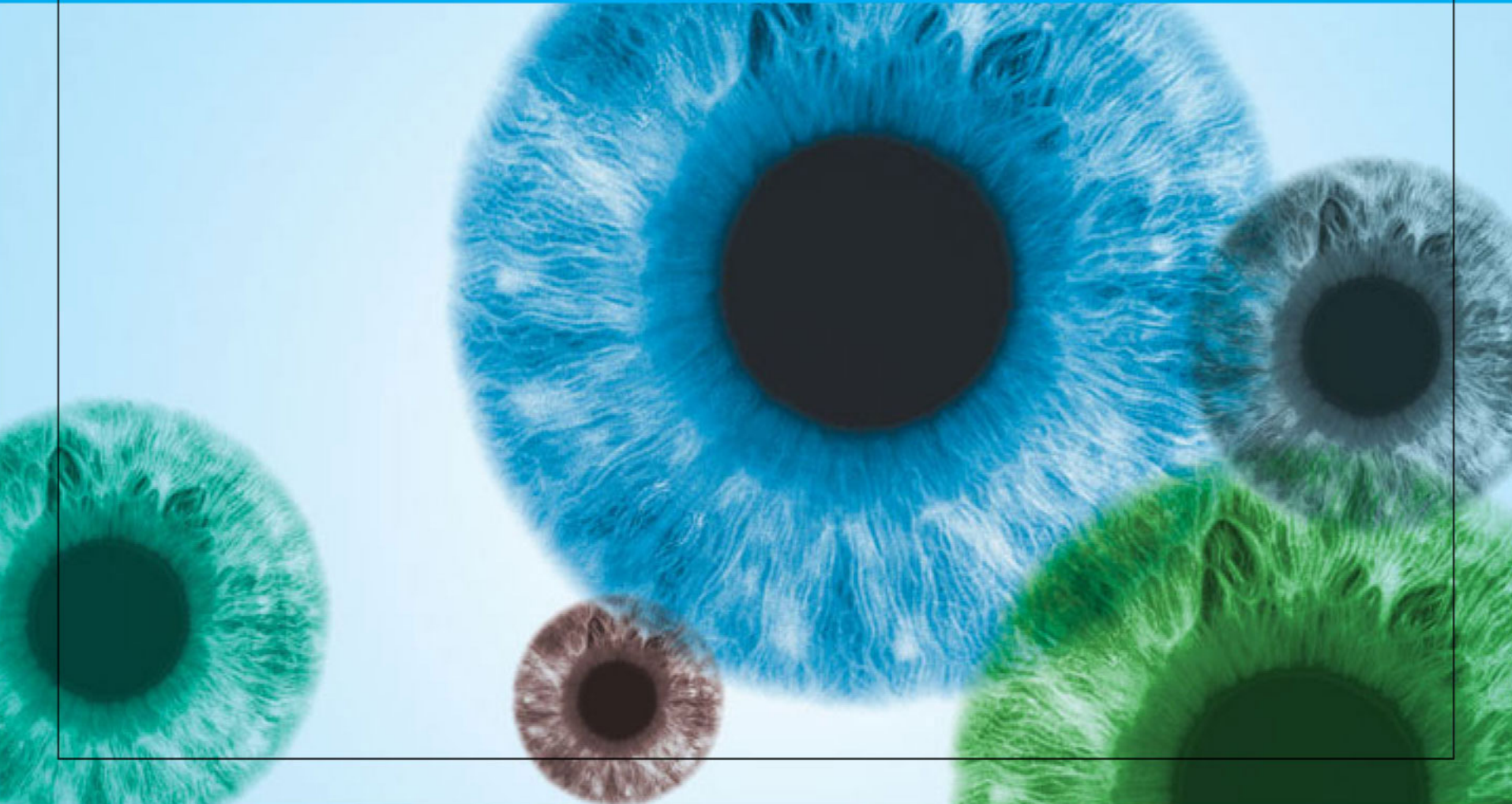


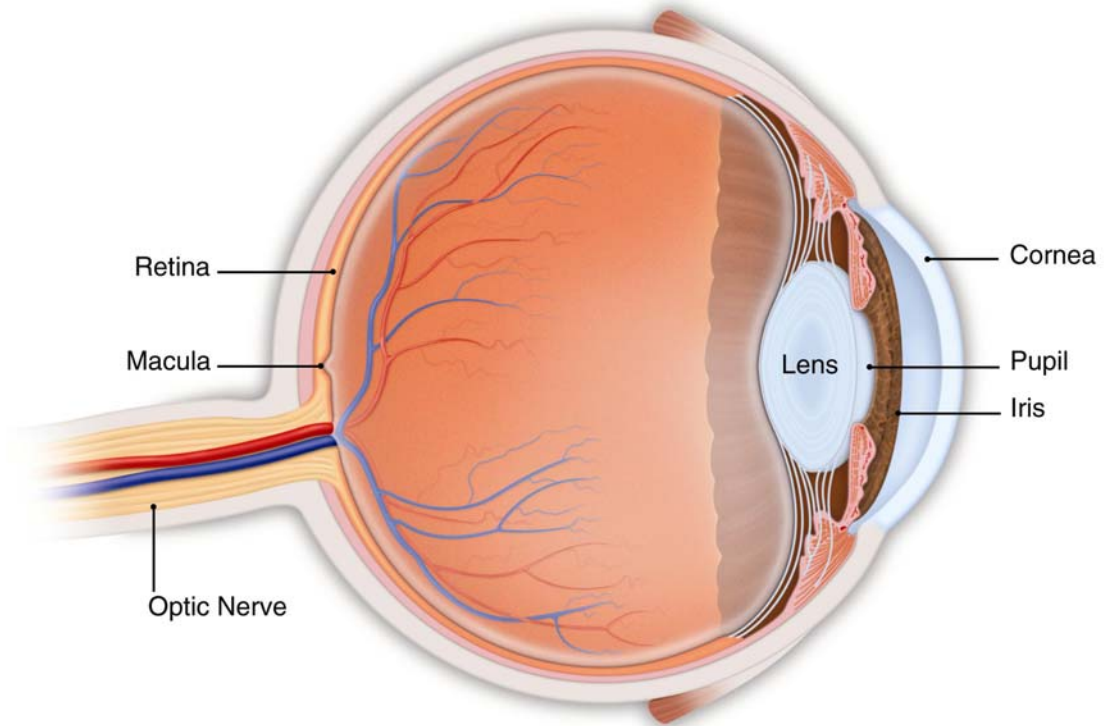
# Age-Related Macular Degeneration



**This presentation is intended for informational purposes only. It is not intended to diagnose or treat any conditions. Consult your medical practitioner for individual advice.**

# The healthy eye

- Light rays enter the eye through the cornea, pupil and lens.
- These light rays are focused directly onto the retina, the light-sensitive tissue lining the back of the eye.
- The retina converts light rays into impulses sent through the optic nerve to your brain, where they are recognized as images.



# The healthy eye

The retina, made of many layers sandwiched together into a smooth surface, consists of two areas, the *macula* and *peripheral retina*.

