Age-Related Macular Degeneration

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Macular degeneration is the most common cause of severe vision loss in people over the age of 50. More than 8 million people in the United States alone have some form of this disease. This booklet is intended to educate patients and their families about macular degeneration, its treatment and low vision rehabilitation.

The term “macular degeneration” includes many different eye diseases, all of which affect central, or detail, vision. Age-related macular degeneration is the most common of these disorders, mainly affecting people over the age of 60. Although age-related macular degeneration is our primary focus here, much of the information also applies to other types of macular degeneration.

We hope that this booklet increases your understanding of macular degeneration and enhances your communication with your ophthalmologist and other health care providers.
The eye is a complex organ composed of many parts. Good vision depends on how these parts work together. It is helpful to understand how the eye works before learning about macular degeneration.

As light enters the eye, it first passes through a lubricating tear film that coats the cornea. The clear cornea covers the front of the eye and helps to focus incoming light.

The iris is the colored part of the eye. As light conditions change, the iris may dilate to make the pupil bigger or constrict to make the pupil smaller. This allows more or less light into the eye.

Light then passes through the lens, a flexible, transparent structure that can change its shape to focus images on the retina.

After being focused by the lens, light passes through the center of the eye on its way to the retina. The eye is filled with a clear jelly called the vitreous.

Finally, light falls upon the retina, a thin, light-sensitive tissue lining the back of the eye. The retina converts light patterns into information the brain can use.
The retina is composed of many different tissue layers, each with a specific function. Some of these layers may not be working properly in an eye with macular degeneration.

Behind the retina, a layer of blood vessels called the choroid supplies oxygen and nutrients to outer layers of the retina.

The optic nerve is a bundle of nerve fibers that carries visual information from the eye to the brain.

The macula is the small central portion of the retina with the densest population of photoreceptors, the light-sensing cells. The center of the macula is called the fovea. With the highest density of photoreceptors, the fovea is what allows one to see fine detail such as small newsprint.

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The photoreceptor layer is composed of light-sensitive cells called rods and cones. Light images are converted into electrochemical signals inside the photoreceptors.

This cross-section shows an enlarged view of the retina.
Age-related macular degeneration is an eye disease that primarily affects the central portion of the retina known as the macula. The risk for developing macular degeneration increases with age and is over 30% by age 75. Other risk factors include a family history of the disease, cigarette smoking, diet, excessive sunlight exposure, high blood pressure and cardiovascular disease.

Under the photoreceptors is a dark layer called the retinal pigment epithelium (RPE). Cells of the RPE absorb excess light and transport oxygen, nutrients and cellular wastes between the photoreceptors and the choroid.

Bruch’s membrane separates the blood vessels of the choroid from the RPE layer.

The choroid is a layer of blood vessels that supplies oxygen and nutrients to the outer layers of the retina.

The sclera is the fibrous, white, outer covering of the eye.

This photograph shows a normal, healthy retina as viewed by an eye doctor during an examination. The ophthalmologist will pay careful attention to the appearance of the macula and fovea when examining the retina.
The majority of people with macular degeneration have an early form of the condition and experience minimal vision loss. For many of these people, macular degeneration will not progress.

In the early stages of macular degeneration, the transport of nutrients and wastes by the retinal pigment epithelium (RPE) slows down. As waste products accumulate under the retina, they form yellowish deposits called drusen.

In the healthy retina, a layer of cells called the retinal pigment epithelium (RPE) supplies the photoreceptors with nutrients and pumps out the waste products created as the photoreceptors convert light into nerve signals.

An eye doctor examining a patient at this stage may note the presence of these drusen, even though most people have no symptoms. Patients with drusen need to be observed over time, although most will not progress to develop vision loss. Many people over the age of 60 will have some drusen.

A portion of people with drusen may begin to experience mild vision loss. At this point, macular degeneration may progress in one of two ways. These two types of degeneration are known as the dry (atrophic) and the wet (neovascular) forms of the disease. Neovascular macular degeneration is sometimes referred to as “exudative” macular degeneration.

This retinal photograph shows numerous yellow drusen in and around the macular region of the retina.
Dry (atrophic) macular degeneration is a slowly progressing condition characterized by the accumulation of drusen beneath the retina with some vision loss. Dry macular degeneration rarely causes severe vision impairment or blindness.

As the retinal pigment epithelium (RPE) continues to slow down in its transport of nutrients and wastes, the overlying photoreceptors become damaged. The size and number of drusen in the macula increase. Vision may be affected as RPE and photoreceptor cells are lost due to atrophy.

In dry macular degeneration, waste products from the photoreceptors accumulate underneath the retinal pigment epithelium (RPE). The waste appears as yellowish spots called drusen.

As areas of retina lose function, patients begin to lose sight in certain areas of their central field of vision. Occasionally, a large region of cells is lost. This is called “geographic atrophy” and it produces a blind spot in the central portion of vision. This blind spot is called a scotoma.

This retinal photograph shows many drusen in the macula. Drusen are typical of dry macular degeneration.
There are certain steps you can take to help slow down the progress of dry macular degeneration. In the Health and Nutrition section on page 65, we recommend dietary changes, taking nutritional supplements, stopping smoking and controlling blood pressure. While there is a great deal of research currently under way, we have no other proven prevention or treatment strategies for dry macular degeneration. Fortunately, the majority of people who have reached this stage of the disease will not progress to the more serious, wet form.

If you have macular degeneration, it is essential that you report any changes in your vision to your eye doctor immediately. Careful self-monitoring with the Amsler grid (see instructions at the end of this booklet) and regular examinations by an eye doctor are crucial for preserving your vision. This is because some people with dry macular degeneration will develop the more severe “wet” form of the disease which requires treatment as soon as possible.

This retinal photograph shows geographic atrophy in the macular region resulting from advanced dry macular degeneration.

Regular use of the Amsler Grid is important if you have macular degeneration (see the “Amsler Grid” section at the end of this booklet). Small blind spots may appear in your vision as dry macular degeneration progresses. The Amsler Grid can help you notice changes in your vision that might otherwise be missed.
For reasons that are not fully understood, a minority of people with macular degeneration develop a more serious form of the disease. People with large “soft” drusen (drusen with indistinct borders), many drusen that run together, or pigment cells in the macula that look abnormal are at greater risk for developing the wet (neovascular) form of the disease.

