AGE-RELATED MACULAR DEGENERATION

An introduction to aging science brought to you by the American Federation for Aging Research
WHAT IS AGE-RELATED MACULAR DEGENERATION?

Age-related macular degeneration (AMD) is the leading cause of severe vision loss in people over 60 in the United States. It affects an estimated 15 million Americans. The retina at the back of the eye receives light rays that have passed through the lens of the eye. The retina's millions of cells then translate those light rays into electrical signals that it sends to the brain through the optic nerve. The macula is near the center of the retina and is the site of our most acute visual perception. It is used when we drive, see faces, read, and do fine detail work.

AMD is associated with aging. It is present in about equal numbers in men and women; whites are more affected than blacks. Smoking and genetic background have been identified as risk factors in the development of macular degeneration.

Two major forms of AMD have been defined. They are the atrophic or “dry” form and the exudative or “wet” form.

Dry macular degeneration
Between 85 and 90 percent of the cases of macular degeneration diagnosed are of the dry type, which progresses slowly. Small yellow deposits of a material called drusen form under the macula. These deposits may interfere with vision. Patches of retina cells may thin out and die off leading to macular atrophy. Dry macular degeneration can sometimes deteriorate into the wet form.

Blurred vision is the most frequent early symptom of the disease, especially blurriness that goes away in bright light. As an individual's light sensing cells begin to degenerate further, however, a small—but growing—blind spot may appear in the center of his or her visual field.

Wet macular degeneration
Only 10 to 15 percent of cases of macular degeneration are of the wet or exudative type. In this form, abnormal blood vessels grow under the macula in a process called retinal or choroidal neovascularization. These abnormal vessels can bleed (sub-retinal hemorrhage) or leak fluid under the retina. This can leave scars. The wet form accounts for 90 percent of severe visual loss and tends to progress rapidly.

Straight lines appearing crooked are often an early sign of wet macular degeneration. The distortion results when leaked fluid under the retina actually lifts the macula. You may also see a small blind spot in the center of your vision, which will worsen over time.

RISK FACTORS

A number of factors can increase your risk for macular degeneration. These include:

- **Increasing age.** Age is the most important risk factor for macular degeneration. AMD is the most common cause of severe vision loss in adults over the age of 60, affecting an estimated 10 to 15 million Americans. With the aging of the population, ophthalmologists predict that it will become an enormous public health problem in the decades to come.

- **Smoking.** Smoking tobacco products increases your risk for AMD two to five times.
The reason? The retina uses a lot of oxygen, but smoking restricts the amount of oxygen that can reach it through the blood vessels. Smoking also causes oxidative (free radical) damage to the eye. The French Pathologies Oculaires Liees a l’Age (POLA) study looked at over 2,000 subjects who lived on the French Mediterranean. The study found that both current and former smokers had the highest risk for developing macular degeneration and that the risk of late-onset age-related macular degeneration remained elevated until 20 years after smokers had quit their habit. A new study, published in the British Journal of Ophthalmology, provides additional evidence that smoking is a leading risk factor of macular degeneration. By combining detailed eye tests with questions about smoking habits, the British research team found that smoking may account for almost 30,000 cases in the UK.

• **Family history.** If an immediate relative of yours has wet AMD, you’re twice as likely as someone with no comparable family history to develop it. Having two family members with wet AMD boosts your risk fourfold. But many patients no longer have to rely on family history alone to assess the likelihood of their developing the disease. RetnaGene AMD is a genetic screening test that can help you make that assessment. It is currently available in many clinics for use with patients over age 60. The test requires either taking a blood sample or swabbing the inside of your cheek, then sending the sample to a lab for analysis. The results will let you know if you should be more vigilant about screening for the onset of AMD, in order to diagnose and treat it before you lose a significant amount of vision.

• **Sex.** Females are slightly more likely to develop AMD than males, but this may be because women live longer than men and thus offer a bigger window for the disease to establish itself.

• **Race.** Whites are more likely than other racial groups to develop AMD. The reasons are unclear.

• **Sun exposure.** Researchers at the University of Wisconsin Medical School, Madison, examined the association between sunlight exposure and sunlight sensitivity and the ten-year incidence of age-related macular degeneration among people aged 43 to 86 years. The study found that people who stay outdoors in the summer sun for more than five hours a day in both their teens and 30s have a twofold greater likelihood of developing early macular degeneration changes (soft drusen or increased retinal pigment), but other studies have not confirmed a strong association between sunlight and AMD. In individuals who have high sun exposure, the

The likelihood of developing early macular degeneration may be reduced by wearing hats or sunglasses.
likelihood of developing early macular degeneration may be reduced by wearing hats or sunglasses at least half of the time when outside in the summer sun.

- **Poor diet.** A diet too high in fat or too low in healthful vegetables has been associated with AMD.

- **High cholesterol or high blood pressure.** A study published in the Archives of Ophthalmology in March of 2000 that looked at 600 patients in the metropolitan New York area found that neovascular (wet) macular degeneration was associated with a history of high blood pressure, and with elevated cholesterol levels. Dry macular degeneration was not related to either high blood pressure or high cholesterol.

- **Obesity.** People with a body mass index (BMI), a measurement of body fat, over 30 increase their risk for AMD by two-and-a-half times. You can calculate your BMI [here](#).

