaucoma, cataracts and retinal detachment, these children—and health-care systems around the world—will face additional challenges as they age. Refractive (Lasik) surgery, a procedure for adults, can correct vision, but does not reduce risks for potentially blinding eye diseases.

Unlike most kids with myopia, Elena isn't waiting for her myopia progression to stop with her growth. She began myopia-control treatment offered through the School of Optometry a couple years after her diagnosis.

"I'm caring for my eyes and my vision," says Elena, now 16 and an aspiring physician. "I think there is potential in myopia control, and I sure hope it helps me out. I'm glad I'm a part of it."

With the May 2017 opening of the Myopia Control Clinic at UAB Eye Care, operated by the School of Optometry, more Birmingham-area children like Elena now have the opportunity to try myopia-control treatments. While research has shown three methods—multifocal contact lenses, orthokeratology lenses and low-concentration atropine drops—can slow myopia progression by

◀ LEFT: ELENA CHESNOKOVA, 16, IS A PATIENT AT UAB EYE CARE'S MYOPIA CONTROL CLINIC. THE CLINIC OPENED IN MAY 2017 AND PROVIDES ITS PATIENTS WITH THREE METHODS OF CONTROL TREATMENT: MULTIFOCAL CONTACT LENSES, ORTHOKERATOLOGY CONTACT LENSES AND LOW-CONCENTRATION ATROPINE DROPS.





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ABOVE: A COUPLE OF YEARS AFTER ELENA WAS DIAGNOSED WITH MYOPIA, SHE BEGAN USING MULTIFOCAL CONTACT LENSES TO CONTROL ITS PROGRESSION. HER EYE CARE NOW INCLUDES ROUTINE EXAMINATIONS THAT MONITOR THE GROWTH OF HER MYOPIA AND THE EFFECTIVENESS OF THE LENSES.

50 to 60 percent, very few clinics offer them.

"We're trying to lead the way in helping general physicians, eye doctors and families understand that we may be able to decrease one's final amount of nearsightedness," says Andrew Pucker, OD, PhD, who directs the Myopia Control Clinic and is an assistant professor of optometry and vision science. "There's a big need to get the word out." Pucker has begun giving public lectures on the topic, including one at the Global Specialty Lens Symposium in Las Vegas in January 2018.

The Myopia Control Clinic also shows fourth-year optometry students how they can incorporate myopia control into their practices and gives them necessary training.

Decades of research, in both animals and humans, at the School of Optometry contributed significantly to myopia-control development and led to the opening of the clinic. With many questions about myopia still unanswered, researchers continue seeking knowledge that could lead to prevention and better control of myopia progression.

VIP service at the Myopia Control Clinic

The Myopia Control Clinic is held twice a month, and optometrists in UAB Eye Care's pediatric clinic as well as clinicians across the community can refer patients.

While myopia control is not new at UAB Eye Care—clinicians have been discussing it with patients and parents since the 1990s—the dedicated clinic time makes more individualized care possible. "It provides those most interested with VIP service," says Katherine Weise, OD, MBA, professor of optometry, who helped develop the Myopia Control Clinic and is director of UAB Eye Care's Pediatric Optometry Service. "Fewer patients are scheduled, so we can spend more time with each."

Pucker and a team of students talk with parents and patients about why controlling myopia is important, perform tests to measure eye length and determine which control method or methods would be best for each child and then discuss options. Pucker also created a consent form that explains myopia and myopia-control goals and provides information about each control method.

"One of the biggest things I've realized is how much patient education is required," says Jonathan Davis, a fourth-year optometry student. "You really have to start at a very high-level view of what myopia or nearsightedness is, and then talk about how it progresses and the risks associated with that. And then you can discuss myopia-control options."