In the wet form of macular degeneration, new blood vessels begin to grow underneath the retina. The proliferation of these new blood vessels is called choroidal neovascularization (CNV).

Wet macular degeneration is classified by where the CNV develops in the retina.

- CNV that develops directly beneath the photoreceptors, which is easily seen by angiography, is referred to as “classic” CNV.
- CNV that develops beneath the RPE layer, which is more difficult to see by angiography, is referred to as “occult” CNV.
- CNV that forms within the retina is sometimes referred to as retinal angiomatous proliferation or “RAP.”
- CNV that results in large, leaky blood vessels is called polypoidal choroidal vasculopathy or “polypoidal.” The polypoidal vessels in this condition tend to cause extensive leakage and bleeding under the retina.
As CNV grows, the new vessels may leak blood or fluid under and into the retina, causing the retinal surface to become uneven. As a result, objects in that portion of the visual field may appear wavy or distorted. The neovascularization may even break through some of the retinal layers. Blind spots may appear in your vision if portions of the retina become damaged by the CNV.

It is believed that the diseased retina stimulates the production of these new blood vessels in response to a decreased supply of nutrients and slow transport of wastes. Unfortunately, the new blood vessels do not improve the health of the retina.

As the surface of the retina becomes uneven, objects may appear blurred, wavy or distorted. As the condition progresses, blind spots may appear.
Eventually, areas of neovascularization and leakage can lead to the death of the overlying photoreceptors and scarring of the macula. Scarring is the final stage of macular degeneration and it frequently results in significant vision loss.

It is important to realize that this entire process occurs only in the macula and affects only central, or detail, vision. Peripheral, or side vision, is rarely affected by macular degeneration. While macular degeneration is the leading cause of legal blindness, it rarely leads to total blindness.

The first indication of fluid or blood under the retina may be a distortion of straight lines. The Amsler grid test, which you can do at home, is an important tool for the early detection of any changes in your vision. Instructions for using the Amsler grid are at the end of this booklet.

Legal blindness means vision is 20/200 or worse in the better eye even with corrective lenses, or peripheral vision is restricted to the extent that only “tunnel vision” remains.

This retinal photograph shows a large yellow scar in the macular region resulting from advanced CNV. A person with this type of scarring would experience a significant loss of vision in that eye.
Eyedrops are given to dilate your pupils. This will allow your doctor to examine the retina through the enlarged pupil. The drops typically take between 20 and 45 minutes to work and will wear off in several hours. While the pupils are dilated, it is usually difficult to read, and bright lights may be uncomfortable. Some patients wear sunglasses after dilation to reduce light sensitivity.

After the dilating drops are administered and given time to work, the eye doctor seats the patient at a device called a slit lamp. The slit lamp is a special microscope that enables the doctor to examine the different parts of the eye under magnification. When used with special lenses, the slit lamp gives the doctor a highly magnified view of the retina.

A thorough examination by an eye doctor is the best way to determine if you have macular degeneration or if you are at risk for developing the condition.

The exam begins with testing of your visual acuity or the sharpness of your vision. There are several different tests for visual acuity. The most familiar one has black letters on a white chart.

Next, your eyes may be tested with an Amsler grid. This test helps your doctor to determine whether you are experiencing areas of distorted or reduced vision, which are both common symptoms of macular degeneration. If you do have macular degeneration, your doctor will use the Amsler grid to determine if your vision has changed. Your ophthalmologist may provide you with a small version of the Amsler grid to carry with you in your purse or wallet. Instructions for using an Amsler grid at home appear at the end of this booklet.

After these vision tests, the front part of your eyes will be examined to determine if everything is healthy. Your doctor may put anesthetic drops in your eyes so that the level of pressure can be measured in each eye.

Examination & Diagnosis

The slit lamp is a microscope that shows a magnified view of the retina. Your eye doctor will look for drusen and other areas of the retina that appear suspicious or abnormal.
A technique called angiography is the most useful test to look for CNV. The procedure is painless and very safe. The patient is seated at a fundus camera so pictures of the retina can be taken. A small IV catheter is inserted into a large vein, usually in the arm. A dye is injected through the catheter into the vein. The dye circulates throughout the blood vessels of the body. As the dye enters the blood vessels of the eye, a series of pictures is taken of the retina. Special filters make the dye stand out against the background of the retina.

The doctor will look for drusen and other areas of the retina that might appear suspicious or abnormal. Because the new blood vessel growth found in the “wet” form of macular degeneration (choroidal neovascularization or CNV) occurs beneath the retina, the blood vessels themselves are not usually visible. But the examination can reveal clues, such as bleeding, elevation of the retina or fluid behind the retina, that suggest the presence of CNV. In these cases, further testing may be necessary.

This retinal photograph shows many drusen and fluid under the retina, which suggests the presence of choroidal neovascularization (CNV). Additional testing would be required for complete diagnosis and treatment.

The fundus camera takes pictures of the retina (see examples at right). The camera may use film or it may be digital, displaying the images on a computer screen.
By looking at the pattern of the blood vessels and observing whether dye leaks from any of the vessels, the ophthalmologist can locate sites of CNV if they are present.

This fluorescein angiogram shows CNV in the macula. The bright area indicates dye leaking from the newly formed vessels.

Two dyes are commonly used in ophthalmology: an orange dye called fluorescein and a green dye called indocyanine green (ICG). These dyes are different from those used for angiograms of the heart or brain. X-rays are not used in this procedure because the blood vessels can be directly viewed and photographed through the pupil.

Most of the time, CNV can be seen with fluorescein dye. Fluorescein angiography is an extremely safe procedure, and it has been performed in millions of patients for more than 25 years. Most patients experience no symptoms when the dye is injected. A small minority may feel flushed or briefly nauseated. Rarely, someone has an allergy to fluorescein and may experience itching or other symptoms that require treatment. After the test, your kidneys remove the fluorescein dye from your body; therefore, your urine will turn orange or dark yellow for up to 24 hours.

