
Seeing What We Don't Know: Macular Degeneration

Richard G. Stefanacci, DO, MGH, MBA, AGSF, CMD

While cataracts are certainly one of the more common causes of vision loss in elderly people, the greatest cause of blindness is macular degeneration. Approximately 10% of seniors ages 66 to 74 years have findings of macular degeneration; prevalence rates increase to 30% in those ages 75 to 85—this is a major issue within the senior community and an important disorder for geriatricians to look for in older patients.

It is often said that we don't know what we don't know—such is the case with the development of new innovative treatments. For years we were taught that there were no good treatments for macular degeneration; as a result, we may have failed to refer patients to specialists for care, believing that there was nothing additional to offer. Today certain types of macular degeneration can be successfully treated. If rendered early enough in the process, these treatments could save a person's vision, allowing him or her to remain independent and avoid morbidity. Since aging is a significant risk factor for macular degeneration, it falls on physicians

to evaluate and treat this leading cause of blindness.

Diagnosis

While macular degeneration progresses slowly, a sudden change in visual acuity may indicate a progression to the disabling exudative form of the disease. Small discrete yellow-white deposits under the retina are the first ophthalmoscopic sign of the disease and develop prior to any change in visual acuity. For this reason, simply performing visual acuity exams, while important, is not enough; a complete ophthalmoscopic exam is required to note the deposits of drusen.

There are two forms of macular

degeneration, the dry and wet forms (Figure 1). Central geographic atrophy, the dry form of macular degeneration causes vision deficit through loss of photoreceptors and cells supporting the photoreceptors in the central part of the eye. And while there is no treatment available for the dry type, it is still important to differentiate this type from the wet form, which is treatable.

Neovascular or exudative macular degeneration is the wet form of the disease. The wet form is also responsible for vision loss that is due to abnormal blood vessel growth under the macula. Irreversible damage to the photoreceptors and supporting cells is caused by bleeding, leaking, and scarring of blood vessels. Innovative new treatments are available for the wet form.

Oftentimes individuals with macular degeneration will first notice blurred central vision. This blurring is most apparent when performing visually detailed tasks such as reading. As the disease progresses, blind spots form within central vision. In most cases,

the blind spots are bilateral because if one eye has macular degeneration, the other eye will also develop the disease. The extent of central vision loss varies according to the type of macular degeneration.

Risk Factors

- Advanced age
- Smoking
- Family history
- Macular degeneration gene
- Hypertension
- Metabolic syndrome (high cholesterol, obesity, hypertension, and insulin resistance)
- High fat intake
- Caucasian race

- Extensive exposure to sunlight

Signs

- Drusen
- Pigmentary alterations
- Exudative changes: hemorrhages, hard exudates, subretinal/sub-retinal pigment epithelium (RPE)/intraretinal fluid
- Atrophy: incipient and geographic
- Visual acuity drastically decreasing by 2 levels or more (eg, from 20/20 to 20/80)