## Macula

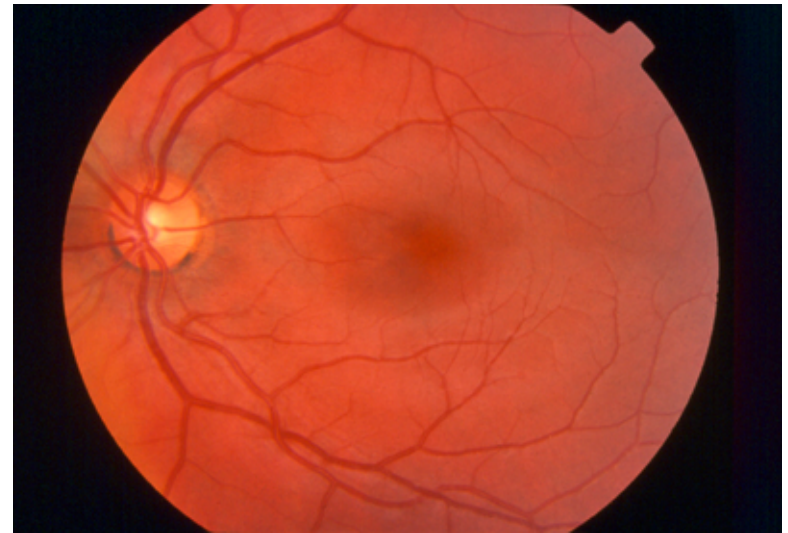
- Small area in center of retina that allows you to see fine details clearly.
- Allows activities like reading small print and recognizing a face.



# The healthy eye

## Peripheral retina

- Gives you side-or peripheral-vision (not detail vision).
- Helps you see someone standing off to your side, but you won't see who the person is.



Normal retina

# What is age-related macular degeneration (AMD)?

- The macula is disrupted by deposits called *drusen*, or other age-related changes.
- These changes, if severe enough, may cause vision to deteriorate.
- When the macula breaks down, you lose your central vision, but it does not affect your peripheral (side) vision.

# Age-related macular degeneration (AMD)

- **A leading cause of severe vision loss in people over 65 years of age.**
- **Associated with the aging process; the macula may lose effectiveness over time.**

# Symptoms of AMD

- **Early AMD may be hardly noticeable, and may only occur in one eye.**
- **Blurring of words on a page**
- **Difficulty recognizing people's faces.**
- **Dark or empty areas may appear in the center of vision.**
- **Straight lines may look distorted.**



**Dark areas may appear in your central vision**

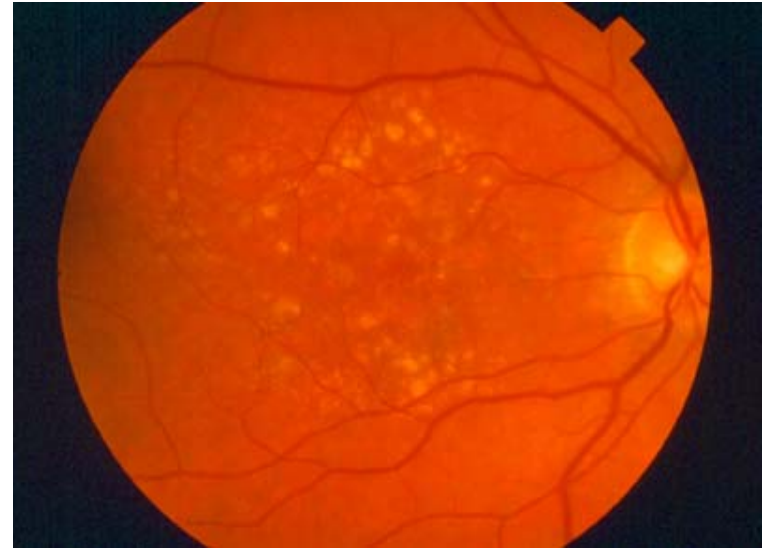
# Two types of AMD

- **Atrophic (“dry”) macular degeneration**
- **Exudative (“wet”) macular degeneration**

# Types of AMD

## Atrophic (“dry”) AMD

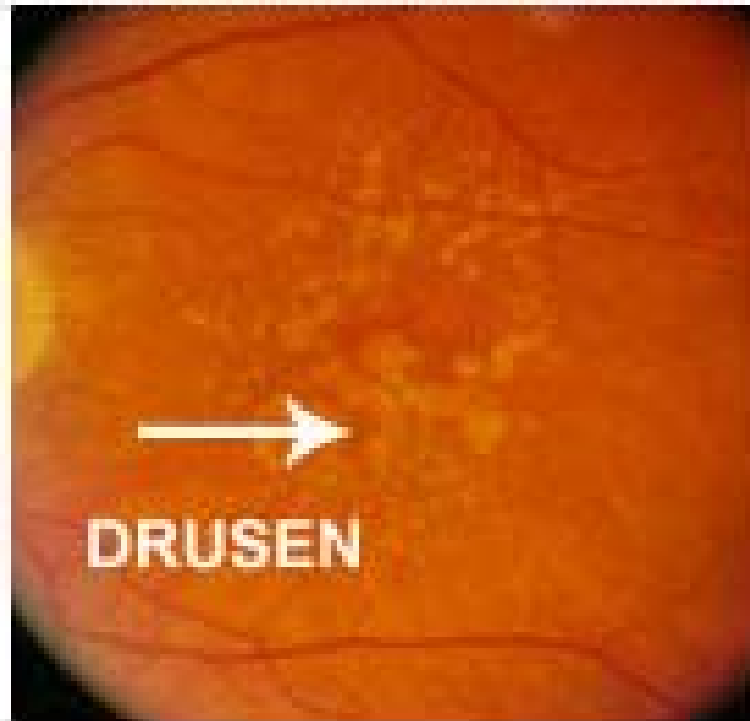
- **Caused by aging and thinning of macular tissues when drusen are present**
- **Most common form**
- **Vision loss is usually gradual**



**With AMD, drusen are seen in the retina**

# Dry AMD

Courtesy of AREDS Research Group.

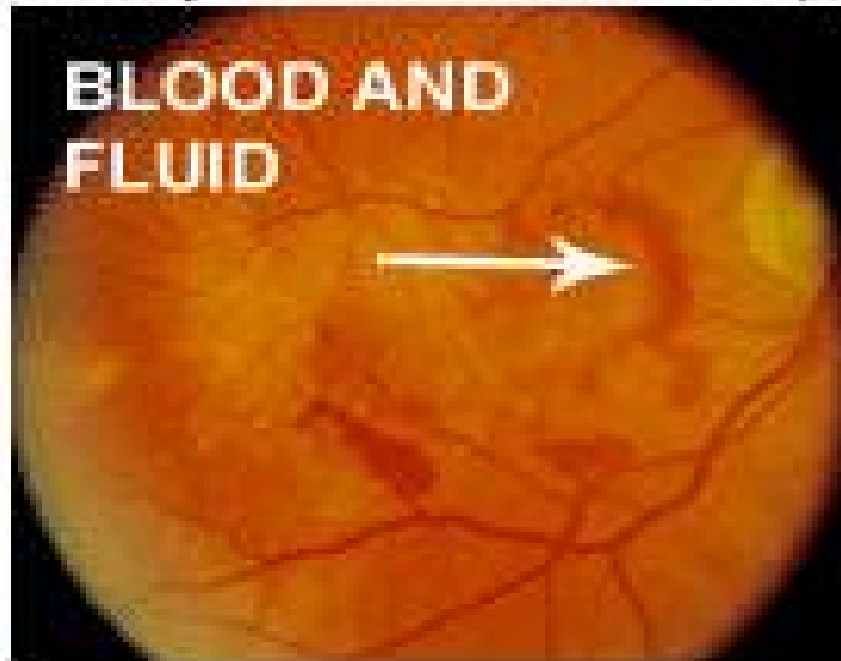


*Dry AMD*



# Wet AMD

Courtesy of AREDS Research Group.



