Macular Degeneration

Avastin® is another medication that is injected into the vitreous cavity. It blocks all types of VEGF-A and was shown in the CATT study to be generally equal to Lucentis® when injected monthly. You may have heard about this medication because it compares favorably to Lucentis® but is much less expensive. It is only available from compounding pharmacies. Avastin® was initially approved for treatment of metastatic colon cancer. It is not FDA-approved for treatment of AMD but is commonly used.

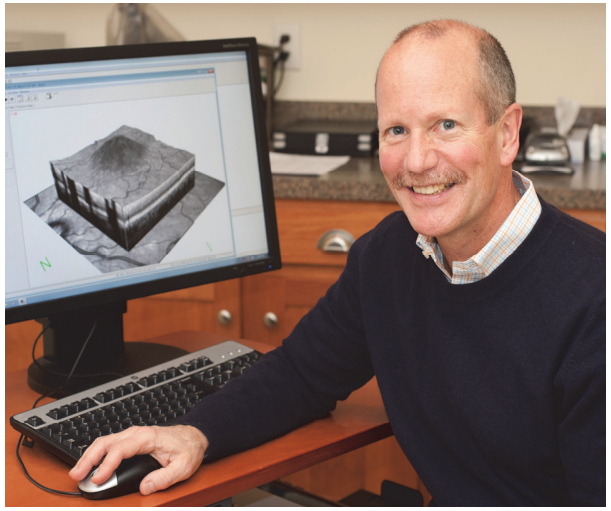
Intravitreal injections carry certain risks. While they are uncommon, the eye may become infected (endophthalmitis) or the retina could tear, leading to retinal detachment.

It is important to understand that most choroidal neovascular membranes reopen. This is the reason that regular examinations in the office with treatment as needed and constant monitoring at home lead to the best outcomes.

In summary, AMD is becoming more common as the population ages. Large epidemiologic studies have documented several risk factors. Caucasians, women, smokers, obese adults, and people with a family history are at the highest risk. **To reduce your risk**:

- **Don't smoke.**
- **Eat a Mediterranean type diet with 'colorful' fruits and vegetables, fish, fowl and limited amounts of red meat or products high in saturated fats or cholesterol.**
- **Maintain ideal weight and exercise regularly.**
- **Eat fish that contain high quantities of omega-3 fatty acids.**
- **Control your blood pressure.**
- **Check central vision in each eye daily, looking for distortion or blind spots.**
- **See your doctor on a regular basis or whenever there is a change in vision.**

Retina & Glaucoma associates



©Lisa W. Cumming Photography

John R. Nordlund, M.D., PhD is a former University of Virginia School of Medicine Faculty Member who has fellowship training in Medical Retina from the Mayo Clinic and Glaucoma from the Johns Hopkins School of Medicine.

Board Certified

Member: American Society of Retinal Specialists

Member: American Glaucoma Society

Member: American Academy of Ophthalmology

Macular Degeneration

Retina & Glaucoma Associates

113-A Bulifants Boulevard
Williamsburg, VA 23188

Phone: (757) 220-3375
Fax: (757) 220-3380

www.rgava.com

Macular Degeneration

Age-related macular degeneration (**AMD**) is a common ocular disease. The retina and the layers beneath it are damaged, making objects appear distorted and blurred. AMD is the leading cause of legal blindness in people ages 50 and older. ***Caucasians, women, smokers, anyone with a positive family history, and obese patients have a higher risk for developing the disease.*** Central vision loss is often seen in patients age 65 and older. AMD is classified as either dry or wet.

Dry AMD is a clinical diagnosis that is made by identifying characteristic changes on a dilated retinal examination. It usually occurs before wet AMD. The earliest signs of dry AMD are found at the junction between the retinal pigment epithelium (**RPE**) and in the part of the choroid called the choriocapillaris. The neurosensory retina, which processes the light signal, rests atop the RPE. The choroid is a blood vessel layer beneath the RPE. The earliest clinical signs of damage are evident where these two layers touch (Bruch's membrane). This is where **drusen** accumulate. Drusen are seen as yellow-white deposits. Their exact composition is unknown, but they have been shown to include debris derived from the RPE, constituents from immune reactions or inflammatory reactions, and other cell components. **Pigment clumping** and **RPE atrophy** are other clinical signs of RPE dysfunction or cell death. The earliest stages of dry AMD are not evident to the patient and can only be found by a dilated retinal examination. Many years may pass before symptoms develop. As AMD progresses, patients may develop blurry vision or waviness in their central vision called **metamorphopsia**. The best way for patients to identify these changes is by examining an **amsler grid** with each eye every day.