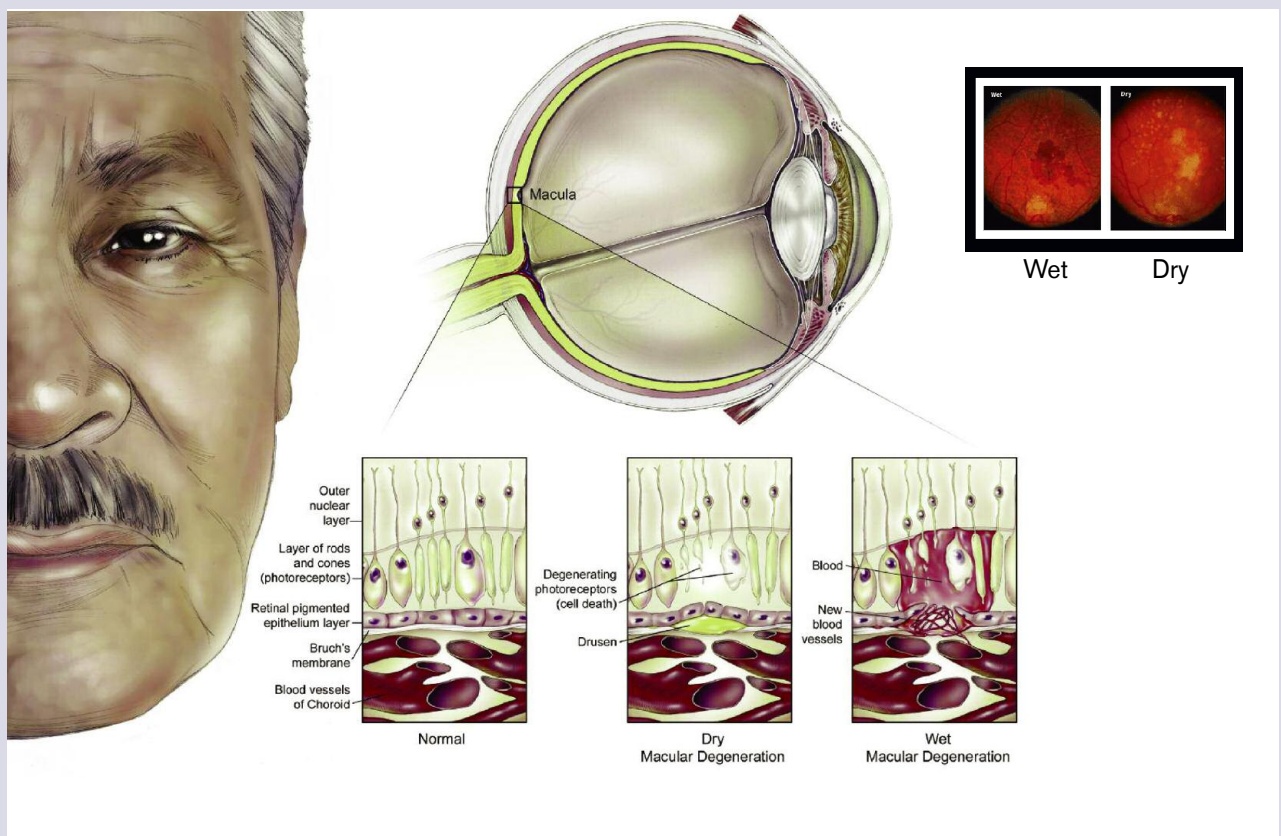
Symptoms

- Blurred vision. Those with non-exudative macular degeneration may be asymptomatic or notice

a gradual loss of central vision, whereas those with exudative macular degeneration often notice a rapid onset of vision loss.

- Central scotomas (shadows or missing areas of vision)
- Distorted vision (ie, metamorphopsia). A grid of straight lines appears wavy, and parts of the grid may appear blank (Figure 2). Patients often first notice this when looking at mini-blinds in their home.
- Trouble discerning colors: specifically dark colors from other dark colors and light from light colors
- Slow recovery of visual function after exposure to bright light

Figure 1. Two types of macular degeneration: wet and dry



Referral to an ophthalmologist should occur if macular degeneration is suspected based on history, reduced visual acuity (less than 20/40), or ophthalmoscopic visualization of retinal pigmentary degeneration. Urgent referrals are required if a patient complains of an abrupt decrease of visual acuity or if there is evidence of intraretinal or subretinal hemorrhage.

The definitive diagnosis is made by an ophthalmologist through a fluorescein angiography, which allows identification and localization of abnormal vascular processes. In addition, optical coherence tomography is now being used by most ophthalmologists in the diagnosis and followup evaluation of the response to treatment by using either bevacizumab (Avastin) or ranibizumab (Lucentis), which is injected into the vitreous of the eye at various intervals to preserve vision.

Management

In June 2006, the drug ranibizumab (Lucentis) was approved for use in the treatment of macular degeneration.¹ Ranibizumab has been shown to halt the progression of the disease in most patients receiving the treatment. Unlike previous treatments, a significant majority (70%) of those receiving ranibizumab had an improvement in vision of at least 1 letter. Up to 40% of patients had a significant vision increase of 3 lines or more. In addition, up to 50% had a vision of 20/40 or better after 12 months of treatment.² This is significant because 20/40 is commonly seen as the vision at which a person can still drive a car. Ranibizumab was

The benefit of early and aggressive diagnosis and treatment of macular degeneration is the ability to maintain vision.

the first therapy to show a statistically significant improvement in patient-reported outcomes.^{3,4} Ranibizumab is given as an injection into the eye by an ophthalmologist. The initial studies required an injection every 4 weeks for 2 years.

Bevacizumab (Avastin), a drug originally approved for use in

colon cancer, has been used by ophthalmologists in the treatment of wet macular degeneration. Bevacizumab and ranibizumab were developed from the same monoclonal antibody parent. However, ranibizumab has been affinity-matured 140 times and is a much smaller molecule than bevacizumab. Being smaller allows ranibizumab to penetrate all layers of the retina and also to systemically clear faster from the eye. Doubts about whether bevacizumab can penetrate the layers of the retina led to the development of ranibizumab. There are also concerns about the safety of bevacizumab because it is known to have significant systemic effects. Before ranibizumab was available, bevacizumab was widely used by ophthalmologists who treat macular degeneration. Some of their experiences with large numbers of pa-

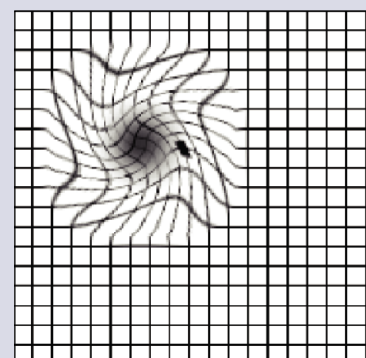
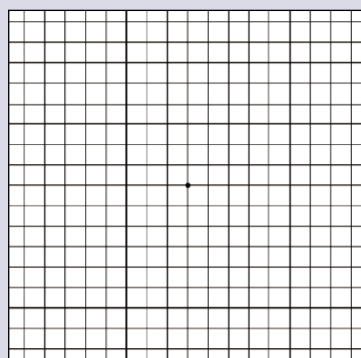
Figure 2. The Amsler Grid

The Amsler Grid is used to test the macula, the very central part of the retina. The test is simply a grid made of evenly spaced horizontal and vertical lines. A small dot is located in the center of the grid for fixation.

