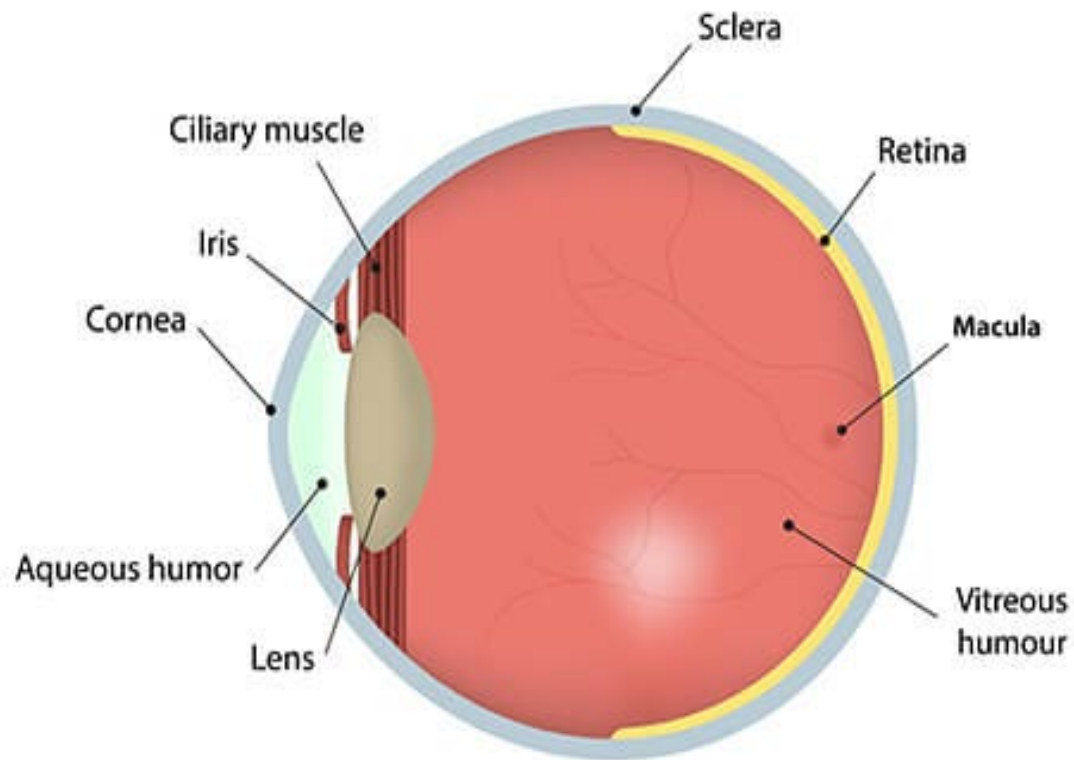
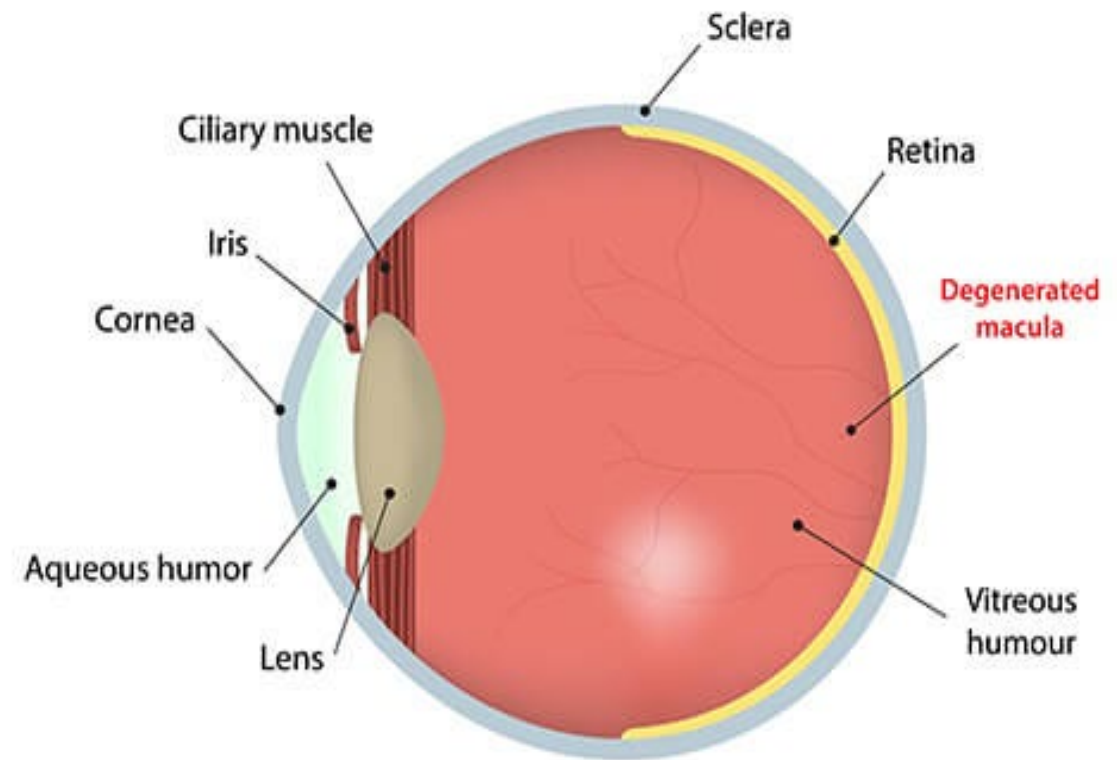


