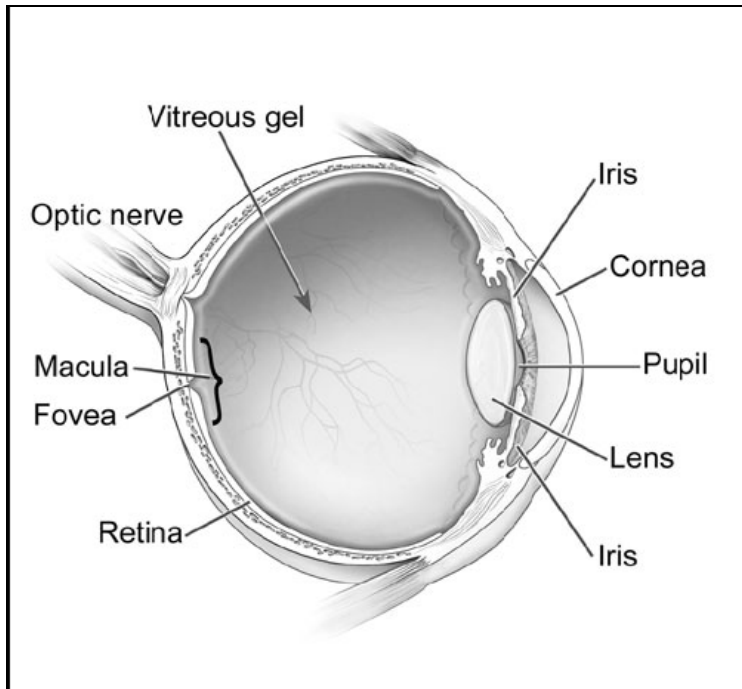




## An Investigational Treatment for Wet Age-Related Macular Degeneration (AMD)



The cornea, pupil and lens are clear, allowing light rays to pass through. The cornea and lens focus the light onto the retina, a layer of light-sensitive cells lining the back of your eye. The retina converts light rays into signals that are sent through the optic nerve to your brain, where they are recognized as images. The retina consists of two areas: the **macula** and the **peripheral retina**. The macula is a small area in the center of the retina near the optic nerve. Even though the macula makes up only a small part of the retina, it is much more sensitive to detail than the peripheral retina. The macula is responsible for focusing central vision in the eye, and it controls our ability to read, drive a car, recognize faces or colors, and see objects in fine detail.

### **Macular Degeneration**

Macular degeneration is caused by deterioration of the macula. As people age, their chance for developing eye disease increases dramatically. Unfortunately, the specific factors that cause macular degeneration are not conclusively known.



Age-related macular degeneration (AMD) is a leading cause of vision loss. This condition may cause permanent loss of your central vision (as illustrated in the picture below).



### **AMD Development**

AMD is one of the leading causes of adult visual loss in the developed world. AMD occurs in a non-neovascular, atrophic "dry" form or neovascular "wet" form. Patients with "dry AMD" have subretinal deposits (drusen), pigment changes, and some retinal atrophy, but their central vision is either preserved or deteriorates slowly.

Approximately 10% of patients with the "dry" form of AMD progress to the "wet" form, characterized by neovascularization, or overgrowth of new blood vessels under the retina. These vessels leak fluid that causes scar tissue to form, which in turn compromises vision - typically the central vision that is essential for reading and functioning. Patients who manifest the neovascular form of AMD represent the majority who develop legal blindness (defined as best corrected visual acuity of 20/200 or worse in the better-seeing eye). Loss of vision has a major impact on the quality of life and independence for those afflicted, causing both economic and personal hardship.



### **Dry AMD**

In the dry type of macular degeneration, the deterioration of the retina is associated with the formation of small yellow deposits under the macula, known as drusen. This leads to a thinning and drying out of the macula, causing it to lose its function. The amount of central vision loss is directly related to the location and amount of retinal thinning caused by the drusen. Vision loss in the dry form of AMD is usually gradual. People who develop dry AMD must carefully monitor their central vision, since this form can change into the more damaging wet form of AMD.

Dry AMD symptoms: Development of drusen  
Slightly blurred vision  
Difficulty recognizing faces  
More light is needed for reading and other activities