Have the patient focus on the dot in the center of the grid with one eye covered and ask the following questions:

- Are you able to see the corners and sides of the square?
- Do you see any wavy lines?
- Are there any holes or missing areas?

If the patient states that the lines of the grid do not look straight or areas appear to be missing or distorted (right), refer him or her to a retinal specialist.



PROVIDER ACTION

Impact to You

Certain types of macular degeneration are treatable. About 10% of seniors ages 66 to 74 years have signs of macular degeneration, and prevalence rates increase to 30% in those ages 75 to 85, making this disorder a significant issue for most geriatric practices.

What You Need to Know

Macular degeneration is the leading cause of blindness, but several forms are treatable. Risk factors for macular degeneration include advanced age, smoking, family history, and others. Signs include drastically decreasing visual acuity by 2 levels or more (eg, from 20/20 to 20/80).

What You Need to Do

Be comfortable performing visual acuity exams and be willing to refer a patient to an ophthalmologist for further examination. Small discrete yellow-white deposits under the retina are the first ophthalmoscopic sign of the disease and develop before visual changes occur.

tients with relatively short followup times were recently published. No randomized controlled clinical trial with systematic safety data collection has been performed to validate bevacizumab's efficacy and safety with the same certainty as those of ranibizumab. Bevacizumab, when administered at the usual cancer treatment doses, has been shown to cause systemic adverse effects. The most common adverse effect is hypertension.

Pegaptanib (Macugen) was approved in 2004 for treatment of neovascular macular degeneration. It targets certain forms of vascular endothelial growth factor (VEGF) molecules and is injected directly into the eye like ranibizumab or bevacizumab.

Photodynamic therapy (PDT) with verteporfin (Visudyne) had been the treatment of choice for neovascular macular degeneration until recently. This was the first treatment shown to decrease the chance of severe vision loss in 2 years in patients with neovascular macular degeneration without first causing immediate vision loss at the time of the treatment. A photosensitive dye with affinity for the abnormal blood vessels is first injected through the veins. A low-energy activating laser is then directed toward the abnormal blood vessels, causing selective damage to those blood vessels. This has also fallen out of favor as newer, more effective treatments became available.

Direct laser treatment for neovascular macular degeneration was shown to decrease the chance of profound vision loss at 2 years in patients with neovascular macular

degeneration, but it is seldom used as the treatment itself because it causes immediate, significant vision loss. Infrequently, abnormal blood vessels outside of the center part of the macula are detected.

Other drugs that are currently under investigation include anecortave (Retaane), squalamine (Evizon), and small interfering RNA (siRNA). Second-generation antisense oligonucleotides iCo-007 targeting the Raf-1 kinase are also under investigation as a target for broad inhibition of multiple proangiogenic signals. Radiation therapy (brachytherapy) and rheopheresis are also being evaluated for wet macular degeneration.⁴

Maintaining an open dialogue with an ophthalmologist is important to understanding the latest treatment options so appropriately timed referrals can be provided.

None of the drugs or laser treatment can restore vision to patients who have already suffered permanent damage to the photoreceptors or RPE cells by advanced forms of macular degeneration; therefore, early detection is critical.

Benefits of Early, Aggressive Treatment

The benefit of early and aggressive diagnosis and treatment of macular degeneration is the ability to maintain vision. Regardless of treatment, improvement of quality of life and function occurs when visual function improves. Thus, many types of functional degeneration observed in older populations, attributed to a decline in vision, can be slowed, or even reversed, when visual function is improved.⁵

MPM

Richard G. Stefanacci, DO, MGH, MBA, AGSF, CMD, is Editor-in-Chief of Medicare Patient Management.

References

1. Food and Drug Administration. FDA approves new biologic treatment for wet age-related macular degeneration [Press release]. June 30, 2006.
2. Brown DM, Kaiser PK, Michels M, et al for the ANCHOR Study Group. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. *N Engl J Med.* 2006;355(14):1432-1444.
3. Rosenfeld PJ, Brown DM, Heier JS, et al for the MARINA Study Group. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med.* 2006;355(14):1419-1431.
4. Macular degeneration R & D. The Eye Digest. 2005. Available at: <http://www.agingeye.net/maculardegen/maculardegennewdevelopments.php>. Accessed March 6, 2007.
5. Brenner MH, Curbow B, Javitt JC, Legro MW. Vision change and quality of life in the elderly. *Arch Ophthalmol.* 1993;111(5):680-685.