Macular Degeneration

Age-related maculopathy, sometimes called **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. Complications often occur after age 75 years. 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 the choroid. 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 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 abnormal deposits associated with atherosclerosis. 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 (AREDS)** showed that taking beta-carotene, vitamin C, vitamin E, zinc oxide, 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 diseasein one eye.

Wet AMD is caused by new blood vessel growth beneath the retina. Vascular endothelial growth factor A (VEGF-A) is a hormone responsible, in part, for stimulating growth of new blood vessels in the body (neovascularization). When VEGF binds to the receptors found on the lining of existing blood vessels, it can stimulate the growth of new blood vessels from the existing ones. This response can be helpful in healing or it can cause disease.

Wet AMD is caused by abnormal new blood vessel growth within the retina or from the choroid (CNM). It 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 the retina.

Testing for wet AMD usually consists of **fluorescein angiography** and Optical Coherence Tomography (OCT). Fluorescein angiography 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 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. These data are used to generate a color image of the involved area. These two tests 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. In the long run, even 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 photoreative 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 is given every 3 months. In 2004, **Macugen** was the first medication approved for use against all types of wet AMD. It blocks the action of a particular type of VEGF and was injected into the vitreous cavity every six weeks. Since it was not very effective, it is rarely used today. **Avastin** is another medication that is injected into the vitreous cavity. It blocks the action of all types of VEGF and has been shown to be effective in small studies. It was originally approved for treatment of metastatic colon and has not yet been FDA-approved for treatment of AMD. However, it is being used off label because it appears to be similar to Lucentis and is 1/20th the cost. A large trial has been started to compare its effectiveness to Lucentis.

Lucentis is a pan-VEGF blocker that was approved in 2006 by the FDA for treatment of all types of wet AMD. It is the current gold standard for treatment of wet AMD. The results from the clinical trials were remarkable. Unlike other treatments, Lucentis prevented moderate vision loss in about 90% 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 every 4 weeks until the vessels close or the retina stabilizes. It is sometimes combined with other treatments.

In summary, AMD is becoming more common as the population ages. Large epidemiologic studies have documented several risk factors: Caucasian women are at the highest risk and family history is important. To reduce your risk:

- Don't smoke.
- Eat 'colorful' fruits and vegetables.
- Maintain ideal weight and exercise regularly.
- Limit your intake of saturated fats and cholesterol.
- 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.