Age-Related Macular Degeneration (AMD)

1. Definition

Age-related macular degeneration (AMD) is a common condition affecting people age 50 years and older. The condition may be associated with varying degrees of central vision impairment and can lead to loss of the ability to read, to drive a car, or see someone's face if it progresses to more advanced stages in both eyes.

The macula refers to the central part of the retina. The retina is similar to film inside a camera. The image one sees is focused by the cornea and lens of the eye on to the macula. Many people with AMD have no visual symptoms and may retain normal 20/20 vision for the rest of their lives. A relatively small percentage of people with AMD will have progression of the disease to the point of losing some degree of central vision over time. Although AMD can cause central vision loss, it typically does not lead to complete blindness.

There are two major types of AMD, a "dry" (non-neovascular) and a "wet" (neovascular) form. The dry form is the early stage. It is the most common form of AMD and all patients with AMD start off with the dry type. There is usually little or no vision loss during this stage although there are exceptions with some people having significant vision loss from more advanced "dry" degeneration. The wet form is a late stage of the condition and affects about 10 percent of all people with the condition. Wet AMD accounts for the majority of central vision loss due to AMD. The wet type implies leakage or bleeding in the macula due to abnormal blood vessels known as choroidal neovascularization. These abnormal blood vessels start to grow beneath the center of the macula and, as they grow, they leak fluid or blood and cause central vision loss with blurring and distortion of vision. Untreated, these abnormal blood vessels typically will grow relatively large and eventually cause scarring with permanent and often severe central vision loss.

The dry form of AMD is characterized by drusen. These are small yellow deposits that the doctor sees when looking at the macula on clinical examination. Drusen are the hallmark of AMD. Most people with drusen alone do not have significant visual changes or vision loss. A minority of people with dry AMD will advance to central vision loss due to geographic atrophy which is the loss of pigment layer under the macula. Currently, there is no treatment or cure for geographic atrophy and the associated vision loss.

The wet form of AMD, however, is treatable and, in general, the best results are achieved when wet AMD is detected and treated early in its course. Medicines injected into the eye are the mainstay of treatment for wet AMD and are highly effective in halting the growth and leakage of choroidal neovascularization. This usually prevents vision loss in most cases and often improves vision to some degree, although not in everyone.

2. Causes and Associations

There are no known specific causes of AMD. It is a degenerative condition that occurs over time. It is typically found in people ages 50 years or more, although drusen sometimes can be seen in younger people. There tends to be familial associations, although just because a family member or blood relative has AMD does not destine someone else in the family to have it as well. Over time, the macula accumulates drusen and pigment changes, and if choroidal neovascularization or geographic atrophy does not occur, then vision tends to remain good. It is the progression to advanced AMD such as with the development of geographic atrophy or choroidal neovascularization (wet AMD) that threatens the loss of central vision.

There are risk factors for people with AMD that may be modifiable or controllable. These include smoking, poor nutritional intake, and high blood pressure. (See section 6 below.)

3. Symptoms

Many people with dry AMD have no visual symptoms at all. However, some people, will require more light to read, have difficulty adjusting between dark and light conditions, or notice mild blurring of vision. Occasionally, significant loss of central vision can occur. Vision loss associated with dry AMD is usually gradual or slow. Because AMD affects the macula, the symptoms typically affect tasks such as reading or driving. Peripheral vision is typically not affected.

People with wet AMD often have more rapidly progressive loss of central vision, typically over weeks or months. Visual distortion is a common symptom of this stage. Occasionally, people may not be aware of these visual changes because the other eye may see well. Therefore, it is important to test vision in each eye separately by covering one eye at a time when checking vision.

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An Amsler grid is a checkered pattern with a central dot in the middle of the pattern. It is a self-monitoring tool that allows people to check their vision one eye at a time to monitor for blurring or distortion that may signify the conversion from dry to wet AMD. People with AMD progression may notice changes on the Amsler grid, and if this occurs, they should to contact their ophthalmologist promptly.

Electronic home monitoring devices are now also available to aid in self-monitoring one's vision in between office examinations (eg. Foresee Home.) If used regularly such devices may work better than an Amsler grid in detecting wet AMD at its earliest stage of development. Early detection and treatment of wet AMD helps to maximize the chances of good vision outcomes.

4. Evaluation

A complete and comprehensive eye examination is important to assess AMD. People will have vision testing, eye drops to dilate pupils, and a complete examination of the front and back of the eye. Pupillary dilation may create near vision blurring, and therefore, it is often best if a driver accompanies the patient, although it is not absolutely required.