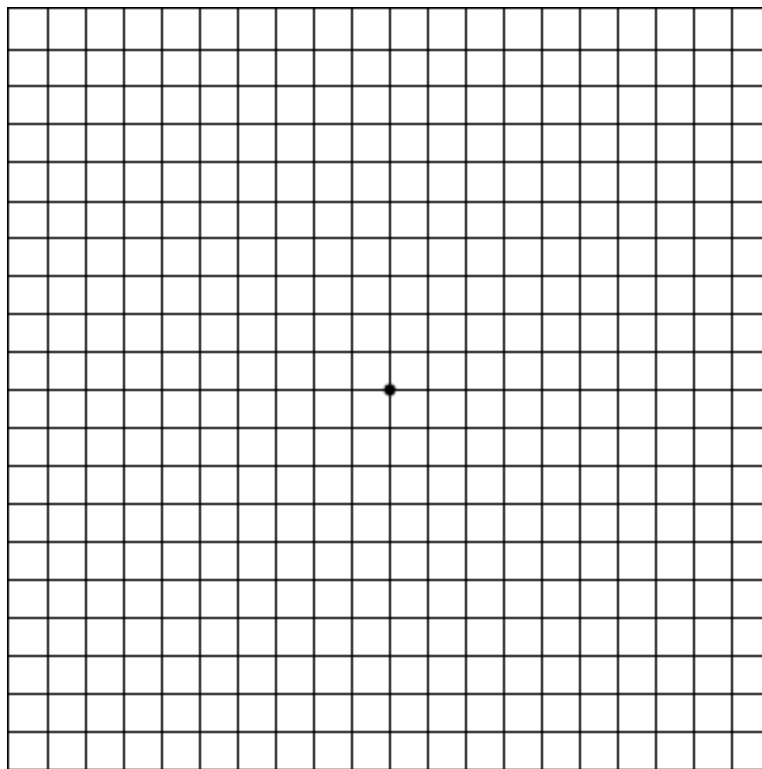
### **Wet AMD**

Wet AMD occurs when abnormal blood vessels begin to grow underneath the retina. These new blood vessels may leak fluid or blood, thereby blurring or distorting central vision. Vision loss from wet AMD may occur faster and be more noticeable than from dry AMD. The longer these abnormal vessels leak or grow, the more detail vision will be lost. The earlier wet AMD is diagnosed, the better the patients' chance of preserving some or much of their central vision.

Wet AMD Symptoms: Difficulty recognizing faces at distance  
Blurred spot or blind spot in center of vision  
Rapid loss of central vision  
Straight lines appear wavy

### **Monitoring Your Vision with the Amsler Grid**

If you have been diagnosed with dry AMD, you should use a chart called the Amsler Grid every day to monitor your vision, as dry AMD can change into the more damaging wet form. This is a simple vision test in which you will look at a chart resembling graph paper:



Cover one eye and look directly at the point in the center of the grid, observing the pattern of vertical and horizontal lines in your peripheral vision. You will look for any visual abnormalities, such as areas of distortion, darkness or blurriness. If you detect any changes when looking at the grid, you should notify your ophthalmologist immediately.

### **Current and Potential Therapeutic Approaches for Wet AMD**

Historically, treatment regimens have focused on directly sealing off abnormal vasculature using laser or laser activated drugs. These approaches have generally not had the broad efficacy levels necessary to be long term clinical solutions. More recently there have been improvements in drug therapy that have demonstrated superior clinical effectiveness over both laser as well as laser activated drugs.

**LASER:** A high-energy laser beam is used to create small burns in areas with abnormal blood vessels. The process can seal off and destroy the CNV that has developed under the macula. The



process is to prevent further damage to the macula and halt continued vision loss. Only a small percentage of people who have wet macular degeneration are candidates for this procedure. Efficacy is a problem. Repeat laser treatment may not be possible in such cases.

**PHOTODYNAMIC THERAPY (PDT):** This procedure combines a cold laser and a light-sensitizing drug called verteporfin (Visudyne®) that's injected into your bloodstream. The drug concentrates in the CNV under the macula. When the doctor directs cold-laser light at the macula, the drug releases substances that theoretically close off the abnormal blood vessels without damaging the macula, and the CNV transforms into a thin scar. The therapy can be repeated if the CNV doesn't close or if it reopens after initial closure. The use of PDT is declining but is not expected to disappear as physicians experiment with combination therapies of PDT with other drug therapies.

**MACUGEN®:** This is the first anti-VEGF ophthalmic drug approved by the FDA. It is delivered by injection to reach the back of the eye. Each patient will receive nine treatments during the year taking up more than 11 hours of physician time during the year with 6-to-7% of patients having up to 3 lines of improved vision.

**LUCENTIS®:** This Genentech drug was recently registered by the FDA with approval for marketing and already has set a high bar for efficacious treatment. Lucentis is already perceived as the standard of care due to the off label use of Avastin, a related drug used to treat colo-rectal cancer. It is estimated that each patient will receive nine to twelve treatments during the year taking up more than 6.5 hours of physician time during the year with 25-34% of patients having up to 3 lines of improved vision.

**AVASTIN®:** This Genentech drug was cleared by FDA for the treatment of colon cancer. Avastin is an antiangiogenic drug like Lucentis. Ophthalmologists began utilizing it for the treatment of wet AMD in mid-2005. This is off-label use.

While these approaches have demonstrated promise for treating the disease, the NeoVista device is being tested to see if it has the potential to provide dramatically more durable treatment without requiring the constant re-treatment necessary with drug therapy alone.