**Wet AMD**

# Diagnosing AMD

- **Many people do not realize they have a problem until vision blurs.**
- **Your eye doctor can detect early AMD during an eye exam that includes:**
  - Dilated eye exam
  - Fluorescein angiography
  - Optical Coherence Tomography (OCT)

# Diagnosing AMD

## Fluorescein angiography:

- Dye is injected into the arm where it travels through the body to the blood vessels in the eye
- Special photographs are taken of the eye; dye will highlight abnormal blood vessel growth under the retina.

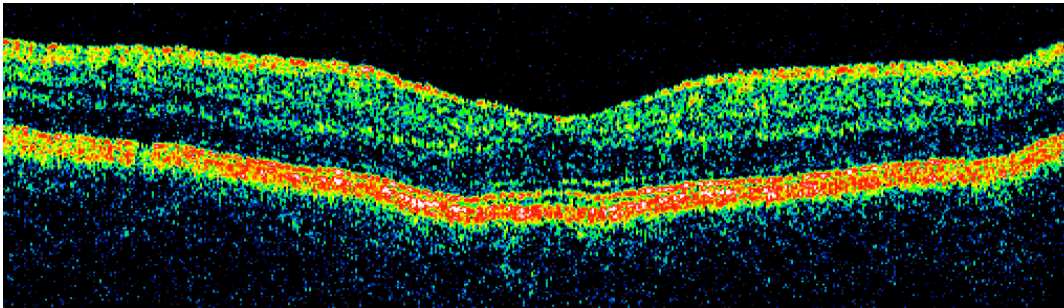


Fluorescein angiogram

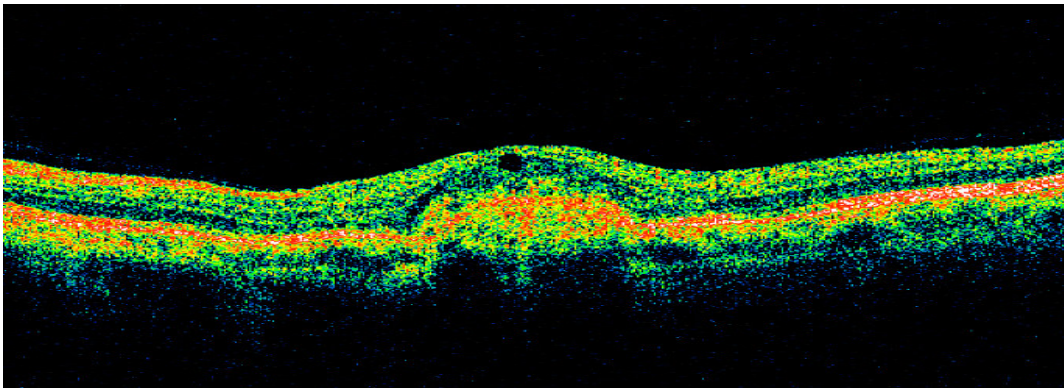
# Diagnosing AMD

## OCT (Optical Coherence Tomography):

- A cross sectional image of retinal tissue
- Provides a virtual biopsy



Normal, healthy  
macula



AMD

# Treating dry AMD

- **There is no treatment for dry AMD, but there are ways to slow the progression.**
- **Nutritional supplements**
  - Vitamins C, E
  - Beta carotene
  - Zinc
  - Lutein

# Treating dry AMD

- The Age-Related Eye Disease Study (AREDS) showed that people with the intermediate stage dry AMD could reduce their risk of progressing to advanced AMD by about 25% by taking a special high-dose formula of the supplements, sold without a prescription.
- **AREDS Formula:**
  - Zinc 80 mg
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - Beta-Carotene 15 mg
  - Copper 2 mg

# Treating dry AMD

- **High-dose vitamins, even when sold without a prescription, may present a risk for some people.**
  - Smokers taking beta-carotene may increase their risk of lung cancer.
  - High Dose Vitamin E (400 IU)
    - 5% higher death rates
    - Bleeding
    - Suppresses body's antioxidants
    - Reduces effect of cholesterol lowering medications
- **We strongly encourage you to talk to your doctor about the risks and benefits of these dietary supplements before taking them.**

# Treating dry AMD

- **Vitamin supplements are not cures for AMD, nor can they restore vision already lost from AMD.**
- **For dry AMD:**
  - Multivitamins with LUTEIN
  - 3 servings of fruit a day
  - Avoid snack foods, smoking, and sunlight
  - Eat fish, spinach, and collard greens

# Evolution of Treatments for Wet AMD

**Thermal “hot” laser**



**PDT “cool” laser**



**Anti-VEGF medication: Macugen**



**Anti-VEGF medication: Avastin / Lucentis**

# Previous Treatments for Wet AMD

## Thermal “hot” laser therapy

- Destroyed abnormal blood vessels by “burning” it with a high-energy laser.
- Scar tissue formed where treatment occurred, creating a permanent blind spot that might be noticeable in your vision.

# Previous Treatments for Wet AMD

## Photodynamic therapy (PDT) “cool” laser

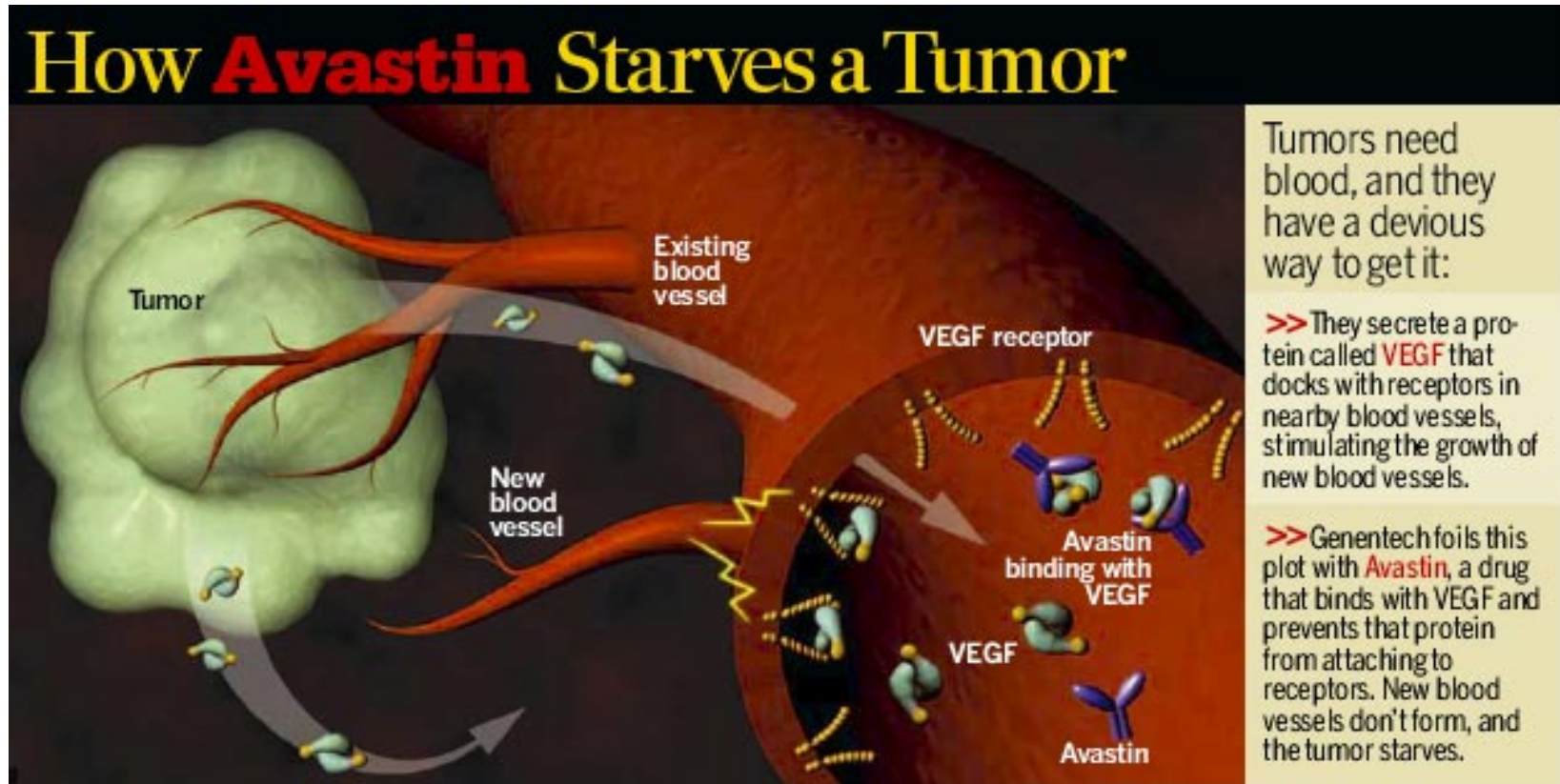
- Used a combination of a medication injected into the arm and a lower-power “cool” laser.
- Laser activated the drug, which destroyed the abnormal blood vessels.
- Better than thermal laser, but still caused scar tissue.