Sometimes, an area of CNV is not clearly defined, or it may be obscured by overlying fluid or blood. In these cases, your ophthalmologist may find it helpful to perform angiography using ICG dye instead of fluorescein. ICG is also useful for visualizing the deeper blood vessels located in the choroid. ICG can show how the choroidal circulation is interacting with other layers of the retina and whether variant forms of CNV, such as retinal angiomatous proliferation (RAP) or polypoidal choroidal vasculopathy are present. ICG angiograms are typically performed using a digital fundus camera or another instrument called a scanning laser ophthalmoscope (SLO). Side effects from ICG dye are rare and similar to those from fluorescein. ICG dye does contain a form of iodine, so if you are allergic to iodine you should tell your ophthalmologist.

Your ophthalmologist may also perform high-speed video angiography. This type of angiography also requires dye, but it captures dynamic “movies” of
Optical coherence tomography (OCT) is an additional technique for imaging the retina. It is a non-invasive test that records the features of the retina and displays this information as cross-sectional views, or optical 'slices.' For this procedure, the patient is seated at the OCT device. Laser light is used to map the anatomy of the retina, and the resulting computer images are saved for analysis. OCT evaluations are not a replacement for angiography. OCT is used as an additional test that provides different information such as whether excess fluid is present in the retina. OCT may be used to monitor how well treatment for wet macular degeneration is working.

Inside the newest OCT instruments, a spectrometer is used along with the laser light to map the blood flow patterns in the retina instead of still pictures. This reveals additional information about CNV. For example, it may provide a view of smaller vessels that are “feeding” the growth of the CNV. The feeder vessels can then be precisely treated, sparing healthier areas of the retina.

The different types of angiography can be used separately or together to provide as much information as possible about the location, size, number and type of CNV areas that may be present in the eyes. Evaluating the specific characteristics of areas of CNV is useful for determining which type of treatment is likely to be most successful.
Autofluorescence imaging of the retina is a new technique that involves capturing a response from molecules in the RPE. There are two ways to obtain these images. One uses a specialized scanning laser, and the other uses special filters attached to the fundus camera. Both types are noninvasive. The images show areas of stress and damage to the retina and can be used to monitor these changes over time.

This is an OCT image of the macula in a normal, healthy eye. The depression in the center is the fovea. Note how smooth and even the layers are.

This is an OCT image of the macula in an eye with wet macular degeneration. Because of fluid build-up, the tissue layers are no longer smooth and flat.

Anatomy of the retina. This technology, known as "spectral domain" or "Fourier domain," allows the instrument to scan the retina much faster, providing very high resolution 3-D images of the retina. The ophthalmologist gets a clearer, more accurate view of individual tissue layers. This is similar to the view of other body parts that is obtained with an MRI. The power of spectral domain OCT also allows repeat examination of the exact same areas of the retina at each patient visit, which results in a more precise measurement of the effects of treatment.

This is an autofluorescence image of the retina in a normal, healthy eye. The macula is at the center.
At this time, there is no way to prevent or cure either the dry (atrophic) or wet (neovascular) form of macular degeneration. However, significant progress has been made in treating the condition, and a great deal of research is currently under way. The most significant advance has been the development of a new class of drugs now being used to treat wet macular degeneration. The drugs are based on the discovery that a group of proteins in the body called vascular endothelial growth factor (VEGF) play a significant role in the formation of the abnormal blood vessels that damage the retina in wet macular degeneration. As explained in the Wet Macular Degeneration section, these abnormal blood vessels are called choroidal neovascularization (CNV).

The anti-VEGF drugs are injected directly into the jelly-like substance that fills the back of the eye, which is called the vitreous. Before the injection, drops are used to numb the eye and a speculum may be put in place to hold the eyelids out of the way. While it may seem scary to receive an injection into the eye, most patients find that they experience minimal discomfort. Once inside the eye, the
Also, many patients in the study gained a small amount of vision, and some experienced significant improvement. It is important to note that the patients in the study had fairly recently diagnosed macular degeneration that had not yet progressed to scarring. Each person responds differently to treatment, depending on his or her individual situation.

Two anti-VEGF drugs have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of wet macular degeneration. The one most widely used is Lucentis (ranibizumab). In the studies that evaluated Lucentis, the results were more favorable than for any other previously FDA-approved treatment. Instead of only slowing the rate of vision loss, the drug appeared to stop disease progression in most people for as long as two years.

Before injection of an anti-vascular endothelial growth factor (VEGF) drug, the eye is numbed and a speculum may be put in place to keep the eyelids out of the way.

The newest drug for the treatment of wet macular degeneration attaches to VEGF molecules in the retina and choroid, preventing them from stimulating more abnormal growth of blood vessels.

medication diffuses throughout the retina and choroid. It binds strongly to the abnormal VEGF proteins, preventing the proteins from stimulating further unwanted blood vessel growth and leakage.
Your ophthalmologist will explain the advantages and disadvantages of all available treatments for wet macular degeneration and choose your treatment based on your individual case.

The FDA-approved anti-VEGF drugs are costly, but the pharmaceutical companies that make them offer assistance programs for patients who qualify. Ask your ophthalmologist for information about these programs.

In the studies of Lucentis, patients were given injections every month for up to two years. More recent evidence suggests that it may be possible to obtain similar results by giving several injections at monthly intervals and then increasing the time between subsequent injections. Retinal specialists are still investigating the optimal timing of injections. Also, research is under way to develop other methods of delivering drugs to the eye to reduce the need for frequent injections.

The first anti-VEGF drug to be approved by the FDA for the treatment of wet macular degeneration was Macugen (pegaptanib sodium). It works in a similar manner to Lucentis, but is not as effective. This is most likely because it acts against only one form of the VEGF protein, called VEGF-165, whereas Lucentis targets all forms of VEGF.

In theory, if Lucentis from the eye were to travel to other parts of the body and interfere with VEGF, it could lead to problems, such as an increased risk of heart attack or stroke. However, the amount of drug injected is small, and no safety problems have emerged with the use of Lucentis.
Off-Label Treatments

The term “off-label” means using a drug to treat a condition for which the drug was not originally intended. For example, aspirin was used to prevent heart attacks and for blood thinning even though for a long time the FDA label did not initially list these specific indications.