- **Eye color.** People who have light colored eyes are at greater risk for AMD, possibly because lighter pigmentation doesn’t shield against UV light as efficiently as darker pigmentation does.

- **AMD in one eye.** Having AMD in one eye increases your likelihood of developing it in the other one.

### DIAGNOSING AGE-RELATED MACULAR DEGENERATION

While the symptoms of AMD suggest a diagnosis, the disease’s presence must be positively confirmed by tests. An ophthalmologist will examine your dilated eyes to look for visible damage to the macula. Vision can also be tested by looking at an Amsler grid—bisecting lines that look like a section of graph paper—and describing how its lines appear to you. If you have macular degeneration, you may see wavy lines, distortions, and blank spaces on the grid.

A test called fluorescein angiography can also be done. A dye, fluorescein, is injected into a vein in the arm. As it passes through the vessels of the eye, photographs of the retinal structures can be taken. Signs of damage from AMD such as new blood vessels or patches of atrophy, indicative of the disease, can sometimes be seen in this way.

Finally, a new test called Ocular Coherence Tomography (OCT) may be used to take cross-sectional images of your retina. During the exam, an optical scan of the retina’s surface is performed and renders images of its layers. OCT takes just a few minutes and is completely painless. Nothing touches the eye. The procedure produces very high quality, detail-rich images that are extremely helpful in diagnosing and managing not only AMD, but other diseases of the eye as well. These
include glaucoma, diabetic retinopathy, and many others.

**TREATMENTS FOR MACULAR DEGENERATION**

At this time, there is no cure for macular degeneration. There are, however, treatments available that can help slow the progression of the disease. How well it can be stopped depends on the location and the extent of the abnormal blood vessels. In most cases, the damage already caused by macular degeneration can't be reversed, making early detection critical.

Treatments for wet macular degeneration include:

**Laser photocoagulation**
The wet form can be treated with laser photocoagulation, which uses a high-energy laser beam to seal off the leaking blood vessels. Unfortunately, this treatment is not effective for everyone. It can slow the rate at which vision is lost, but it cannot prevent a recurrence.

**Surgical treatments**
Very new surgical treatments to relocate retinal tissue away from the areas of damage are showing some promise. These are used only in extreme cases of bleeding under the retina. One procedure, still in the experimental phase, inserts tiny prostheses into the retina. These can stimulate the brain into producing visual images, taking over the function of the damaged eye tissue.

**Nutritional treatments**
In 2001, the National Eye Institute’s (NEI’s) Age-Related Eye Disease Study (AREDS) found that taking high doses of particular vitamins and minerals could help prevent individuals with intermediate dry AMD from progressing to advanced or wet AMD. The formula contained 500 milligrams of vitamin C, 400 international units of vitamin E, 15 milligrams of beta-carotene, 80 milligrams of zinc as zinc oxide, and two milligrams of copper as cupric oxide. The supplements offered no benefit to people with early-stage AMD. Researchers believe that AREDS formula works by providing antioxidants that help maintain healthy cells and tissues. Select patients who have intermediate AMD in both eyes or advanced AMD in one eye can receive the formula. The preventative benefits are modest.

The NEI is now conducting AREDS2 clinical trials, which are evaluating the benefits of adding lutein, zeaxanthin, and omega-3 fatty acids (DHA and EPA) to the original AREDS formula. The estimated AREDS2 completion date is December 2012, but researchers will follow up for at least five years.

**Anti-VEGF treatments**
Vascular endothelial growth factor (VEGF) is a protein that cells secrete to stimulate the creation of new blood vessels. Too much VEGF can contribute to disease, including blood vessel disease in the eyes. Treatment to inhibit the over expression of VEGF is now becoming the mainstay of treatment for wet macular degeneration. There are currently two FDA approved drugs, ranibizumab (Lucentis) and aflibercept (Eylea), that do this. Both are administered into the eye monthly or bi-monthly in an ophthalmologist’s office. Although these drugs don’t work to the same degree for everyone, a computer model study published in the June 2011 issue of Archives of Ophthalmology suggested that

A study by the National Eye Institute found that high doses of particular vitamins and minerals were helpful in some individuals.
monthly ranibizumab usage would reduce the incidence of visual impairment among people with wet AMD in two years by 37 percent. Early clinical tests of ranibizumab and aflibercept showed that well over 90 percent of patients treated with either drug maintained or improved their vision over the year-long course of the trial.

THE FUTURE OF MACULAR DEGENERATION RESEARCH

Some of the areas of research into macular degeneration that show promise for the future include the exploration of the role of diet and vitamins in the prevention or treatment of the disease. If vitamins do prove valuable, scientists will explore further to find out if those vitamins should be taken as supplements or in the diet. Another promising area is the role of estrogen replacement therapy in the prevention of age-related macular degeneration in women, although recent studies have called the value and safety of estrogen replacement therapy into question.

The role of genetics in macular degeneration has been a fruitful area of research. Through genome-wide association studies (GWAS), researchers continue to discover genes that significantly increase AMD risk. These studies scan the entire DNA of individuals to find genetic variants related to specific diseases. The hope is that genetic interventions can be developed that will stop and perhaps reverse the damage these diseases cause.

Studies are underway to test the effect of drugs to slow the progression of dry AMD.

Several experimental treatments that may someday help to improve low vision are now being tested in clinical trials. Among these are retina chips, implanted electrodes, and miniature implanted telescopes.