# Anti-VEGF Treatments

- Non-destructive treatments for wet AMD
- Not a laser
- A medication injected directly into the eye.
- **Macugen** approved by FDA in **Dec 2004**
- **Avastin** approved by FDA in **Feb 2004** for the treatment of **colon cancer**, but was used “off-label” in the eye since **Nov 2005** while Lucentis was awaiting FDA approval.
- **Lucentis** approved by FDA in **July 2006**

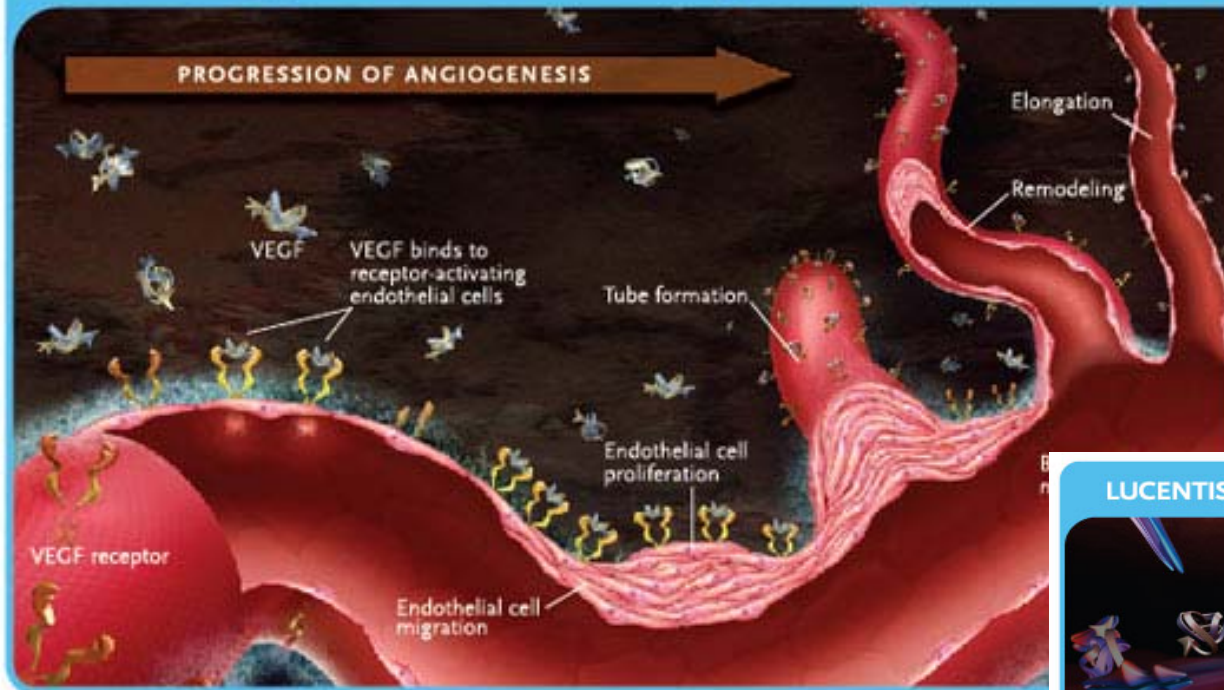
# VEGF Antagonists

These drugs block a protein called **VEGF** (vascular endothelial growth factor) which causes the growth of abnormal blood vessels in wet AMD.