Physicians may use any available drug to treat macular degeneration, including drugs approved for other reasons. A drug commonly used off-label for the treatment of wet macular degeneration is Avastin (bevacizumab). Avastin is similar to Lucentis because it is an anti-VEGF drug. It is approved by the FDA for the treatment of certain kinds of cancerous tumors, which, like CNV, form and grow with the help of abnormal blood vessels.

Before the FDA approval of Lucentis, retinal specialists had started using Avastin to treat wet macular degeneration. Like Lucentis, Avastin is injected into the back of the eye. Avastin is being used worldwide in the treatment of wet macular degeneration, and the results appear to be similar to the results achieved with Lucentis. However, there has been a great deal of media attention and some controversy surrounding these drugs. Although both may help in wet macular degeneration, Avastin is far less expensive. On the other hand, Avastin has not been evaluated by a large, formal macular degeneration study the way Lucentis has. The National Eye Institute is currently conducting a study, called the CATT Trial, to directly compare the safety and effectiveness of Lucentis and Avastin in wet macular degeneration. The results of the study should help to provide a final answer to the question of which of these drugs should be routinely used.

Another off-label treatment used for wet macular degeneration is the injection of a steroid, often triamcinolone, into the back of the eye. Steroids fight inflammation, which recent research has indicated plays a role, along with VEGF, in macular degeneration. Steroids are typically used in combination with other macular degeneration treatments, such as photodynamic therapy (PDT) (see next page) and/or an anti-VEGF drug. If your ophthalmologist uses steroids as part of your macular degeneration treatment, he or she will closely monitor you for potential side-effects, which may include the formation of cataracts and elevated pressure inside the eye.
Photodynamic Therapy (PDT)

Photodynamic therapy (PDT) is a treatment for some forms of wet macular degeneration approved by the FDA in 2000 and still used in some cases today. Unlike the anti-VEGF drugs, which affect the underlying disease process, PDT targets only the results of the process, the newly formed, abnormal, leaking blood vessels known as choroidal neovascularization (CNV). PDT couples low-intensity laser with a light-sensitive drug to close the leaking blood vessels beneath the retina.

To begin the treatment, a special light-sensitive drug called Visudyne (verteporfin) is infused into a vein in the arm and allowed to circulate throughout the body. In the bloodstream, the drug attaches itself to molecules of low-density lipoprotein (LDL) that are present in the abnormal blood vessels (CNV) in eyes with wet macular degeneration.

Next, eye drops are used to numb the eye and a special contact lens is placed on the eye to focus the laser. At this point, low-intensity laser energy is directed through the contact lens onto the area of CNV. The laser energy activates the drug that has accumulated in the abnormal blood vessels causing the vessels to close and stop leaking. Using this low-intensity laser spares the overlying retina from damage.
Usually, the entire PDT procedure takes less than 30 minutes. For the next several days, as the drug is clearing from your system, you should not expose yourself to direct sunlight or other bright lights.

Typically, several sessions of PDT are required to control CNV. It is common for patients to have as many as three or four treatments in the first year of therapy. Your ophthalmologist will use angiograms and/or optical coherence tomography (OCT) imaging of your retina to determine if additional treatments might be beneficial. The goal of treatment is to stabilize your vision. Your ophthalmologist will discuss the risks, benefits and limitations of PDT and alternatives for your particular case.
Combination Therapy

It is increasingly common for wet macular degeneration to be treated with a combination of therapies. An anti-VEGF drug may be used in conjunction with both a steroid and PDT. PDT and steroid or PDT and an anti-VEGF drug may also be used together. The initial results of using steroids in combination with PDT, for example, have shown better vision results than would be expected with PDT alone. Also, adding a steroid to PDT has been shown to decrease the number of PDT treatments required to control CNV. Several large studies are under way to confirm these findings.

Combination therapy appears to be effective because the different treatments combat CNV in different ways. PDT closes already leaking vessels, steroids act against inflammation and possibly VEGF, and anti-VEGF drugs address the underlying molecular events that lead to CNV. The goal of combination therapy is to control CNV while decreasing the number of times it must be treated.

Thermal Laser

Another treatment for wet macular degeneration used today in a limited number of cases is thermal laser therapy. In this treatment, a thermal (heat-producing) laser is used to coagulate CNV and stop the vessels from leaking and spreading. In some cases, the area of involvement may be too extensive or too close to the fovea to treat. Your doctor will discuss with you the risks, benefits and limitations of thermal laser treatment and alternatives in your particular case.

When thermal laser is used to treat wet macular degeneration, a series of precisely controlled beams of laser energy are directed through the pupil. Only minimal discomfort is felt as several pulses of energy are directed at the area of CNV.
Thermal laser treatment for wet macular degeneration is done on an outpatient basis with anesthetic eye drops. To begin the procedure, the patient is seated at a special slit lamp. A lens is placed on the eye to give the ophthalmologist a magnified view of the retina through the pupil. Next, the laser is aimed directly at the CNV under the retina. Only minimal discomfort is felt as several small pulses of laser light are directed at the CNV.

During treatment with thermal laser, the laser light (shown in green) passes through the tissues of the retina. In the area of CNV, the laser energy is converted into heat (white spot). This heat burns the CNV and some of the surrounding retinal tissues.

The laser light passes through the tissues of the retina where the light is absorbed by the CNV and pigmented tissues of the retinal pigment epithelium (RPE) and choroid. The absorption of laser energy produces heat that burns the CNV and some of the surrounding retinal tissues, causing a small scar to form. After treatment, the scarred area may appear as a permanent blind spot in your vision.

This fluorescein angiogram shows a well-defined area of CNV underneath the macula before treatment.

This fluorescein angiogram shows the same eye after thermal laser treatment. The CNV beneath the macula has been successfully treated.
While the efforts of the scientific community have already produced new treatments for macular degeneration, the search for even better therapies continues. Many new treatment strategies are being developed and tested. Some of these strategies have not yet lived up to expectations, but others continue to show great promise. This chapter provides an overview of ongoing research.