People with AMD may have several types of tests to assess the disease. People may undergo color photography of the macula to document drusen, pigment changes, and other characteristics of AMD.

Fluorescein angiography is a commonly used, office-based diagnostic test that can help determine the extent of macular degeneration and help distinguish between the dry and wet forms of the condition. Fluorescein angiography is performed by injecting sodium fluorescein dye into a peripheral vein (usually in the arm) with a small needle. This dye then goes through the blood vessels of the body and eyes. Choroidal neovasculation in the macula can be seen as a leaking blood vessel complex under the retina. It is regarded as a safe test, but people should expect some yellowish skin discoloration and orange urine. Most people have no difficulty with this testing, although a small percentage of people will experience some nausea. Any angiogram test, however, can be associated with allergic or even more severe reactions, and therefore, this test is typically reserved for people in whom wet AMD is noted or suspected. Fluorescein is not a radiologic contrast dye, and is safe for people with kidney disease. Occasionally, retinal angiography is performed with a green dye (indocyanine green) when fluorescein angiography alone does not provide sufficient information for the evaluating the condition.

Optical Coherence Tomography (OCT) a non-invasive, office-based imaging technique that uses low energy laser to scan the macula and determine whether there is fluid in the macula, potentially signifying wet AMD. It is a commonly used test as an adjunct to fluorescein angiography to help diagnose wet AMD. It can also be used to assess how the eye is responding to treatment. OCT has no risk to the patient.

5. Prognosis

Most people with AMD will retain good central vision and the ability to read in their lifetime. This is because 90% of people have dry AMD, which is associated with a more favorable prognosis. Without treatment people with wet AMD will suffer central vision loss. If it affects both eyes with associated vision loss, then the patient may progress to legal blindness, although AMD does not lead to total loss of vision. Thankfully, the new treatments have vastly improved the prognosis for people with wet AMD.

6. Treatment

Dry AMD

There is no treatment yet to halt the progression or recover any vision loss from dry AMD. However, the two Age Related Eye Disease Studies (AREDS) demonstrated that a specific formulation of anti-oxidant vitamins and minerals can reduce the risk of progression of dry AMD to more advanced stages and associated vision loss. The components of the AREDS formulas are as follows:

AREDS (Original):
15 mg Beta-carotene; 500 mg Vitamin C; 400 IU Vitamin E; 80 mg Zinc oxide; 2 mg Copper oxide

AREDS II:
Lutein 10 mg; Zeaxanthin 2 mg; 500 mg Vitamin C; 400 IU Vitamin E; 80 mg Zinc oxide; 2 mg Copper oxide

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Both formulas are beneficial in treating dry AMD, but only one of the two should be used. Your eye care provider should help you to decide which formula is best for you. It is also important to check with your medical doctor before starting treatment with either AREDS formula. A multivitamin in addition to either AREDS vitamins is ok. However, taking more than the recommended doses may be harmful. In general, Vitamin E supplementation should not exceed 400 IU, and current or recent smokers should not be on any Beta-carotene supplementation due to an increase risk of lung cancer. (Therefore, current or recent smokers should not be using the original AREDS formula.) Chewable products of the AREDS formula are now available if you have trouble swallowing the pills.

Based on epidemiologic studies, certain lifestyle and nutritional changes may be beneficial. Based on what is known to date, the following recommendations may be made in hopes of improving the prognosis of dry AMD:

1. Stop smoking. Smoking has been associated with vision loss and more advanced forms of AMD.
2. Control blood pressure. High blood pressure is associated with more advanced AMD.
3. Be physically active. People with AMD who are physically active several times a week may reduce their risk for progression to advanced AMD and vision loss.
4. Eat a diet rich in colorful vegetables (including dark green leafy vegetables such as broccoli and spinach) and fruits which contain natural antioxidants. These food groups have been associated with lower rates of progression to advanced AMD.
5. Consider eating food rich in Omega 3 fatty acids. Omega 3 fatty acids are found in cold water fish such as tuna and salmon along with nuts. Studies show that a diet with high omega 3 fatty acid intake is associated with less advanced AMD.

Wet AMD

The prognosis for people with wet AMD is improving. There are more effective treatments now than there were just a few years ago but still no cures exist for AMD. Treatments include new medications aimed at blocking growth factors, nondestructive laser-drug combinations, and traditional laser photocoagulation.