# VEGF

## VEGF-A triggers CNV and vascular leakage



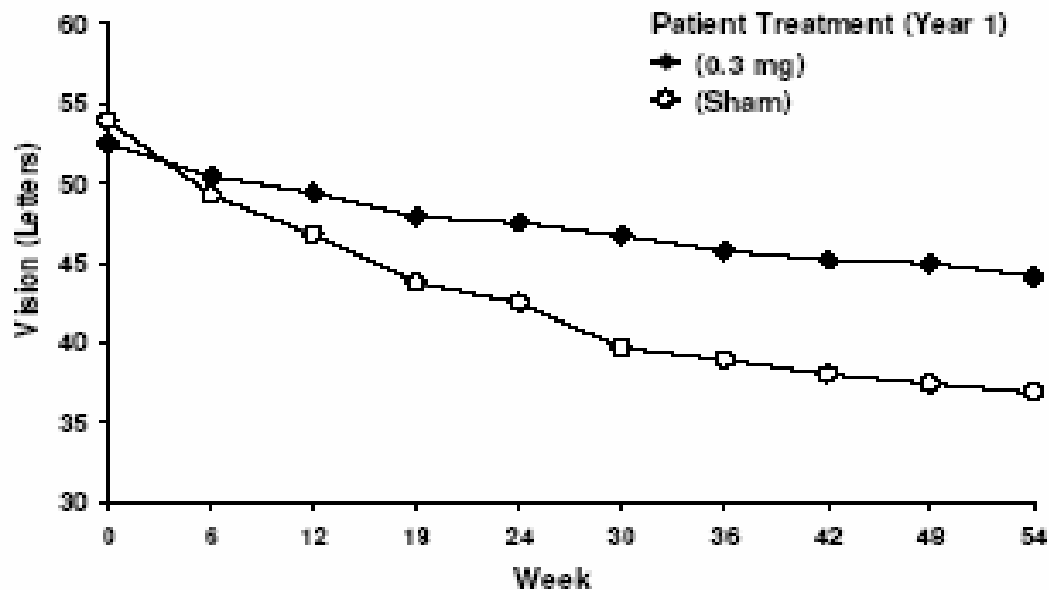
## LUCENTIS™ binding to VEGF-A



# Macugen – Vision Year 1

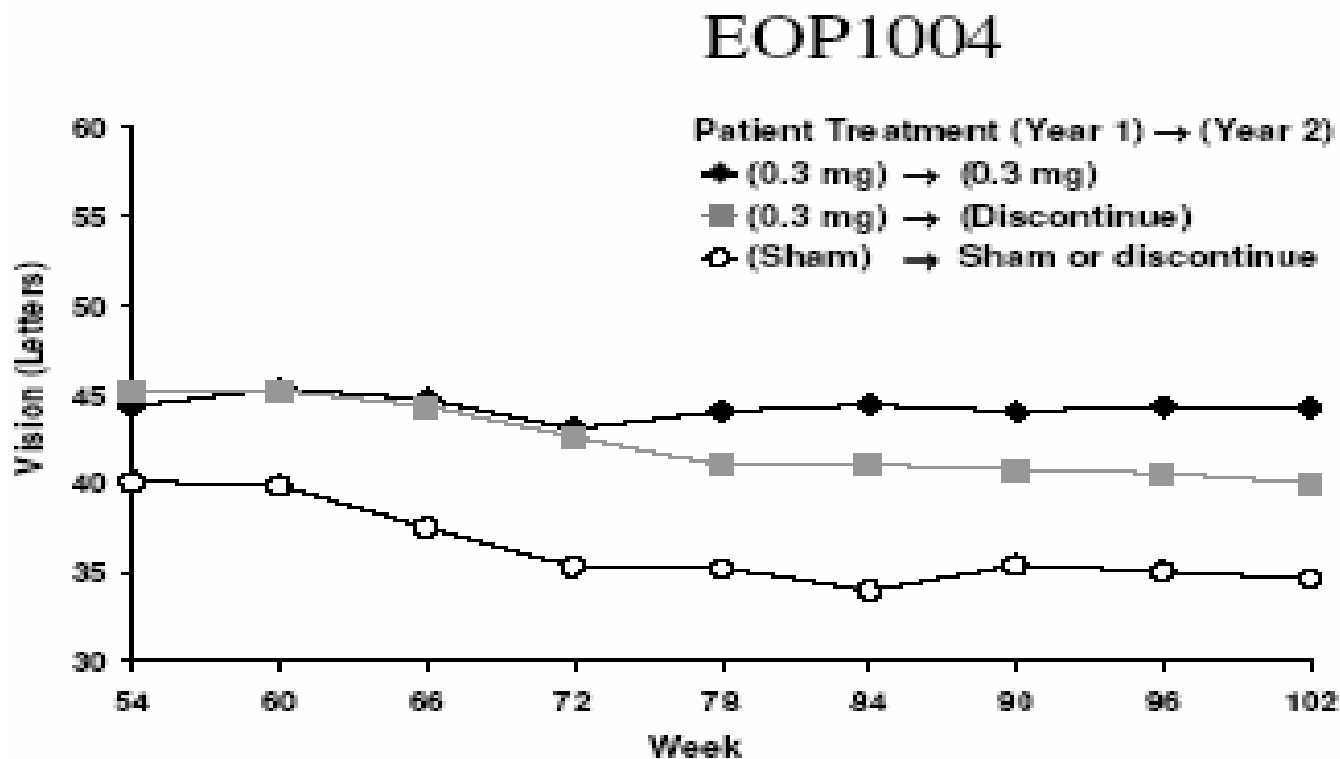
Given every 6 weeks

EOP1004



**27% decrease in the rate of vision loss**

# Macugen – Vision Year 2



Only a small group of patients  
(about **5-10%**) had an **improvement** in vision.

# Lucentis

- The first and only treatment proven to **improve vision** of 15 or more letters on the eye chart in up to **40%** of patients with wet AMD.
- Up to **96% maintained vision**

# Our Experience with Anti-VEGF

## CASE 1

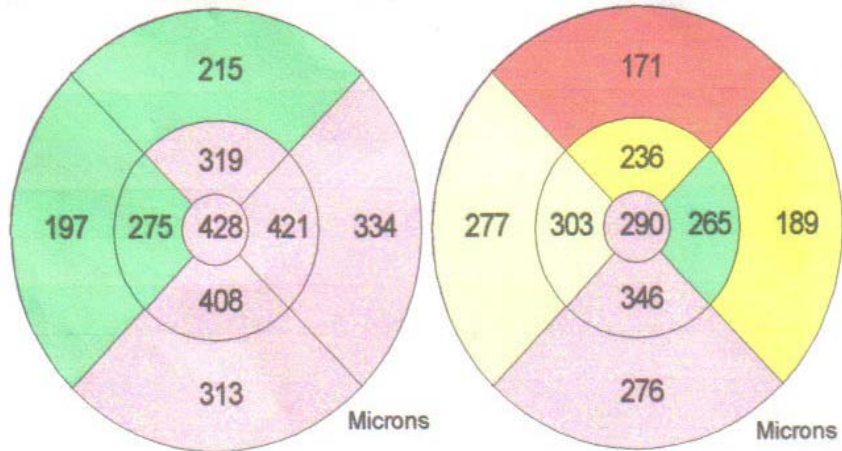
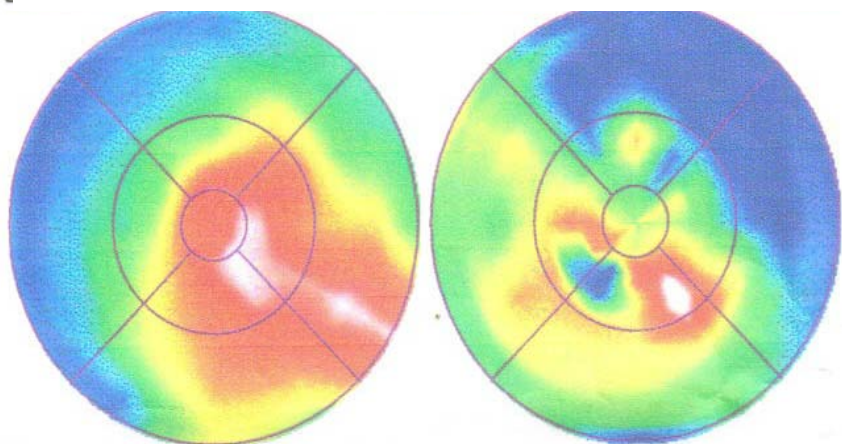
- **73 year old woman**
- **New onset wet AMD right eye**
- **No previous treatments**