Macular Degeneration

Healthy Eye



Eye with Degenerated Macula



Objectives: Upon completion of this presentation the learner will be able to:

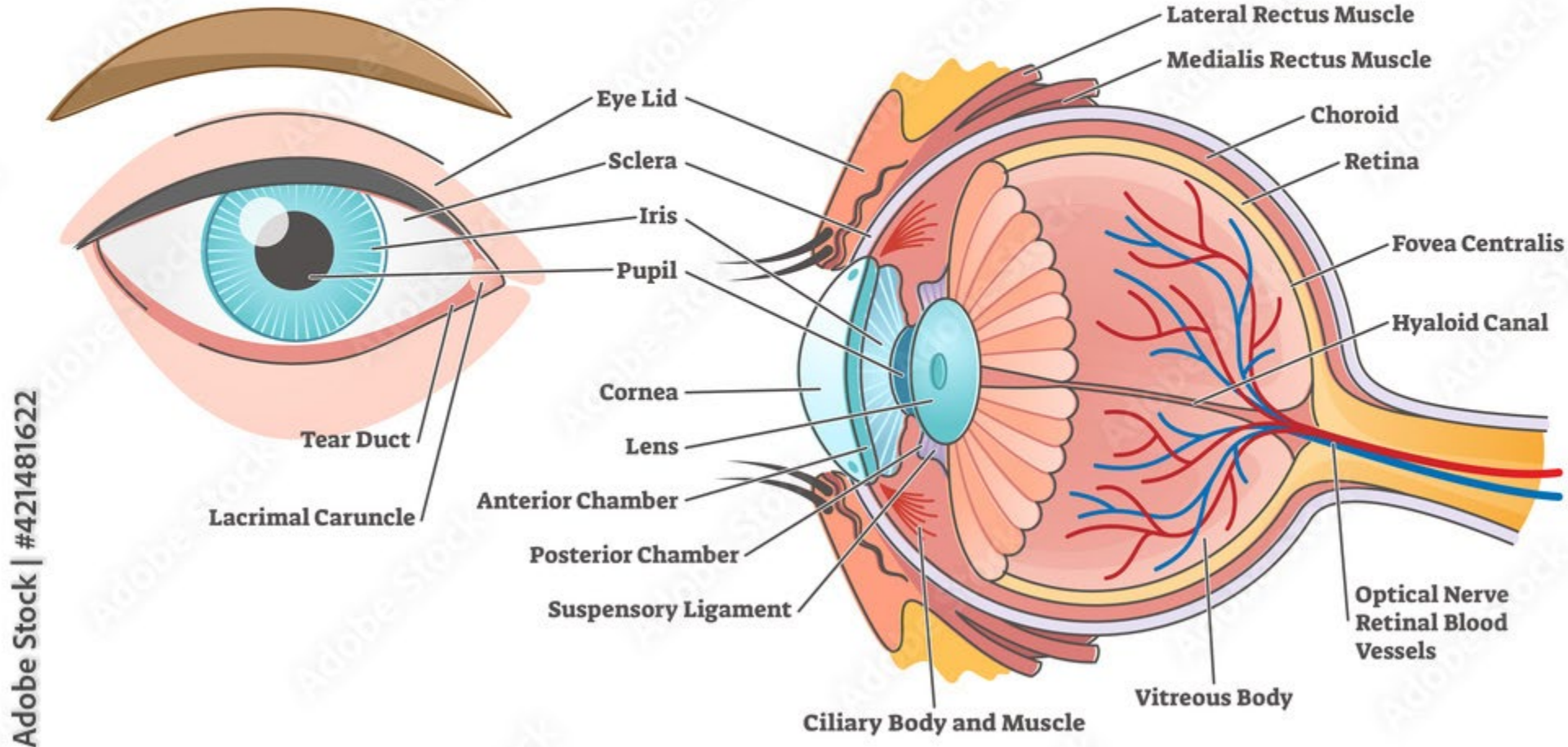
- 1. Define Age-Related Macular Degeneration (ARMD).**
- 2. Discuss what parts of the eye are involved with the macular degenerative changes.**
- 3. List eight Sociodemographic risk factors for ARMD.**
- 4. The Age-Related Eye Disease Study (AREDS) documented what two supplementations decrease the risk of ARMD progression?**
- 5. What two clinical forms has ARMD been classified into?**
- 6. List the Age-Related Macular Degeneration Disease Stages and four groups based on clinical examination of the macula.**

