Jing Chen, PhD, of Boston Children’s Hospital, Harvard, is looking for the culprit that causes leaky blood vessels to grow uncontrollably near the retina in wet age-related macular degeneration (AMD), which can lead to vision loss.

She thinks it may stem from signaling by small regulatory RNAs, known as “microRNAs” (miRNAs). RNA (ribonucleic acid) translates our genetic blueprint for our cells to know how to take action. miRNAs are short-term fixes to these gene blueprint translations that either help or harm our bodies as they adjust to changing conditions and stressors.

Stressors that may lead to wet AMD include inflammation, lipid and nutrient imbalances, cumulative environmental wear and tear, and reduced cell maintenance functions due to age and/or lifestyle factors. Dr. Chen believes these conditions may bring about harmful miRNA signaling, which in turn may trigger AMD.

She and her colleagues have identified a strong miRNA candidate for errant blood vessel growth, miR-145. Their experiments showed that in a mouse model of AMD, miR-145 levels more than doubled compared with normal controls. When they injected an miR-145 inhibitor, new blood vessel growth was cut in half. Similarly, human cell cultures showed greatly reduced blood vessel growth once miR-145 was inhibited.

This approach has not yet been through clinical trials, but the results strongly suggest that inhibiting miR-145 could help stop abnormal blood vessel growth in wet AMD. Thanks to findings made possible by her Macular Degeneration Research grant, Dr. Chen has now received funding from the National Eye Institute to carry this promising work forward.
PRESIDENT’S CORNER

I’m excited about the progress we’re making against AMD!

As our cover story shows, a researcher we fund has identified a culprit that may trigger abnormal blood vessel growth in the eye. This important discovery could ultimately save the sight of millions of Americans who are at risk of irreversible vision loss from wet AMD.

I’m also delighted by the symposium that BrightFocus Foundation spearheaded recently at the world’s largest meeting of vision researchers. Scientists discussed research showing how diet, vitamins, and other lifestyle factors can impact the development of AMD. It was the brainchild of BrightFocus Foundation, of which Macular Degeneration Research is a program.

Vitamins

More than 200 scientists heard from experts like Emily Chew, MD, of the National Eye Institute (NEI), who helped lead the landmark Age-Related Eye Disease Studies (AREDS I and II). This led to the AREDS “eye vitamin” regimen for early-to-moderate AMD.

She addressed the interaction between diet and genetics in AMD. Several dozen genes have been linked to an increased risk for AMD. One study assessed AREDS in combination with a modified Mediterranean diet high in vegetables, fruits, and fish, and low in processed meats, alcohol, and saturated fats.

While overall this diet was linked to a lower risk for advanced AMD, results for genetically susceptible individuals weren’t conclusive. Dr. Chew is designing additional NEI research in this area.

Lifestyle

Louis Pasquale, MD, of Harvard, stressed that “genetics is not destiny” in AMD. Although there is a genetic link, he speculates that it could be modified by lifestyle factors—much like obesity, which is linked to genes but can be managed through diet and exercise. Future discoveries may furnish “powerful insights into ophthalmic disease and can lead to cost-effective primary prevention measures,” he said.

Diet

Julie Mares, PhD, of the University of Wisconsin-Madison, has led large, long-term studies assessing the impact of diet on AMD. As she discussed, scientists believe that vitamins C and E, carotenoids like lutein and zeaxanthin, and zinc help protect the retina against oxidative damage from stressors such as lifelong light exposure, changes in energy metabolism, inflammation, and reduced cell waste removal functions.
In a recent BrightFocus Chat, Priyatham Mettu, MD, a retina specialist at Duke University, answered callers’ questions.

**Q:** How can patients make the most out of their doctor’s appointment?

**A:** Many patients are referred to a retina specialist by another doctor. Bring in-hand any records of prior evaluations, imaging, or treatment. That helps the doctor give an informed opinion about what’s best for you.

Also, write down questions in advance so you remember to ask them. If at the end of your visit you didn’t fully understand anything, say, “Here’s what I wasn’t sure about: Could you tell me more about this, could you give me more information about that?” That way, when you leave, you feel comfortable with what you’ve learned.

**Q:** What are long-term side effects of eye injections for wet AMD?

**A:** For most patients, the current anti-vascular endothelial growth factor (anti-VEGF) treatments are safe. All the available data for those who have been treated for 7 to 10 years suggests patients can receive these injections with very few ill side effects.

**Q:** What is the right frequency for shots?

**A:** We typically inject once a month for three months and then re-evaluate. If there’s no sign that the blood vessel is getting bigger or bleeding, we can gradually extend the interval between shots. If not, we have to consider switching to another anti-VEGF treatment or adding other therapies, such as laser treatments.