# Before anti-VEGF

# After anti-VEGF

Right eye

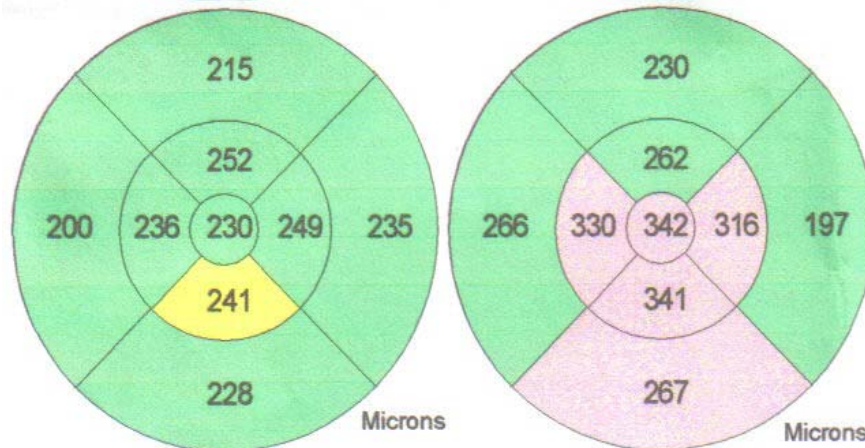
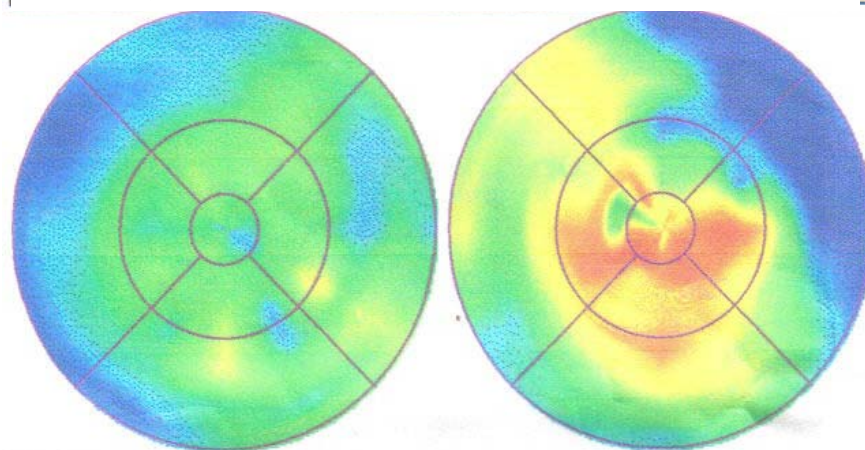
Left eye



Vision = 20/200

Right eye

Left eye



Vision = 20/60

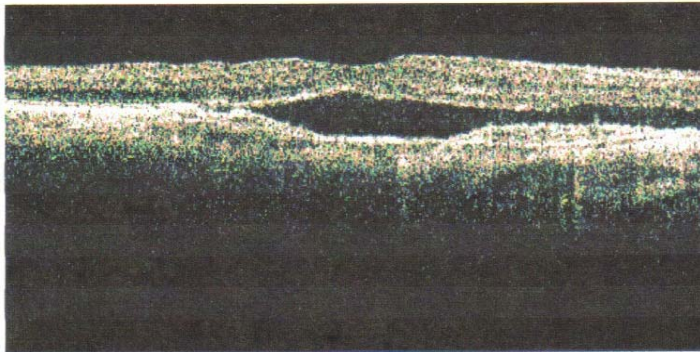
# Before anti-VEGF

# After anti-VEGF

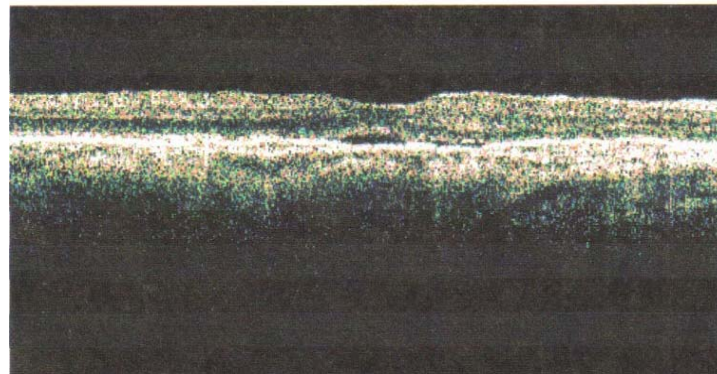
Vision = 20/200

Vision = 20/60

OCT Image

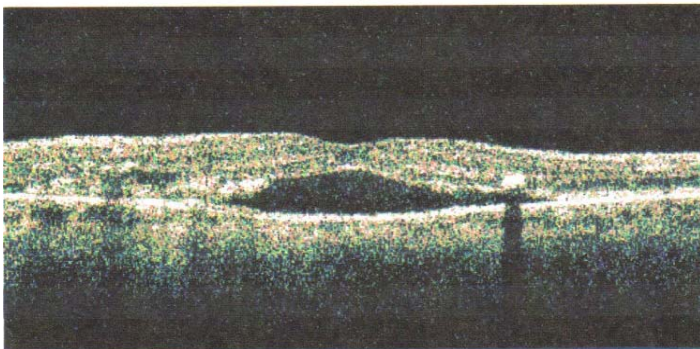


OCT Image

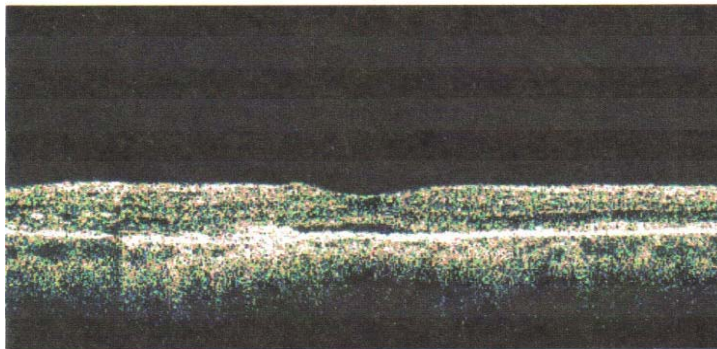


180°  
scan

OCT Image



OCT Image



90°  
scan

# Our Experience with Anti-VEGF

## Case 2

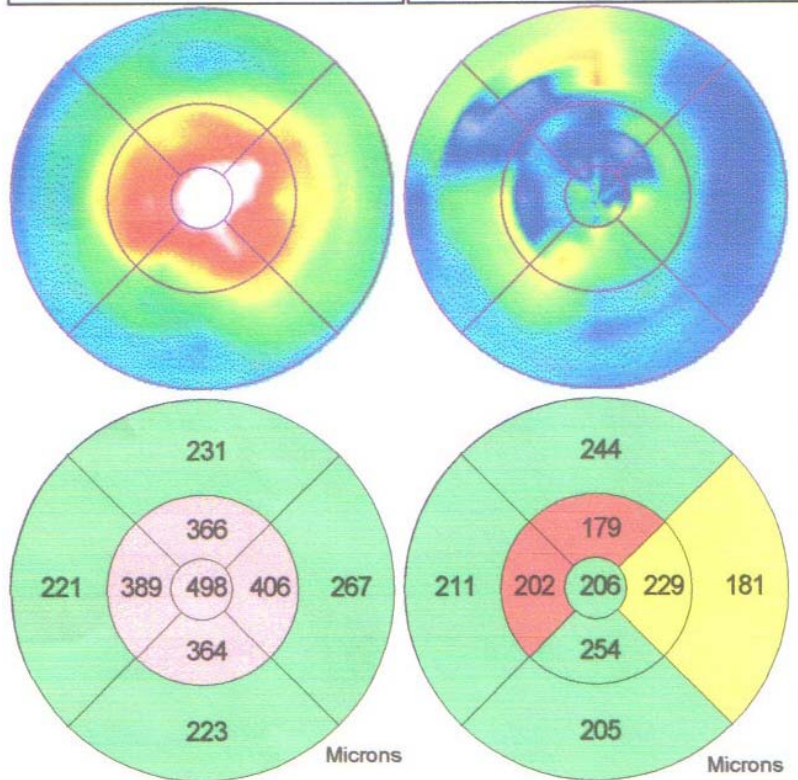
- 84 year old woman
- Prior history of wet AMD right eye
- Previous treatments:
  - PDT x 2
  - Macugen
- **Despite these treatments, vision continued to worsen**