Age-Related Macular Degeneration (ARMD)

- **ARMD is the most common cause of blindness in developed countries in people over 60 years of age. Affected 196 million people in 2020. 288 million people by 2040.**
- **Macular degenerative changes involve the central part of the retina that is the fovea.**
- **The Central vision is affected, resulting in difficulty driving, reading etc.**
- **ARMD accounts for 8.7% of all types of blindness worldwide.**
- **More common in people of European Ancestry than in Asians.**



EYE ANATOMY



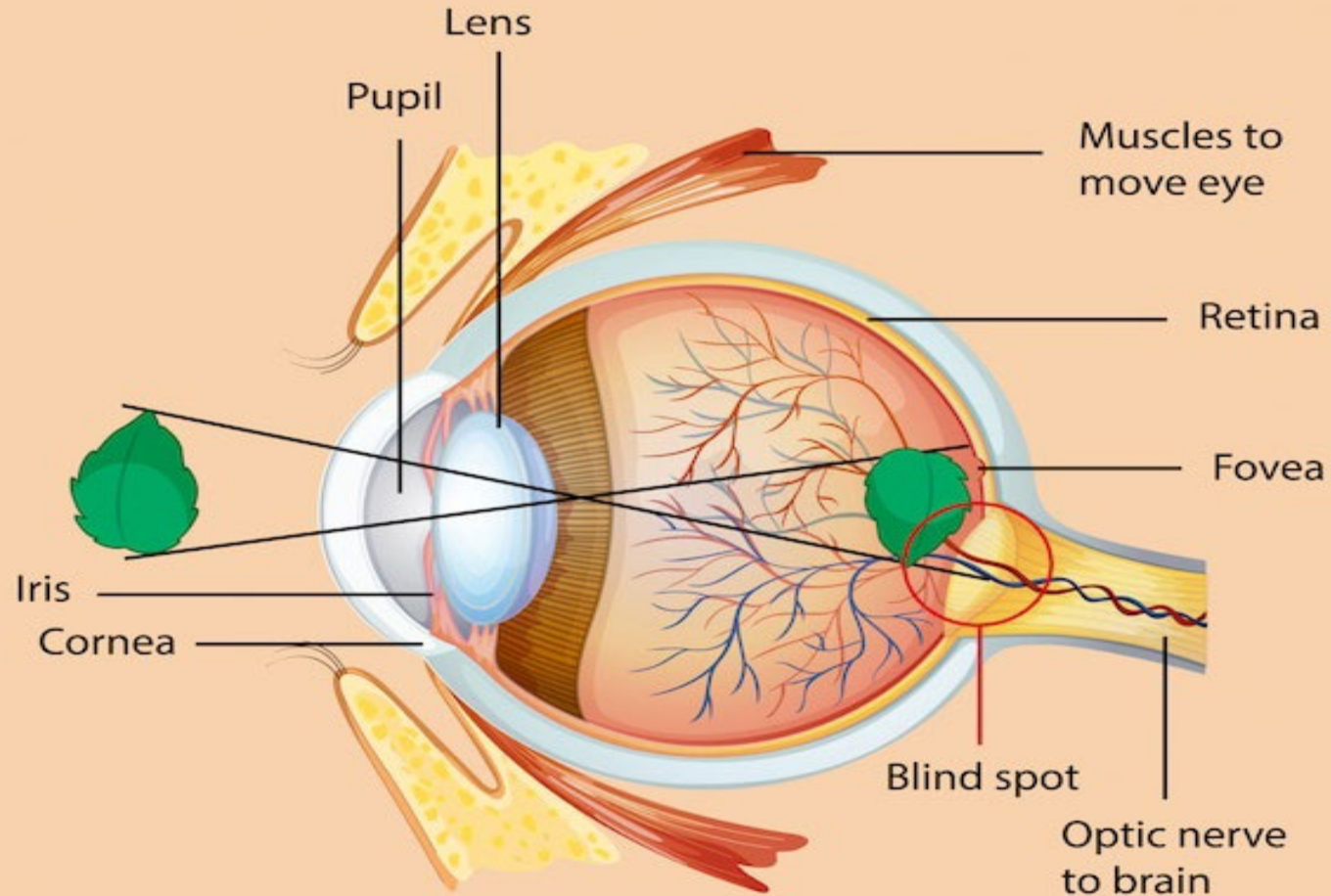
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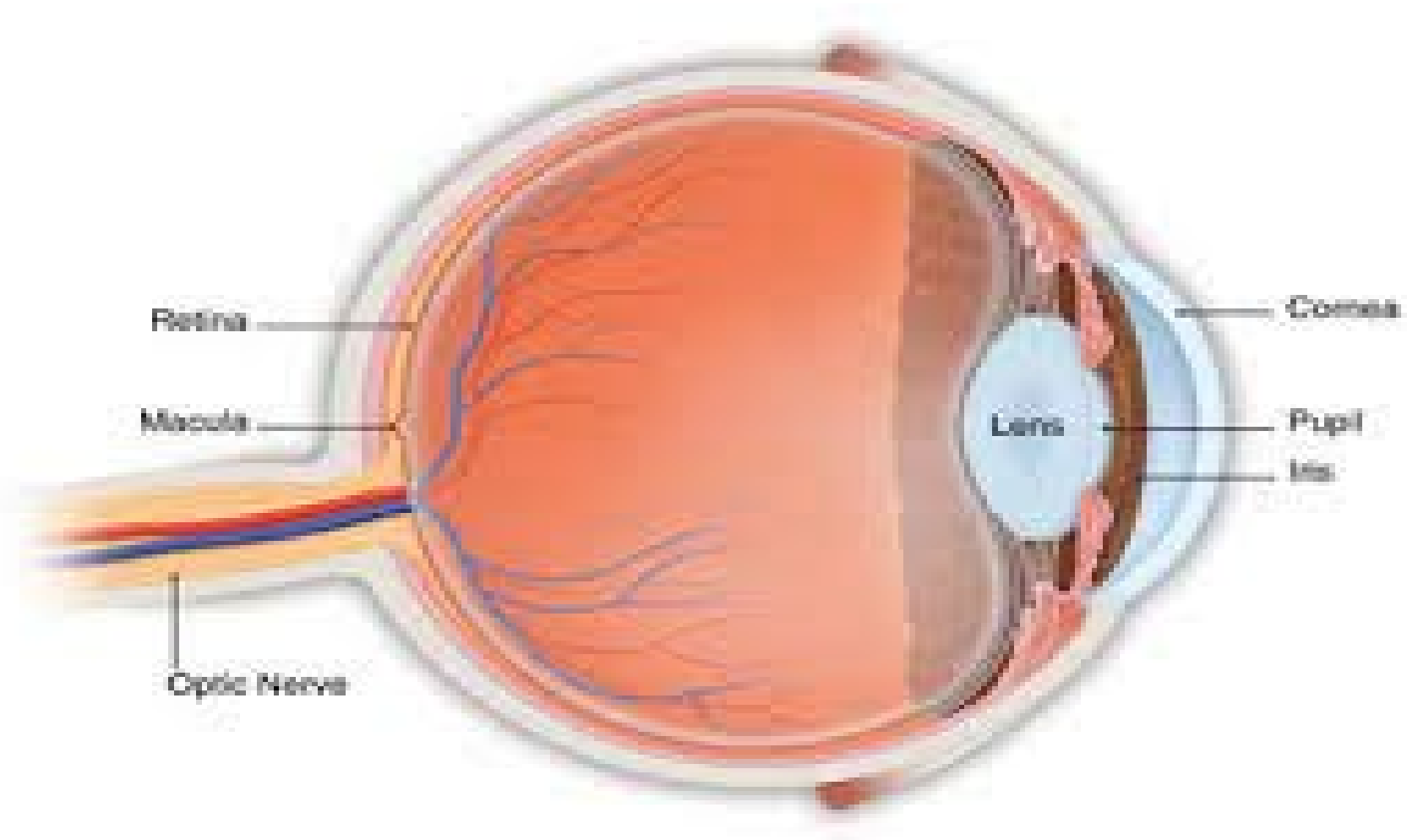