**Q:** Is there any new research that would eliminate eye injections?

**A:** I think on the horizon there are going to be a host of new treatments around extended-release treatments. Instead of coming once a month, you might come once every six months.

**Q:** How can I take part in a clinical trial?

**A:** Ask your eye doctor what stage of AMD you are in, what you can expect going forward, and if he or she is aware of any clinical trials. Your doctor should be able to highlight potential trials and if you might be a good candidate for them.
LIVING WITH AMD AS A PATIENT OR CAREGIVER

Leona and her daughter, Sharon, were guest speakers at a recent BrightFocus Chat.

When Leona was first diagnosed with AMD, she didn’t notice any difference in her vision. She continued teaching, driving, and living her normal life.

But after retiring, Leona realized she needed more help. She moved closer to her eldest daughter, Sharon.

“It was a while before I realized how important it was to attend doctor appointments with her,” says Sharon. Now she would advise other caregivers to attend every doctor’s visit, take notes, and ask questions that the patient may forget to ask. Also, counseling can help, since there is a risk for depression for the patient as well as the caregiver who is suddenly thrust into a new role.

Unfortunately, when Leona’s AMD changed from dry to wet, she didn’t realize she was having a bleed. “I didn’t get to my eye doctor right away, thinking that the graying of my vision was from cataracts. By the time I got [there], I had lost more vision. Who knows, but it might have been prevented. So, even if you don’t want to be one of those patients who calls with every symptom, I encourage you to be one,” she says.

There have also been positive experiences. Occupational therapists provided Leona with mobility training, helped her learn how to cross the street, and so on. “That was enormously helpful in keeping her independent,” says Sharon. “She can leave her apartment in good weather and walk downtown.”

Leona has also remained independent at home, thanks to technology like magnifiers, computers, reading machines, and labels on appliances.

She appreciates the “little things,” like being able to cook and do laundry. “You just have to be patient,” Leona says. “I can’t do things nearly as quickly as I used to, but to do them at all is still a triumph.”

Register for BrightFocus Chats

Recently diagnosed with AMD? Know someone who has it? Receive helpful information from our FREE monthly phone call with doctors, researchers, or experts in the field on timely topics. You can submit questions before or during the event. Transcripts and audio recordings are available afterward on our website.

To register, call 800-437-2423 or go to brightfocus.org/eyechats.
HOW DO CLINICAL TRIALS WORK?

As part of our ongoing series of articles about clinical trials, we will look at the three phases of clinical trials. Each has a specific purpose in determining the safety and efficacy of a treatment for use by the public.

**Phase 1 Clinical Trials** evaluate the safety of a drug or treatment to determine that it is not harmful to people. This testing normally takes place with a small group of healthy volunteers, and negative effects may lead the Food and Drug Administration (FDA) to discontinue the trial.

**Phase 2 Clinical Trials** test the right dosage and effectiveness in treating a disease. A small group of volunteers who have the disease are assigned to different treatment groups, with each group receiving different doses. The results are then compared to control groups (trial participants who did not receive treatment). If the results show either adverse outcomes or no improvement, the trial can either be suspended or discontinued.

**Phase 3 Clinical Trials** test whether a treatment is safe and effective for a wide variety of people. With a larger number of volunteers, there can be many groups, especially if the treatment involves a combination of drugs or different components. Again, the results are compared to control groups. If the drug works and the trial is successful, the trial sponsor may now apply to the FDA for approval to manufacture and sell these new treatments, making them available to patients.

Today’s clinical trials can lead to better treatments tomorrow. For more information about clinical trials or to find one near you that you may be able to participate in, please visit brightfocus.org/AMDtrials.

This series of articles promoting awareness of clinical trials is supported in part by an educational sponsorship from Biogen. BrightFocus is solely responsible for the content of this article.
People often want to make a philanthropic gift but feel they can’t afford it. Here are two common obstacles we hear… and some solutions.

**Obstacle:** “I have children and grandchildren to worry about. They come first.”

**Solution:** You can support our future work by remembering us in your will or living trust. It’s simple to do and you can change your mind at any time.

**Obstacle:** “I am not rich. There is only so much money to go around.”

**Solution:** Rather than making a gift of cash now, consider the options below, which can offer important tax savings for you and your family.

**Stock.** For gifts of appreciated stock owned longer than one year, you receive an income tax charitable deduction for their full fair market value—not the price you originally paid for them.

**Life insurance.** You can name our organization as the beneficiary of a policy you no longer need.

**Retirement plan assets.** Highly taxed when left to heirs, this makes an excellent charitable gift after your lifetime.

We can help you identify a gift to fit your goals. To learn more, contact Lauren Fields, Manager, Planned Giving, at 855-345-6637 or Lfields@brightfocus.org.

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