Anti-Vascular Endothelial Growth Factor (VEGF) Agents:

Lucentis (ranibizumab)

Lucentis (ranibizumab) was FDA approved for the treatment of wet AMD in 2006. This was the first treatment shown to improve vision in many people with wet AMD. Lucentis is administered in the office by an intraocular injection and typically administered monthly for the first few treatments. The eye is prepped with antiseptic solutions and topical anesthetic drops. The injection is very well tolerated being relatively painless and only rarely associated with any complications. Treatment may need to continue indefinitely depending on the nature of the wet AMD and response to treatment, although the frequency and total number of injections may vary considerably among patients.

The risks of intraocular injections such as with Lucentis include hemorrhage, retinal tear, and infection, all of which are very rare. Anyone who receives an injection and subsequently has increased pain or loss of vision should contact their doctor immediately as these symptoms could indicate one of these rare complications.

Lucentis is a humanized antibody fragment that works by blocking an important growth factor of choroidal neovascularization called vascular endothelial growth factor (VEGF). By blocking VEGF, both the growth and leakiness of the abnormal blood vessels is reduced. Studies with patients on a course of Lucentis showed that 70% of people on treatment will maintain or improve vision and 30% to 40% of people have relatively large degrees of visual improvement. However, there can still be vision loss despite ongoing Lucentis therapy.

Eylea (aflibercept)

Eylea (aflibercept) is the second FDA-approved anti-VEGF agent to treat wet AMD. Eylea is a fusion protein that acts like an antibody to bind VEGF. In clinical trials it had equivalent effectiveness and safety to Lucentis. See above (under Lucentis) for details regarding the benefits and potential risks Eylea injections for treating wet AMD.

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Avastin (bevacizumab)

Avastin (bevacizumab) is another drug used to treat wet AMD. Avastin is FDA-approved for use in people with certain types of cancer by intravenous infusion. Like Lucentis, Avastin is an antibody to VEGF. Retina specialists have been performing intraocular injections of Avastin to treat wet AMD for about as long as Lucentis. Although the use of Avastin injected into the eye is considered off-label, there are now studies that show Avastin to be as safe and effective to Lucentis.

Photodynamic Therapy (PDT)

Photodynamic therapy (PDT) with Visudyne (verteporfin) is another treatment for wet AMD. It utilizes an intravenous injection of a photosensitizing drug called Visudyne (verteporfin) and a non-thermal laser light to try and reduce leakage from certain types of choroidal neovascularization. It typically does not improve vision as when used alone, however, it is used in rare circumstances in combination with anti-VEGF therapy.

PDT is a timed, office-based procedure. The Visudyne drug is infused into the vein over 10 minutes and then allowed to collect within the choroidal neovascularization over another 5 minutes. The choroidal neovascularization is then exposed to a low energy laser light for about 90 seconds to activate the drug only within abnormal blood vessels in the macula. This produces a chemical reaction within these abnormal blood vessels to reduce blood flow and leakage. The treatment is often repeated at 3 month intervals.

Visudyne clears itself completely from the body over several days. The skin and eyes must be protected from sunlight with clothing and special sunglasses for 2 days after the treatment. No driving is allowed while wearing the sunglasses. Sometimes PDT is combined with other treatments such as anti-VEGF agents or steroids to attack choroidal neovascularization using several different mechanisms of action.

Laser Photocoagulation

Thermal laser photocoagulation may be used in very uncommon, specific cases of choroidal neovascularization where the abnormal blood vessels are located relatively far from the center of the macula. Thermal laser treatment attempts to heat and destroy choroidal neovascularization but also damages overlying vision cells to some degree. Accordingly, this procedure is typically considered only when the abnormal blood vessels are far from the center of the macula. A major problem with thermal laser treatment is recurrent choroidal neovascularization which can develop in 50-60% of people.

Miscellaneous treatments

Low vision aids may help improve the quality of life for people whose vision is impaired to the point that they cannot carry out important visual activities of daily living such as reading mail or writing checks. Low vision rehabilitation involves using specific magnifying optical devices and lighting aids to assist in performing specific vision functions. Although low vision aids are no cure for AMD, they may be helpful in performing essential visual tasks. Low vision centers can also be a good resource for non-optical aids such as books on tape, large print reading materials, and writing guides. Computers and electronic readers (iPad, Kindle, etc) are often found to be very useful in the setting of vision loss from AMD. An implantable miniature telescope was approved by the FDA and may be useful in certain patients with inactive or stable macula scars from AMD.

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