Redefining Retirement Living

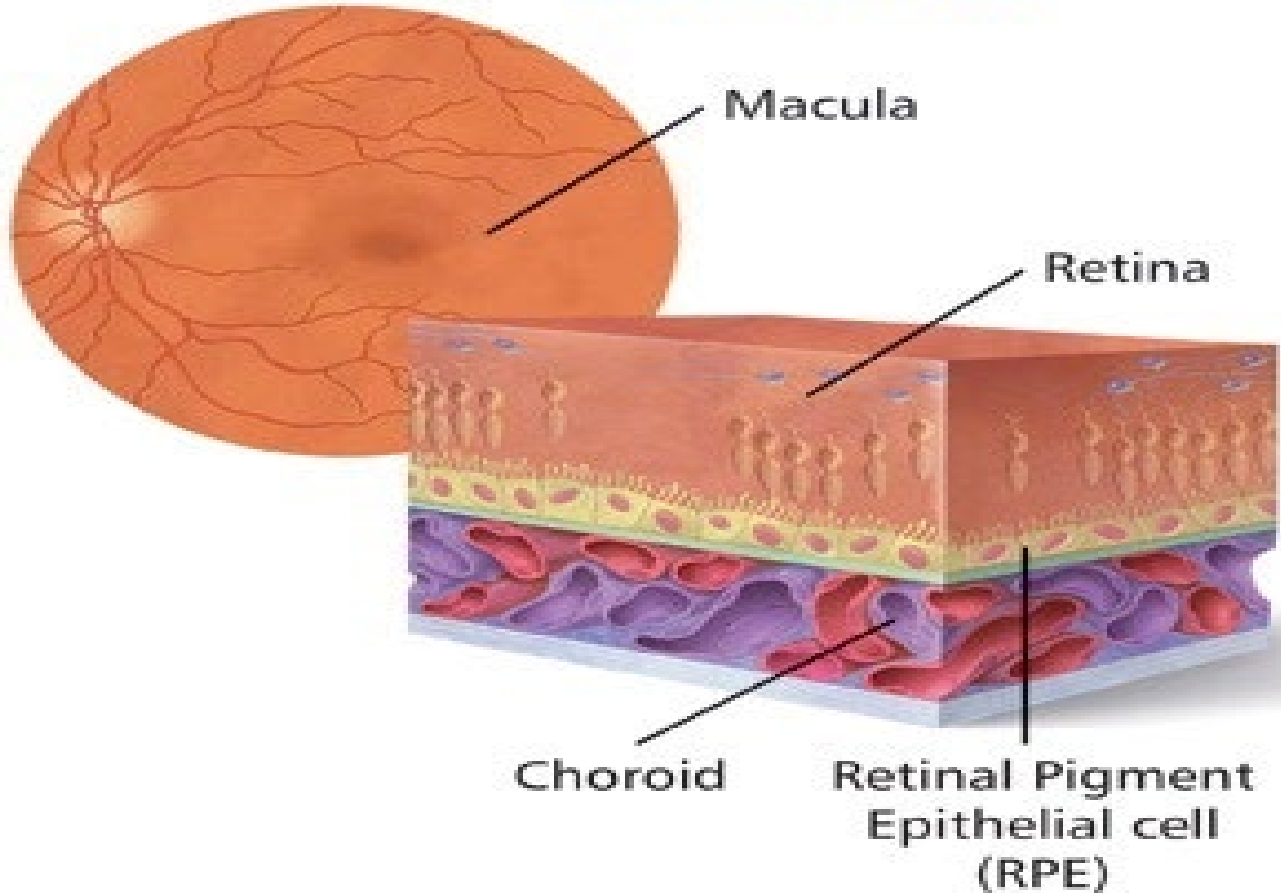
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Cross section of Human Eye