In the wet (neovascular) form of macular degeneration, the retina is damaged by the growth of abnormal blood vessels called choroidal neovascularization (CNV). It has recently been discovered that a protein called vascular endothelial growth factor (VEGF) is a main culprit in this process. Three treatments that inhibit the activity of VEGF, Lucentis (ranibizumab), Avastin (bevacizumab) and Macugen (pegaptanib sodium), are currently available, but other methods of blocking it are now being studied.

It is important to realize that laser treatment generally doesn’t improve your vision. Laser treatment is a compromise: a small portion of retina is sacrificed in order to prevent more widespread damage that would occur if the CNV were allowed to continue growing. When laser treatment is successful, the scar produced by the laser is smaller than the scar that would have resulted if the CNV had been left untreated.

Even if successful, thermal laser therapy treats the CNV but not the underlying disease process of macular degeneration. Therefore, it is common for CNV to come back in the future. Following laser treatment, it is often necessary to use angiography and OCT to detect any recurrences of CNV. If new CNV is found, your eye doctor may recommend additional treatment to preserve your remaining vision.

Inhibiting the Growth of Abnormal Blood Vessels

In the wet (neovascular) form of macular degeneration, the retina is damaged by the growth of abnormal blood vessels called choroidal neovascularization (CNV). It has recently been discovered that a protein called vascular endothelial growth factor (VEGF) is a main culprit in this process. Three treatments that inhibit the activity of VEGF, Lucentis (ranibizumab), Avastin (bevacizumab) and Macugen (pegaptanib sodium), are currently available, but other methods of blocking it are now being studied.
One such method is called RNA interference (RNAi). RNAi, also known as “gene silencing,” is being studied for the treatment of a variety of diseases. RNA, which is similar to DNA, helps to direct the functions of genes, in particular their production of proteins in the body. Fragments of RNA, called short interfering RNA (siRNA) have been engineered to disrupt the production of VEGF once they are injected into the eye. The potential advantage of siRNA treatment would be its ability to prevent the production of VEGF. Other anti-VEGF treatments work at a later stage in the macular degeneration disease process when excess VEGF has already been produced. Some researchers have described this difference as “turning off the faucet” instead of “mopping up the floor.” SiRNA may also produce fewer unwanted side effects because it works inside specific cells.

Another anti-VEGF treatment which has entered late-phase clinical trials is called VEGF Trap-Eye. This drug binds more tightly to VEGF than other anti-VEGF drugs so, hopefully, its effects will last longer before repeat treatment is needed.

While VEGF plays a major role in CNV, other substances and/or processes in the body may also be involved. Researchers are exploring other targets such as Placental Growth Factor, $\alpha_{5}\beta_{1}$ integrin, and the nicotinic acetylcholine (nACh) receptor pathway in hopes of finding even better treatments.

An experimental treatment known as AdPEDF represents a somewhat different approach to inhibiting the growth of abnormal blood vessels and causing those that are already present to regress. AdPEDF uses an adenovector, which is a carrier of DNA, to deliver the Pigment Epithelium-Derived Factor (PEDF) gene to the eye. Once inside, this gene promotes increased production of PEDF, which serves two important functions: regulation of normal blood vessel growth and protection of the photoreceptors from damage. Protection of the photoreceptors is a unique aspect of this potential treatment.
**Targeting the Immune System and Inflammation**

Strong evidence has emerged that a large percentage of macular degeneration cases can be explained by variations in a gene called Complement Factor H (CFH). This gene is important for helping the body's immune system respond to threats. When a variant, or mutated, form of this gene is inherited, the body is less able to control inflammation, which is now believed to be a major contributor to the development of macular degeneration. Multiple pharmaceutical companies are currently conducting research in this area.

Other genes at work in the immune system have also been linked to the risk of developing macular degeneration. This body of new knowledge can potentially lead to earlier detection and treatment of both the wet and dry forms of the disease.

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**Retaane**

Retaane (anecortave acetate) is a medication similar to but not the same as a steroid. It inhibits the formation of new blood vessels (CNV) that occurs in wet macular degeneration.

Retaane is very safe, lasts up to six months, and, unlike Lucentis, Avastin, and Macugen, it is delivered behind the eye through a curved flexible tube called a cannula. The cannula is slid alongside the eye until the end is resting directly underneath the macula. The cannula does not pierce the eye like an injection. Once the medication is in place, the cannula is removed.

Retaane has so far not lived up to expectations.
In many cases of macular degeneration, it appears that the retinal pigment epithelium (RPE) is the first component of the retina to fail. RPE transplantation is an attempt to replace diseased RPE tissue with healthy RPE cells.

First, a vitrectomy is performed to remove the vitreous gel from the eye. Then, a small incision is made in the retina to gain access to the space beneath the retina. At this point, RPE cells are injected into that space. As time passes and the retina heals, it is hoped that these transplanted RPE cells will arrange themselves properly to replace lost or diseased RPE.

Although RPE cells can be implanted successfully, they may not form the necessary connections with neighboring cells and tissues. Additionally, rejection of these cells by the body is possible.

Radiation therapy for wet macular degeneration is under investigation in a number of research centers. Because growing blood vessels are sensitive to radiation, it has been suggested that radiation may stop or slow CNV. The studies completed so far have not yielded consistent results. Several small studies have demonstrated some beneficial effects of radiation while other trials have shown no benefit.

Because growing blood vessels are sensitive to radiation, it has been suggested that radiation may stop or slow choroidal neovascularization (CNV).

The type of radiation and the method of delivery are key factors in how successful such treatments can be. The ideal radiation therapy would target and affect only areas of CNV and spare surrounding healthy tissue and blood vessels. Radiation therapy utilizing precisely delivered strontium 90 is currently making its way through clinical trials. It is being studied in conjunction with an anti-VEGF therapy.

For many surgeries involving the retina, the vitreous gel must first be removed from the eye in a procedure called vitrectomy.

Low Dose Radiation Therapy

Cell Transplantation
Surgical strategies for treating wet macular degeneration have also been explored. For example, submacular surgery is an attempt to remove CNV, scar tissue and blood from underneath the retina. After a vitrectomy to remove the vitreous, a small incision is made in the retina to gain access to the area underneath. Using fine microsurgical instruments, the surgeon removes the abnormal vessels from the eye. Early results using this technique have been somewhat disappointing. A series of large studies known as the Submacular Surgery Trials failed to show any significant benefits for these techniques. Vision is rarely significantly improved, and the blood vessels tend to grow back.