# Before anti-VEGF

# After anti-VEGF

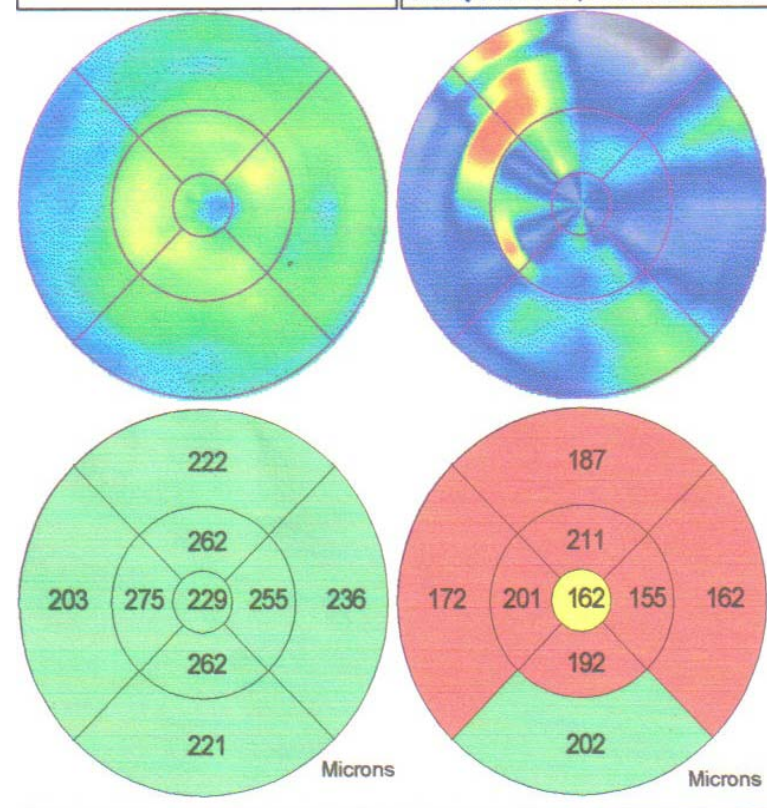
Right eye

Left eye



Right eye

Left eye



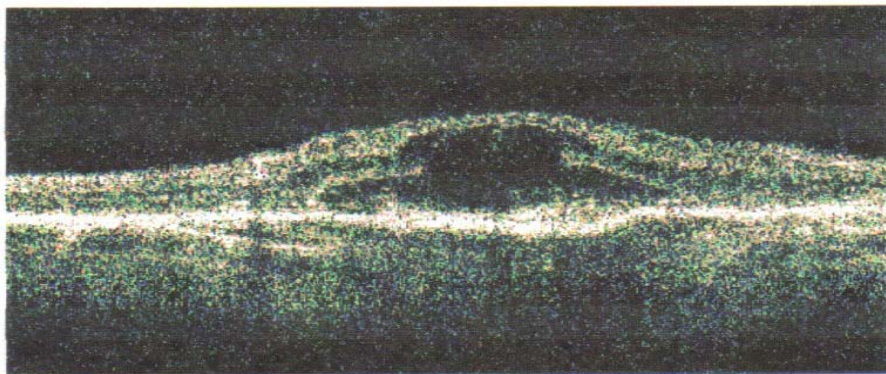
Vision = 20/300

Vision = 20/300

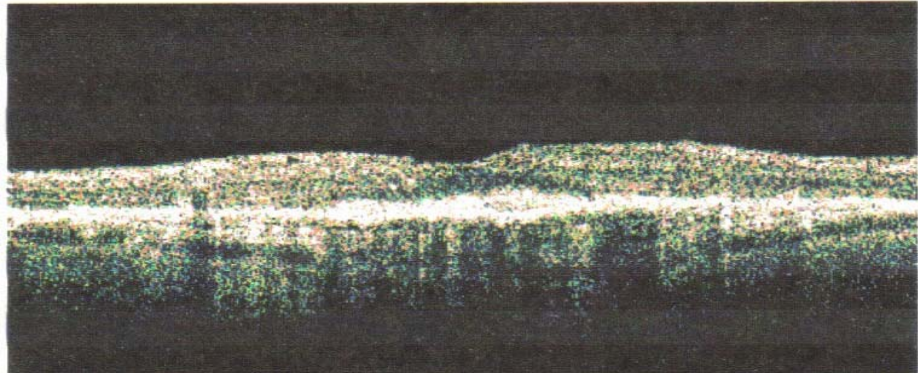
# Before anti-VEGF

# After anti-VEGF

OCT Image



OCT Image



# Side Effects of Intraocular Injections

**Serious adverse events related to the injection procedure occurring in <1% of injections:**

- **Infection**
- **Retinal Detachment**
- **Traumatic Cataract**

# Are anti-VEGF medications right for you?

- Only patients with the wet form of AMD can benefit from it
- An eye examination along with special testing can determine if you have the wet form of AMD
- Treatment outcomes are better when treatment is initiated in the early stages of the disease

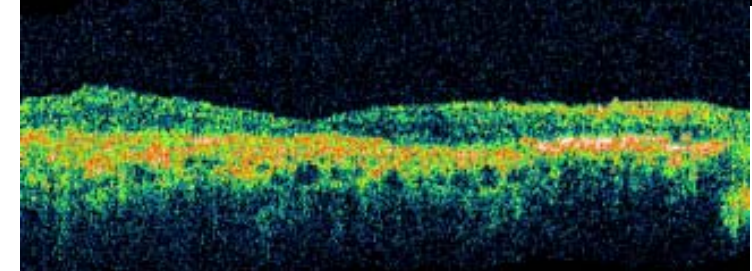
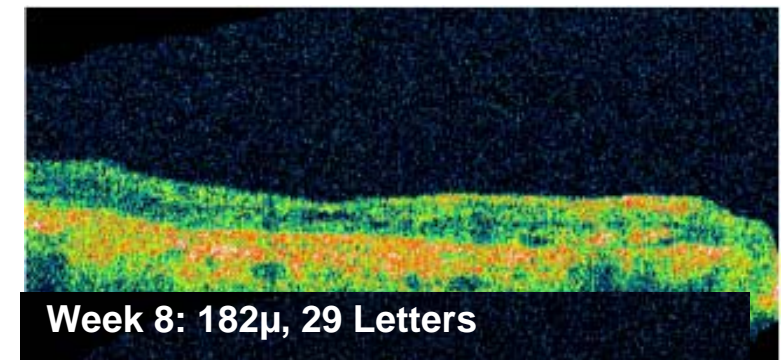
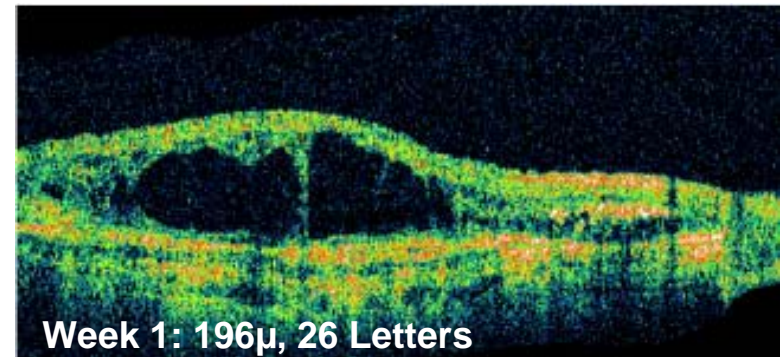
# What EFEI offers to treat Wet AMD