Treatments offered at the clinic are:

- Multifocal contact lenses, which studies show reduce myopia progression approximately 50 percent by improving image focus in the retinal periphery.
- Orthokeratology contact lenses, hard contact lenses typically worn at night that reshape the cornea, allowing a person to see clearly during the day without glasses or contact lenses. Research has shown orthokeratology contact lenses also slow myopia progression an average of 50 percent by improving peripheral retinal-image focus.
- Low-concentration atropine (0.01 percent), which studies have shown reduces myopia progression an average of 60 percent. Full-strength atropine (1 percent) is an eye drop that typically dilates the pupil, causing light sensitivity and blurring near vision. At 0.01 percent concentration, however, pupil size does not increase and near vision is not dramatically affected.

Patients are encouraged to return to the clinic every six months for treatment evaluation. "Close monitoring of the success of these treatments is important," Pucker says. "We've developed a patient-recall system to make sure we're contacting them when we need to and checking up to make sure they're happy with their treatment."

All this could help with patient adherence, he says. "If you're coming to this clinic specifically to slow eye growth, you're more likely to follow the treatment," he says.

Student education was another driving force in the decision to open the Myopia Control Clinic. It is one of several clinics at UAB Eye Care that expose students to specialty areas and current hot topics in the field.

In groups of three or four, students attend the Myopia Control Clinic four times over half a semester. Pucker gives a one-hour lecture before each clinic, then students spend the next two to three hours working with patients. "They're getting education beyond what they would get in class—more clinically oriented education," he says.

Davis says he had considered offering myopia-control treatments in his practice, but thought he would need additional training to become proficient. "I assumed I would cross that bridge when I got out there in my practice and decided to begin treatment," he says. "But I feel like this course has caused that not to be necessary. I definitely have enough experience and knowledge now to be comfortable at least getting it started in my clinic."

Emma Wilhite Scott, another fourth-year optometry student, says she learned an easier method of

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ABOVE: ELENA IS EXAMINED BY HER OPTOMETRIST, KATHERINE WEISE, OD, MBA, PROFESSOR OF OPTOMETRY AND DIRECTOR OF UAB EYE CARE'S PEDIATRIC OPTOMETRY SERVICE. WEISE HELPED DEVELOP THE MYOPIA CONTROL CLINIC AND HAS PLAYED AN INTEGRAL ROLE IN RESEARCH OF MYOPIA CONTROL METHODS.

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FROM TOP, TIMOTHY GAWNE, PHD, ASSOCIATE PROFESSOR OF VISION SCIENCE, AND THOMAS NORTON, PHD, PROFESSOR EMERITUS OF VISION SCIENCE

fitting orthokeratology lenses. She plans to offer her patients myopia-control treatments as well. "They should always be given all the options," she says.

Past research: Laying the foundation

In the late 1950s, when he was at the University of California, Berkeley, Henry B. Peters, founding dean of the School of Optometry, led the Orinda study, pioneering research exploring myopia prevalence and progression in children. At UAB, he strongly advocated for both basic and clinical research as a basis for developing treatments, says Thomas Norton, PhD, an emeritus professor who joined the School of Optometry faculty in 1978.

Norton says Peters encouraged him to apply for grants for animal research because he understood animal models were important. "Animal models have driven the idea that you could control myopia," Norton says. "Many people thought it was only genetic."

Wendy Marsh-Tootle, OD, MS, who served as director of UAB Eye Care's Pediatric Optometry Service from 1994 to 2004, recruited clinical faculty and got them involved in myopia-related clinical research through the National Institutes of Health and other funding agencies, Norton says. "We have a strong pedigree in the nearsighted world here at UAB," says Weise, who filled Marsh-Tootle's position after her retirement.

Early animal studies

Animal models were—and still are—essential for myopia-control research because it's the only way to get data fast enough, says Tim Gawne, PhD, associate professor of vision science. He says that human trials are great, but ideally, kids would be followed up to at least age 16 because nearsightedness tends to grow between the ages of 7 and 16.

"You just couldn't do many different human trials in a lifetime," he continues. "Whereas with an animal that develops quickly, like a chick or a tree shrew, in a year you could test a dozen different combinations of things to see what their effects are."