In macular degeneration, as in other areas of medicine, using stem cells to treat or cure disease is an exciting possibility. Current efforts are aimed at generating replacement RPE cells from stem cells. The cells could then be inserted into the retina where they would hopefully develop into functional cells and photoreceptors, restoring lost vision.

Another potential strategy for using human cells to treat macular degeneration is known as encapsulated cell technology. This treatment is an implant that is inserted into the eye. The implant contains human cells that have been genetically engineered to produce a protein called CNTF. This protein is believed to protect the retina’s specialized nerve cells, the photoreceptors, from damage due to the dry form of the disease. The implant would regularly release CNTF for an extended period of time, approximately 18 months.

In one surgical strategy, fine microsurgical instruments are used to remove neovascular vessels from underneath the retina.
Another kind of macular degeneration surgery that has been performed is called “macular translocation.” This technique aims to move the macula when it overlies diseased subretinal tissues. After a vitrectomy, a flap of retina is detached from the underlying tissues, cut, and rotated into a new position. The rotated retina is reattached to an area of healthier subretinal tissue. In most cases, a second surgery, involving the muscles of the eye, must also be performed.

While this experimental technique has helped some patients, it has been associated with a high percentage of serious complications. It is only performed at a handful of medical centers around the country.

**Implantable Miniature Telescope**

The Implantable Miniature Telescope (IMT) is a tiny optical device that is implanted directly into the eye. It magnifies the central visual images onto a larger retinal area than normal to improve vision and the quality of life for patients who have lost significant vision to macular degeneration. After surgical implantation, patients undergo a vision rehabilitation program.

A second IMT-like device is also currently being tested. It functions in a similar manner but addresses a shortcoming of the original design, the loss of peripheral vision in the IMT eye.
Artificial Vision

Because macular degeneration results in impaired functioning of the retina, researchers are attempting to bypass the retina using electronics or silicon chips to send signals to the brain to improve vision. Typically, surgery is required to implant such devices. This type of technology is many years away from helping people with macular degeneration, but it may offer hope for improved vision in the future.

Drug Delivery Methods

Most of the available and experimental drug therapies for macular degeneration currently require injections into the eye. The injections are safe but do carry some risks such as the potential for infection, especially when they are given frequently. Therefore, a major goal of ongoing research is the development of less invasive and longer-lasting ways to deliver drugs to the eye.

Eye drops are one attractive possibility. To be effective against macular degeneration, an eye drop formulation must be able to travel from the surface of the eye into the back of the eye, which has remained a challenge.

Rheopheresis

Rheopheresis is a procedure that attempts to remove abnormal, harmful circulating proteins from the bloodstream. Blood is removed from the veins in the arm and filtered with a machine to remove heavy proteins. The rest of the blood is returned to the bloodstream. This treatment was being evaluated for dry macular degeneration, but the studies have been suspended due to financial difficulties within the sponsoring company.
Laser Treatment of Drusen

As explained in previous chapters, most people with macular degeneration have some drusen or yellow deposits underneath the retina. It had been proposed that applying low intensity laser treatment to the drusen might cause them to shrink or disappear, thus eliminating the potential for advancing disease. This theory was evaluated in a large study known as CAPT. Unfortunately, in this study, the treatment was neither harmful nor helpful.

A different kind of laser treatment may hold more promise. In a method called “selective RPE laser treatment” (SRT), short laser pulses are applied to damaged areas of the RPE. Researchers believe the laser will not affect the retina’s other layers or cells, and the treated areas of the RPE will renew themselves and function normally.

Risk Factors

A number of factors are known to increase the risk of developing age-related macular degeneration. These risk factors are: age, family history of the disease, smoking, high blood pressure, history of cardiovascular disease, elevated serum lipids, variants of the Complement Factor H gene, and excessive exposure to bright sunlight. Some of these factors are within an individual’s control and can be modified through changes in behavior.

The following factors may increase the risk of developing age-related macular degeneration:

• age
• family history of the disease
• smoking
• high blood pressure
• history of cardiovascular disease
• elevated serum lipids
• variants of the Complement Factor H gene
• excessive exposure to bright sunlight
Elevated serum lipids (cholesterol and triglycerides) have been associated with an increased risk of macular degeneration. If you have either of these conditions, it is important to follow your doctors’ recommendations for diet and medication.

The Complement Factor H gene is involved in regulating inflammation in the body. Abnormalities in this gene have been linked with macular degeneration. Ongoing research may lead to new insights, diagnostic testing or treatments.

Excessive exposure of the eyes to sunlight, particularly the blue and ultraviolet wavelengths, is considered to be a risk factor for both macular degeneration and cataract formation. To protect the eyes from excessive exposure to sunlight, sunglasses that block UVB and UVA light should be worn. It is also advisable to wear a hat with a wide brim.

The rate of macular degeneration in the population clearly increases with age. By age 75, the odds of having this condition are greater than 1 in 3.

If your parent or sibling has macular degeneration, you have an increased risk of developing the disease yourself.

Smoking has been identified as a strong risk factor for macular degeneration in many studies. Smoking triples the risk of developing macular degeneration. Even secondhand smoking doubles the risk of macular degeneration compared with the general population. It is good to know that stopping smoking will reduce the risk. And, after 20 years of not smoking, the risks are no different than for non-smokers. It is particularly important for people with macular degeneration to try to stop smoking in order to protect their vision and to improve their overall health.

Hypertension (high blood pressure) and cardiovascular disease may place additional stress on the blood vessels of the eye, which could accelerate the development of macular degeneration and vision loss.
Nutritional Supplements

The role of nutrition in the development of macular degeneration is of great interest to patients and researchers. Many studies have been conducted over the past several years to test whether nutritional supplements can prevent or slow the progression of macular degeneration.

The largest research study of its kind, the Age-Related Eye Disease Study (AREDS), showed that one group of age-related macular degeneration patients, those who are at high risk for developing advanced age-related macular degeneration, may be helped by taking a specific combination of antioxidants and zinc. In this study, patients in this high-risk group lowered their risk for disease progression by approximately 25 percent when they took the recommended high doses of both zinc and antioxidants.