- **Intraocular injections**
  - Macugen
  - Avastin
  - Lucentis
  - Clinical Trial: Regeneron Study
- **Intravenous injections (no injection in the eye)**
  - Avastin

# Intravitreal AMD Phase I - Bioactivity

## Case 1 – VEGF Trap 1 mg

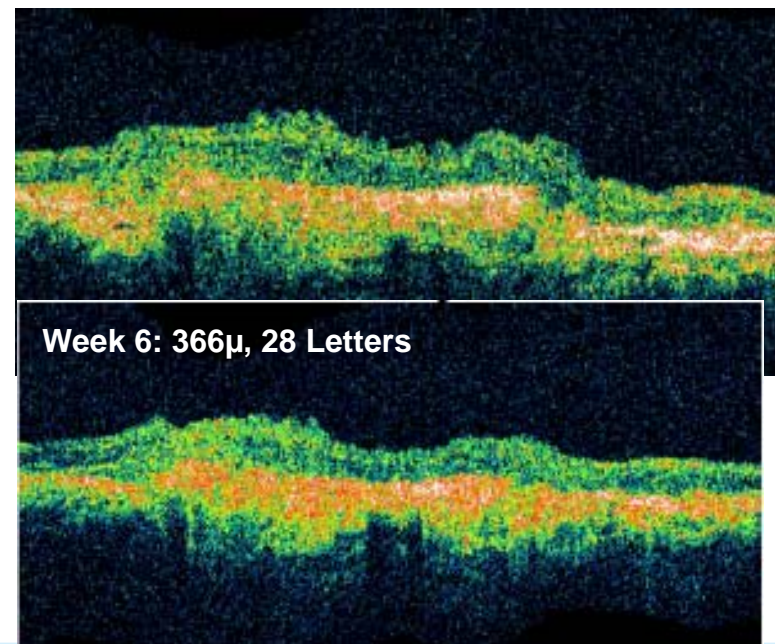
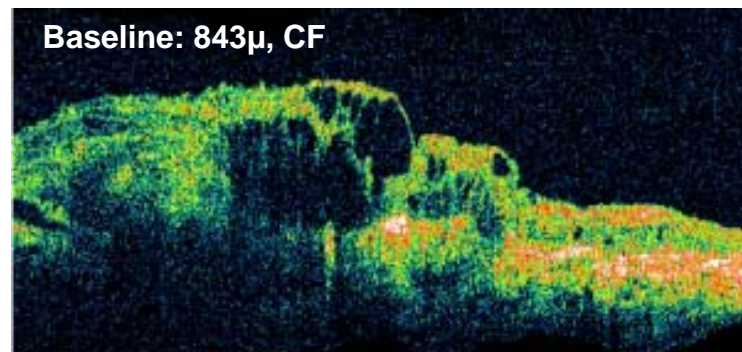
- 76 year old WF
- Bilateral neovascular AMD
- Time from diagnosis: 6 years
- Prior Treatment:
  - PDT x 1
- VA
  - Baseline: 20/320
  - Week 6: 20/250



# Intravitreal Phase I - Bioactivity

## Case 2 – VEGF Trap 4 mg

- 84 year old BM
- Neovascular AMD OD
- Time from diagnosis:  
1 week
- Prior Treatment:
  - None
- VA
  - Baseline: CF\* at 2 ft.
  - Week 6: 20/250



# VEGF Trap vs Lucentis -- Which One NOW?

## •Dosing Interval

- Lucentis is injected once a month.
- PIER data suggests that 3-month interval is insufficient to maintain vision gain
- In the VGFT-OD-0508 study, the “continued dosing phase” allows for PRN dosing. This means that there is a possibility that the subject will not need to be dosed every 4 weeks.
- Possibilities of less injections and improved VEGF binding leading to faster improvement (potentially).

## •Cost

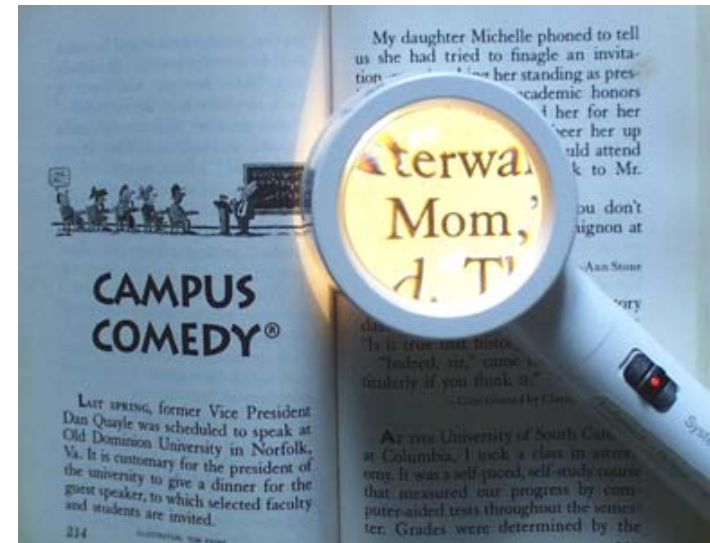
- Lucentis cost \$1950.00 per injection Medicare allows \$1560.00 which means the patient is out of pocket \$390.00 if they don't have a supplement insurance.
- There is no cost **to the subjects** if they participate in VGFT-OD-0508.

# What if AMD cannot be treated?

- **People with wet or dry AMD who cannot be treated will not become totally blind—they will still have peripheral (side) vision.**
- **With special low-vision rehabilitation, devices and services, people can often learn how to “see” again with remaining vision.**

# Low-vision aids

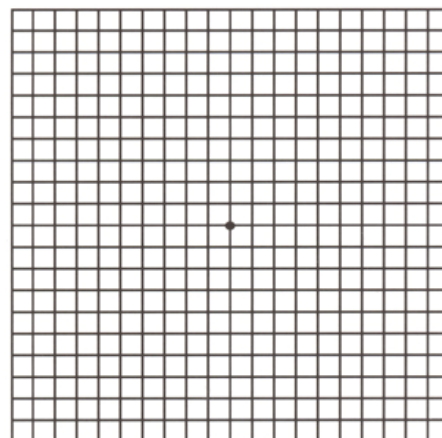
- **Optical low-vision devices use lenses to magnify objects:**
  - Magnifying spectacles
  - Hand magnifiers
  - Stand magnifiers
  - Video magnifiers
  - Telescopes



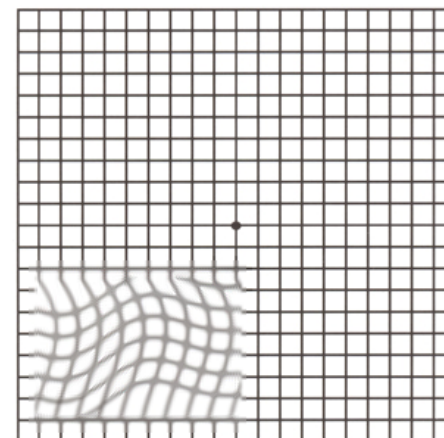
**Illuminated magnifier**

# Monitoring your vision at home

- If you have been diagnosed with AMD, you must monitor your vision every day with an Amsler Grid.
- With AMD, the Amsler Grid may contain blurry or wavy lines.



Amsler Grid, as seen through a normal eye



Amsler Grid, as might be seen through an eye with AMD

**\* Preserve good vision with regular eye exams \***