Myopia-related animal research at the School of Optometry began in the early 1980s, and most of it has been conducted with tree shrews, squirrel-like mammals that were once classified as primates. Unlike monkeys, they mature quickly, so studies in the juvenile phase—when eye growth occurs—can be completed fairly rapidly. "The tree shrew has a lot of advantages that no other current, commonly used model has," Gawne says. "They are the closest non-primate species to a primate. They're diurnal, like humans, and they have good vision—20 times better than a mouse."

When Norton left Duke University for UAB, he drove from North Carolina to Birmingham with about 20 tree shrews in the back of his car. The 100 animals in UAB's current tree shrew core—one of only three tree shrew research colonies in the United States—descended from those animals. Norton had discovered, by accident, in 1976 that myopia could be induced in tree shrews. He was doing unrelated neuroscience research that involved raising animals with one eyelid closed. The closed eye elongated, resulting in nearsightedness.

"Having realized we can cause the eyes to get long, then that becomes a test bed for, how can you stop it?" Norton says.

As humans and other animals are growing, the normal eye uses signs of defocus to adjust its length to its optics, keeping vision accurate. Early animal studies demonstrated this active emmetropization process. When researchers put a minus lens on an animal, the eye would adapt to achieve good focus with the lens in place. When they removed the lens, the myopic eye would recover by slowing its growth.

In human myopia, the eye responds inappropriately to defocus, growing longer when growth should be slowed. Traditional glasses and contact lenses correct focus on the fovea, sharpening central vision, but fail to correct blur on other parts of the retina, in fact worsening defocus in the visual periphery. Animal studies showed correcting the refractive error in the periphery can slow down myopia, Norton says.

Milestones in human research

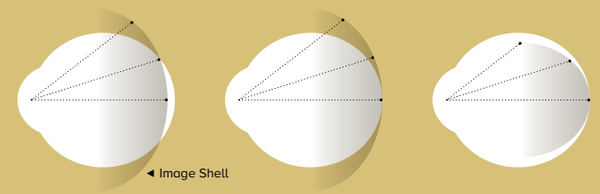
This animal science at the School of Optometry laid the groundwork for two large, NIH-funded studies of children at UAB and other sites across the country: the Collaborative Longitudinal Evaluation of Ethnicity in Refractive Error (CLEERE) study, which involved 4,927 kids and took place from 1989 to 2009, and the Correction of Myopia Evaluation Trial (COMET), which included 469 children and lasted from 1996 to 2015.

These studies provided much-needed basic information about myopia development—for instance, nearsightedness grows at an average rate of about 0.50 diopters per year for about nine years and stops by age 18 for about 75 percent of children. In addition, the COMET study proved that correcting defocus on the peripheral retina could slow myopia development in children as it had in animals. "We came up with the idea for the COMET study and put it together with three other schools of optometry," Norton says.

Kids ages 6 to 12 were recruited in Birmingham, Philadelphia, Boston and Houston, and half were given regular glasses while the other half were given glasses with progressive-addition lenses that regionally improved peripheral focus. After five years, myopia had slowed 20 percent in kids with the progressive-addition lenses compared to the control group.

"It was definitely a cornerstone study for optometry, and UAB was leading the way," Weise says. "We laid the groundwork for a lot of future nearsightedness studies. We showed proof of concept for using multifocal contact lenses to slow down nearsightedness."

How does overnight corneal reshaping help slow myopia progression?



Traditional glasses and contact lenses correct focus on the fovea but fail to correct blur on other parts of the retina. Orthokeratology contact lenses—hard contact lenses worn at night—reshape the cornea, allowing a person to see clearly without glasses or contact lenses. In addition to correcting focus on the fovea, the lenses correct the refractive error in the periphery, which can slow myopia progression.

Adapted from: Lipson, Michael. "Overnight Corneal Reshaping in 2014 and Beyond." *Contact Lens Spectrum,* Volume: 29, Issue: May 2014.

Myopic mystery: why is nearsightedness increasing?

Based on current trends, half the world's population—5 billion people—are likely to be myopic by 2050 and approximately 1 billion will fall into the high myopia category, according to researchers at the Brien Holden Vision Institute. Why is myopia advancing at such a shocking pace? It depends on who you ask, says Katherine Weise, OD, MBA, professor of optometry and director of UAB Eye Care's Pediatric Optometry Service.