A nutritional supplement that contains a specific list of ingredients has been shown to slow the progression of macular degeneration in some people. It is important to talk with your doctor before taking supplements.

The supplements used in AREDS appeared to be safe when taken for the duration of the study. Several brands of supplements containing the AREDS ingredients are available over-the-counter, but patients with macular degeneration should consult with their eye doctor before taking them. It is important to note that the supplements only benefit people with certain macular degeneration characteristics. Since the supplements contain 5 to 15 times the recommended daily dietary intake of Vitamin E, Vitamin C, copper, zinc and Vitamin A.

Supplements Used in the AREDS Study:
- Vitamin C 500 mg
- Vitamin E 400 IU
- Vitamin A as 15 mg beta-carotene ~ 25,000 IU*
- Zinc 80 mg as zinc oxide
- Copper 2 mg as cupric oxide

*Individuals who smoke should not take supplements containing beta-carotene or Vitamin A because they have been associated with an increased risk of developing lung cancer in smokers. Individuals with other forms of macular degeneration such as Stargardt’s Disease should consult their ophthalmologist before taking any supplements.
A/beta-carotene, they can be harmful for some people, such as those with certain health conditions or those taking certain medications such as blood thinners. Additionally, high doses of beta-carotene/Vitamin A have been shown to increase the risk of lung cancer in individuals who smoke. Also, there are concerns that excessive beta-carotene/Vitamin A could aggravate a juvenile form of macular degeneration known as Stargardt’s Disease.

The National Eye Institute is currently conducting a second AREDS research project called AREDS2. This new study is testing the effects of supplements containing macular xanthophylls (lutein and zeaxanthin) and/or long-chain Omega-3 fatty acids (docosahexaenoic acid and eicosapentaenoic acid) on the progression to advanced age-related macular degeneration. AREDS2 involves 4,000 people who have either large drusen in both eyes or large drusen in one eye and advanced macular degeneration (neovascular or geographic atrophy) in the other eye.

Based on your particular case and the information already available about nutrition and age-related macular degeneration, your eye doctor may recommend that you use supplements containing lutein/zeaxanthin and/or Omega-3 fatty acids.

Research has shown that people who eat diets high in spinach or collard greens are less likely to develop macular degeneration. These and other green leafy vegetables, such as kale, mustard greens, turnip greens and romaine lettuce, are good sources of two important macular pigments: lutein and zeaxanthin. These recommended nutrients are also found in orange peppers, yellow corn, broccoli, avocados, oranges and egg yolks.
Lutein and zeaxanthin supplements were not available at the time of the first AREDS study and therefore could not be tested. They are being tested now in AREDS2, and many physicians recommend taking supplement formulations containing these ingredients or adding these nutrients to your diet.

Some people with macular degeneration have diets deficient in the mineral zinc. Zinc is found naturally in shellfish, fish, meat, oats, beans and peas.

Research has shown that patients who eat diets high in Omega-3 fatty acids are less likely to develop macular degeneration. These compounds may also have a protective role against ongoing retinal damage. Good dietary sources of Omega-3 fatty acids are fish, fish oils, walnuts and certain plant oils such as flaxseed and canola. Further research is being conducted to obtain a more complete understanding of the impact of these unsaturated fatty acids on macular degeneration.

For macular health, it is recommended to eat a well-balanced diet with plenty of fruit, fish and green leafy vegetables and to avoid excessive saturated fats and cholesterol. You should talk with your doctor about also taking a daily multivitamin such as Centrum.

Several substances such as bilberry, ginkgo biloba, bioflavinoids and shark cartilage have received attention in the popular media. There is no good scientific evidence regarding the safety or effectiveness of these preparations in preventing or treating macular degeneration. If you have questions about such claims, ask your eye doctor.
Age-related macular degeneration and other types of macular degeneration can cause central vision to deteriorate. When central vision deteriorates, it may be difficult to perform tasks that require detailed sight, such as recognizing people’s faces and seeing street signs and curbs. Also, it may be difficult or impossible to read a newspaper or small print on a pill bottle. Vision impairments such as these cannot be fixed with regular eyeglasses or contact lenses. When they interfere with daily activities, they are referred to as “low vision.”

Reading the small print on a pill bottle may be difficult or impossible for someone with low vision.

The pictures on the following pages illustrate how the world might look to people with different kinds of vision impairments that can cause low vision, including macular degeneration.

A person with normal vision or vision corrected to 20/20 with glasses sees this street scene.

A cataract occurs when the normally transparent lens of the eye starts to become opaque. This street scene looks blurred because of reduced visual acuity, and the colors do not seem as vivid. These effects become more noticeable in glaring light.

With cataracts, print may appear hazy or lacking in contrast.
Vision deterioration and low vision can be frightening. You may fear the loss of your job, a decrease in your quality of life or the loss of your independent lifestyle. Thankfully, people rarely lose all of their vision as a result of macular degeneration alone. Even if you are “legally blind,” which means your visual acuity on an eye chart is 20/200 or worse even with glasses, you can continue to lead a productive and satisfying life. Low vision doesn’t signal an end to independent living for most people.

There are many things you can do to help yourself. For example, you can see a low vision specialist or participate in vision rehabilitation, both of which help you to learn skills and strategies for making maximum use of your vision. Also, a wide variety of low vision optical devices and non-optical devices are available to help you with everything from reading, cooking and performing other daily activities to completing work-related tasks, using a computer and enjoying leisure activities.
A Low Vision Evaluation

If you have experienced some vision loss from macular degeneration, your eye doctor may refer you to a low vision specialist for an evaluation. The specialist will begin your evaluation by asking you about your medical, eye and vision history.

To get a better idea of exactly what you can see, the specialist will perform vision tests. Special charts will be used to evaluate the acuity, or sharpness, of your near and distance vision. Functional vision tests will also be performed. Functional vision tests evaluate not only how well you see letters on an eye chart, but also how well you see faces, clocks, street signs, newspaper print and many other visual cues that help guide all of us through the day.