Dry AMD cannot be prevented or cured. In some patients the rate of progression can be slowed by the use of antioxidant vitamins and zinc. The **Age-Related Eye Disease Study 2 (AREDS 2)** showed that taking a specific mixture of vitamin C, vitamin E, zinc oxide, perhaps lutein/zeaxanthin and cupric oxide reduced the risk of developing advanced AMD by 25 percent, over a five-year period, in patients who had at least intermediate disease in one eye. Other studies studies suggest that **omega-3 fatty acids (fish oil)** are helpful. See Separate handout for details.

Wet AMD is caused by new blood vessel growth. The new blood vessels either start beneath the retina as a choroidal neovascular membrane (**CNM**) or within the retina as retinal angiomatose proliferation (RAP). **Vascular endothelial growth factor A (VEGF-A)** a local hormone is responsible, in part, for stimulating growth of these new blood vessels (neovascularization). When VEGF binds to the receptors found on the lining of existing blood vessels, it stimulates growth of new blood vessels. This response is helpful in healing but in AMD it makes matters worse, transforming dry AMD into wet AMD. Wet AMD almost always causes visual symptoms. Most patients describe a rapid development of a blind spot (scotoma) or distortion of the central vision (metamorphopsia). The retinal examination may show blood, yellow deposits (exudates), or thickening of retina.

Testing for wet AMD usually consists of fluorescein angiography and Optical Coherence Tomography (OCT). **Fluorescein angiography (FA)** is the gold standard for identifying the presence of new blood vessel growth and for defining its size and type. It consists of injecting a vegetable-based dye (fluorescein) into a vein in the arm and taking pictures of the retina with a camera as the dye passes through the blood vessels. It identifies new blood vessels and other areas where fluid may be leaking from the retina. It is a simple and easy test that is done in the office. Millions of these tests have been done throughout the world with few complications. **OCT** is a newer imaging modality that bounces light off the layers of the retina. The data are used to generate cross sectional images of the macula. These images identify the retinal layers where fluid accumulates and can be compared to assess effectiveness of treatment. FA and OCT along with the clinical examination are used to determine the most effective treatment for that eye.

Treatment for wet AMD has come a long way. Prior to the 1980's, patients were told there was 'nothing we can do'. The untreated eye usually developed a macular scar and did not see well enough to identify the 'big E' on the eye chart. The first major improvement came in 1981 when thermal lasers were used to cauterize the CNM. If the CNM was not beneath the center of vision, most treated eyes retained good sight, at least for a while. However, if the CNM was beneath the center of vision, treatment caused an immediate permanent loss of vision. Even so, treatment of subfoveal CNMs was helpful because it limited the size of the scotoma.

The next major step was the approval by the FDA in 1999 of **Photodynamic Therapy with Visudyne® (PDT)**. Visudyne is a photoactive dye infused through a vein in the arm for ten minutes and then activated five minutes later by a cold laser focused on the CNM. The dye binds preferentially to new blood vessels and when activated by a 'cold' laser it causes a clot to form within the CNM that closes it. Treatment used to be given every 3 months. When used today, PDT is generally given as an adjunct to intravitreal injections.

Lucentis® was the first effective intravitreal medication for treating CNMs. It is a pan-VEGF-A antibody approved by the FDA in July 2006 for treatment of all types of wet AMD. The results from the clinical trials were remarkable. Unlike other treatments, Lucentis prevented moderate vision loss in about 90% of patients treated during a two-year trial period. Nearly 1/3 of patients regained some of their lost vision. The drug is injected into the vitreous cavity as often as every 4 weeks until the vessels close or the retina stabilizes. It is sometimes combined with Photodynamic Therapy with Visudyne® (PDT) or intravitreal steroids. Combination therapy may reduce the number of treatments needed.

The latest FDA approved intravitreal medication is **Eylea®**. Eylea® targets all VEGF-A types, VEGF-B and platelet derived growth factor. It was shown to be equivalent to Lucentis® and has a potential advantage of requiring less frequent injections.