Research has provided a few agreed-upon facts:

- Genetics plays a role. A child with no myopic parent has a 10-percent chance of developing myopia; a child with one myopic parent has a 25-percent risk; and a child with two myopic parents has a 50-percent risk.
- Higher education levels are linked to an increased risk for myopia.
- More time spent outdoors correlates with decreased risk of becoming myopic.

Beyond this, theories abound. Here are some:

- Near work: For a long time, near work was thought to contribute to myopia, with use of electronic devices perhaps accounting for accelerated prevalence in the past few decades. But recent studies show near work alone isn't likely the issue.
- Looking at shorter distances indoors compared to the distances seen outdoors.
- Less vitamin D or ultraviolet light as a result of more time spent indoors.
- Less intense light indoors: "Light outdoors is orders of magnitude brighter than it is inside," says Tim Gawne, PhD, associate professor of vision science. Even on a cloudy day, light outside can be 25,000 to 35,000 lux vs. 500 lux inside.
- Less dopamine because of less time spent outdoors: More light could cause an upregulation of dopamine receptors, and retinal dopamine is thought to reduce myopia.
- Artificial light indoors and from electronic devices: Natural light has a broad, smooth spectrum, but artificial light spectra are choppy and spiky, Gawne says. "We might see colors fine, but the emmetropization system might not get it," he says. ■

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> Katherine Weise, OD, MBA, professor of optometry

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RIGHT: ANDREW PUCKER, OD, PHD, MEASURES THE CORNEAL SURFACE OF A YOUNG PATIENT IN UAB EYE CARE'S MYOPIA CONTROL CLINIC. IN ADDITION TO CONDUCTING RESEARCH STUDIES THAT EXAMINE HOW THE CILIARY, OR FOCUSING, MUSCLE IS INVOLVED IN MYOPIA DEVELOPMENT, PUCKER HELPED TO JUMP-START AND NOW DIRECTS THE MYOPIA CONTROL CLINIC.

Multifocal contact lenses are better than glasses at controlling myopia because they improve focus in more of the visual periphery. The use of orthokeratology lenses in myopia control also stemmed from COMET research because flattening the cornea improves peripheral focus as well.

Weise and the School of Optometry are playing an integral role in another large NIH-funded study that began in January 2018. Weise is the protocol development chair for the Myopia Treatment Study 1, through the Pediatric Eye Disease Investigator Group, a consortium of 300 pediatric optometrists and ophthalmologists dedicated to facilitating multicenter clinical research in eye disorders affecting children. The group chose to investigate nearsightedness and atropine, and the School of Optometry is one of 10 sites selected for the 2.5-year study that will include 200 children.

Past research shows atropine slows myopia in children, but most large studies have been conducted in Asia. The eye drop hasn't been studied in the United States in a concentration with few-to-no side effects.

The study will recruit an ethnically diverse group of children, reflective of the U.S. population, and two-thirds of them will use 0.01 percent atropine while the others use a placebo. "The big hot topic in the United States now is atropine," Weise says. "Part of our question is, in U.S. kids, whether they're Asian or African-American or Hispanic or Caucasian, does atropine slow down the progression of nearsightedness to a meaningful degree?"

Current animal research: clues to a confounding question

It's known that the juvenile retina, without input from the brain, is interpreting the pattern of images throughout the day and trying to guess whether the eye is too long, too short or just right, and adjusting growth accordingly, Gawne says. "We know it's visual," he says. "The secret is what is the retina looking at and what is it getting wrong? And that's the thing that has been surprisingly hard to understand."

Much of current myopia-control research centers on better understanding this system—or finding ways to override it.

Light studies

Most of Gawne's research involves tree shrews and ambient light. One way he's hoping to fool the retina takes advantage of the fact the eye suffers from longitudinal chromatic aberration—meaning it focuses light of different wavelengths at different points. Long-wavelength, red light is focused farther back in the eye than short-wavelength, blue light. Therefore, if the red light were in better focus than blue light, this might signal the eye that it is long enough. "Maybe we could trick the eye," he says, by giving it only red light. "It would say, 'hey, I see sharp red, but nothing blue at all.' Maybe that would tell the eye, 'I need to stop growing.'"