In addition, the low vision specialist will test a very important aspect of vision called contrast sensitivity. Contrast sensitivity is a measurement of the ability to visually separate objects from their backgrounds. For example, seeing a large bold black letter on a white page is easier and requires less contrast sensitivity than seeing a gray car coming over a foggy horizon. The black letter stands out from its background; the gray car does not. Contrast sensitivity declines as we age and as a result of macular degeneration. Poor contrast sensitivity interferes with tasks such as reading and seeing a restaurant menu in dim lighting. It also impedes the ability to move around safely and travel independently.

During the evaluation, it is important to tell the specialist what activities you need or want to do but are having difficulty with because of your vision limitations. Also, let the low vision specialist know if you have difficulty adapting to changing levels of light when you come indoors or go outside. Tell him or her if glare bothers you or if you can’t seem to find good lighting for a particular task.

During a low vision evaluation, special charts are used to assess your ability to detect contrast.
Helpful Devices for Work, Home and Hobbies

After performing the vision tests and talking with you about your interests and what you are having trouble doing, the low vision specialist will help you test some optical devices that can help.

The types of optical devices the specialist can prescribe include:

- strong reading lenses, also known as microscopic lenses
- hand-held and stand magnifiers that have contrast-enhancing illumination systems
- electronic magnification devices
- computer software that includes screen magnification, voice output or speech recognition
- telescopic devices
- absorptive lenses

Examples of low vision optical devices appear on the following pages.

Strong reading glasses are a convenient option because both hands are free to hold and move reading material or to work on a project.

If strong reading glasses do not provide enough magnification, hand-held magnifiers can also be used. Some have a built-in light source that provides increased contrast for reading.

Stand magnifiers rest directly on a page of print. As long as the magnifier sits on the page, the letters remain in focus. Stand magnifiers are more powerful than hand-held magnifiers.
Electronic magnification devices may also be referred to as reading machines or video magnifiers. They provide the greatest possible magnification and highest contrast for reading and performing close-up tasks.

Some models are designed to sit on a desktop; others are portable. Recent advances in flat screen technology provide higher resolution, which is an important advantage compared with older monitors.

Also, with an electronic magnification device, you can make black letters appear on a white background or vice versa, whichever is more helpful for you. Advanced models can scroll words in continuous lines or up the screen like a teleprompter used by TV newscasters.

Telescopic devices make an object appear closer than it really is. Hand-held telescopes are monocular (for use with one eye) and are useful for looking at items like a street sign, a building directory or a fast-food menu.

Some kinds of electronic magnification devices are hand-held. Others are worn on the head, similar to a pair of glasses, and can be focused to see objects at a distance, up close or any range in between.

Telescopes can also be mounted on spectacles for one or both eyes. They allow the hands to remain free, making them useful for activities such as going to the theater or playing cards. In some states they can be used for driving.
If you have low vision, you may also benefit from non-optical devices. Hundreds of these products, such as large-print books, cooking aids, talking clocks, writing guides and special lighting, can make everyday living easier. Examples of non-optical low vision devices appear on the following pages.

Also known as tints, filters and sunwear, absorptive lenses block different wavelengths of light, making it easier for some people to see. Absorptive lenses may be used indoors or outdoors to reduce glare, to block ultraviolet or infrared light or to enhance contrast.

Large-print books can be purchased or borrowed from many sources.

Telephones with large buttons are easier to use. Voice-activated telephones are also available.

Writing guides can be used for tasks such as addressing an envelope or writing a check.

Many talking devices, such as this calculator, can make daily tasks easier for the visually impaired.
A Team Effort

The low vision specialist or your eye doctor may connect you with other professionals who can help you in a variety of ways. Such professionals may include:

- certified low vision therapists
- occupational therapists
- vision rehabilitation specialists
- orientation and mobility instructors
- social workers and mental health professionals
- technology specialists
- employment specialists

Vision rehabilitation specialists, for example, teach a skill called eccentric viewing, which would allow you to “look around” dark spots in your vision and use a more healthy area of your retina to see. Orientation and mobility instructors teach strategies and techniques for important actions, such as finding your place in a room or moving around indoors or outdoors safely. The ultimate goal of the team of professionals is to enable you to make absolutely the best use of the vision you have and to make sure you receive all of the services that meet your needs.

Resources

If you have low vision due to macular degeneration, you may find the following types of resources helpful. You can also ask your eye doctor for a list of resources.

Books

Making Life More Livable: Simple Adaptations for Living at Home After Vision Loss
Edited by Maureen A. Duffy, M.S.
American Foundation for the Blind Press

Macular Degeneration: The Complete Guide to Saving and Maximizing Your Sight
Lylas G. Mogk, M.D., Marja Mogk, Ph.D.
The Random House Publishing Group

Mayo Clinic Guide to Better Vision
Edited by Sophie J. Bakri, M.D.
Mayo Clinic Health Solutions

Coping With Vision Loss: Maximizing What You Can See and Do
Bill Chapman
Hunter House Publishers
Information and Support

Lighthouse International
(212) 821-9200
(800) 829-0500
www.lighthouse.org

American Foundation for the Blind
(800) 232-5463
www.afb.org

Association for Macular Diseases, Inc.
(212) 605-3719
www.macula.org

The Macula Foundation, Inc.
(800) 622-8524
www.macula.org

Large Print and Audio Materials

The American Printing House for the Blind, Inc.
(800) 223-1839
www.aph.org

Eyes Only Quarterly Newsletter
Association for Macular Diseases, Inc.
(212) 605-3719
www.macula.org

Library of Congress
National Library Service for the Blind and Physically Handicapped
(888) 657-7323
www.loc.gov/nls
The Amsler Grid

The Amsler grid is a quick and simple test you can take at home to monitor changes in your vision. People with macular degeneration should test their eyes with the Amsler grid several times a week.

Directions for using the Amsler grid:

1. If you wear reading glasses, put them on for this test.
2. Hold this book at a comfortable reading distance.
3. Cover one of your eyes.
4. Look at the grid. Keep your eye focused on the white dot at the center of the grid throughout the test.
5. Without moving your eye from the center dot, notice the lines that make up the grid. All of the lines should be straight and all of the squares should look the same. There shouldn’t be any blank, dark, or distorted areas on the grid.
6. Call your eye doctor right away if you notice anything unusual or abnormal in your vision.
7. Use the same procedure to test your other eye.
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