The experiment worked in tree shrews, with even one hour per day of red light having about a 1-diopter effect. In late 2017, he submitted an NIH grant proposal for a large study in tree shrews that could move the therapy closer to human trials. He hopes to evaluate parameters including timing, spectral purity and intensity to arrive at a practical therapy for kids. "Maybe if we could get it down to 15 or 20 minutes of red light, maybe they could read during that time," he says. "We need to flesh it out with animal experiments."

Gawne is already conducting a small-scale study of tree shrews exposed to high-intensity red light—15,000 lux instead of 1,000 lux. Preliminary findings of the study, begun in June 2017, are promising, he says. Red-light studies in monkeys show success as well, he notes.

Another study he began in 2017 involves 7-methylxanthine, a substance similar to caffeine that thickens the posterior sclera and has been shown to slow myopia in monkeys and Danish children. Gawne is testing it in tree shrews in combination with other therapies, including red light.

Recent research also has examined the function of dopamine in relation to myopia. Increased time spent outdoors correlates with a decreased risk of myopia, although why is unclear. More light is thought to cause an upregulation of dopamine receptors, Norton says, and dopamine could help reduce elongation of the eye. A study Alexander Ward, a PhD student at the School of Optometry, Norton and two others published in 2016 showed injecting a dopamine-like substance in tree shrews reduced myopia.

Genetic pathways and the ciliary muscle

Pucker is working on three studies to see how the ciliary, or focusing, muscle is involved in myopia development.

Association studies have shown the ciliary muscle in humans with longer eyes is bigger and doesn't function as well compared to ciliary muscles in normal, emmetropic eyes. In one study, Pucker is inducing myopia in guinea pigs and monitoring effects on their ciliary muscles as well as whether genes are turning on or off in ways that could affect the muscle's growth.

In another study, he's using a device to stretch guinea-pig eyes, simulating exaggerated eye growth, so he can look at mechanically induced genetic pathways. In a third study, which will begin soon, he'll put human ciliary-muscle cells in a dish, stretch them and then compare them to unstretched cells to see what genetic pathways are affected.

"A specific pathway could be upregulated, causing the ciliary muscle to grow bigger and thicker," Pucker says. "A bigger muscle could be restricting equatorially eye growth, which would only allow the eye to grow longer, a disproportionate growth that could be causing nearsightedness. If we understand this mechanism, we could potentially deliver a drug to the front of the eye, where that muscle is located, and potentially stop that muscle restriction from happening, which would allow the eye to grow proportionally and avoid becoming myopic."

Norton says patients at the Myopia Control Clinic will eventually benefit from research currently taking place at the School of Optometry. "As we learn more about how this works, other treatment options are likely to come forward, and I'm sure one of the first places to adopt them—once they've been shown to work in clinical trials—would be the Myopia Control Clinic," he says.

Elena Chesnokova looks forward to that future. "It's really exciting," she says. "I'm glad that we're coming up with new ways to combat myopia. I hope that in the future people won't have to deal with myopia as much." ■



How to talk with patients about myopia (say 'nearsightedness')

The general public doesn't have a good understanding of myopia.

That's the finding of a 2017 public-health survey conducted by Andrew Pucker, OD, PhD, assistant professor of optometry and vision science, and Stephanie Cox, OD, clinical assistant professor of optometry, and they say it has implications for myopia-control treatment.

In the electronic survey of 330 people who had visited UAB Eye Care, only 68 percent could accurately define nearsightedness and myopia. "We found that nearsightedness is more commonly correctly answered than myopia is, so if you're talking to patients, maybe you want to say the word nearsighted," Pucker says. "There were no predictors of who would get it right; not education, age or income."

Clinicians need to explain the basics to improve chances patients will comprehend and follow treatment plans. "If you want to have your patients do your treatments, and do them consistently and correctly, they first need to understand what myopia is," he says. ■