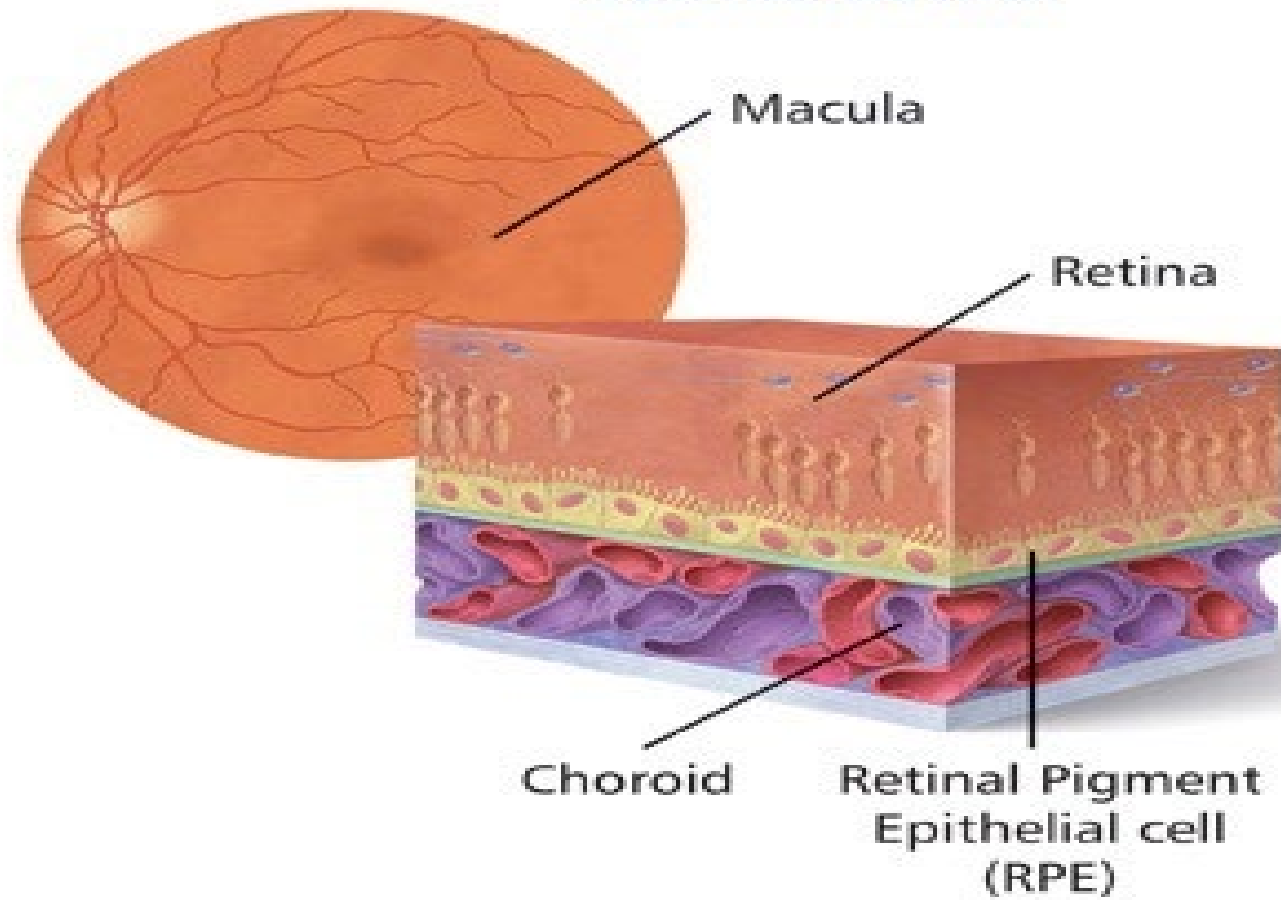
Normal Retina



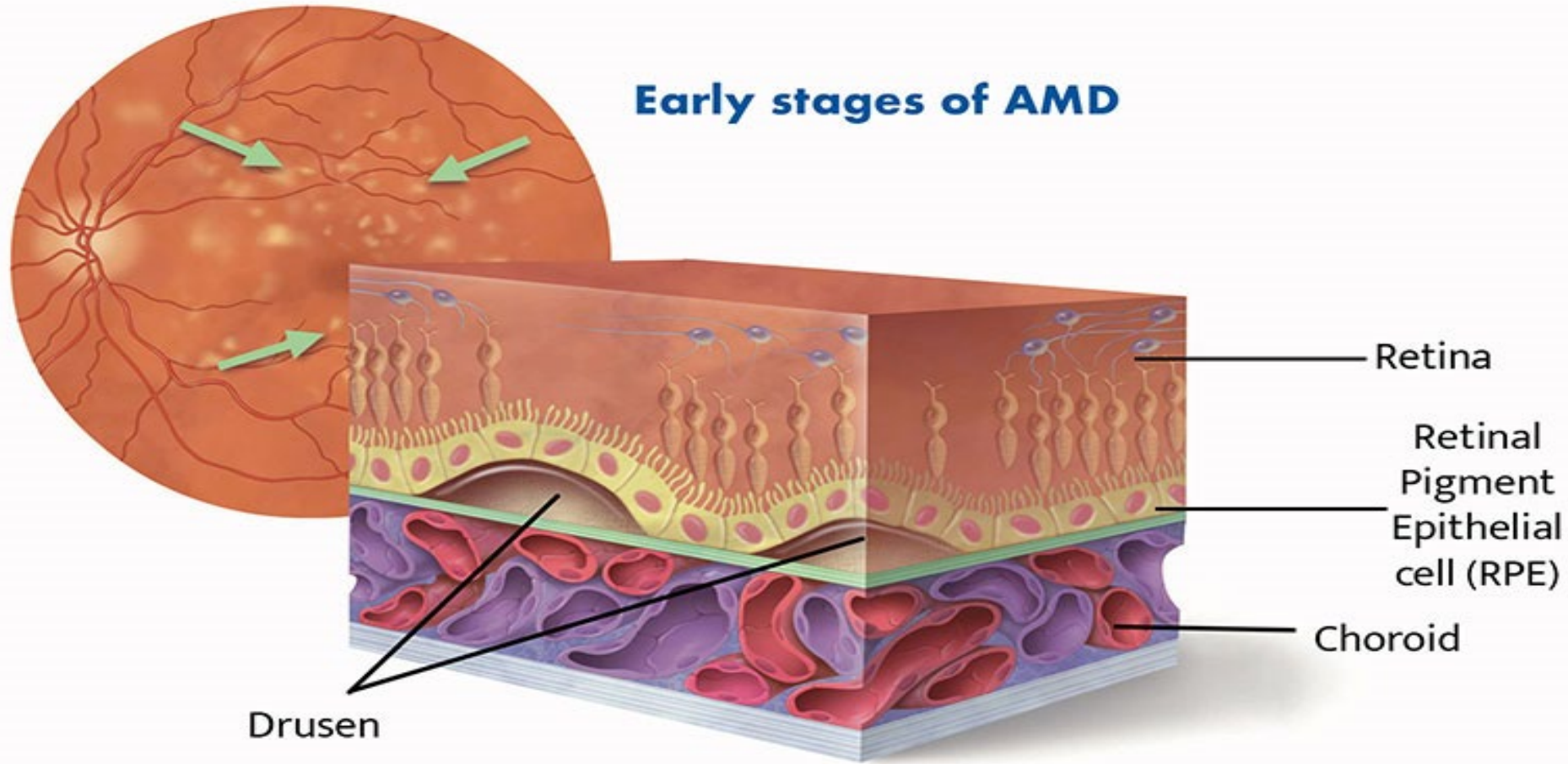
Definition of Age-Related Macular Degeneration

- Age -related macular degeneration (ARMD or AMD) is:
- Complex eye disorder. ARMD occurs when extracellular deposits accumulate in the outer retina, ultimately leading to photoreceptor degeneration and loss of central vision.
- Leading cause of incurable blindness worldwide in elderly. Bilateral Disease.
- ARMD initially affects the Central area of the Retina, known as the Macula.
- ARMD is classified as early stage to late stage.
- Advanced ARMD is classified into the:
 - 1. Nonexudative or atrophic form DRY ARMD.
 - 2. Exudative or neovascular form WET ARMD. More serious form.
- (Genes and Diseases, Science Direct Volume 9, Issue 1, January 2022)

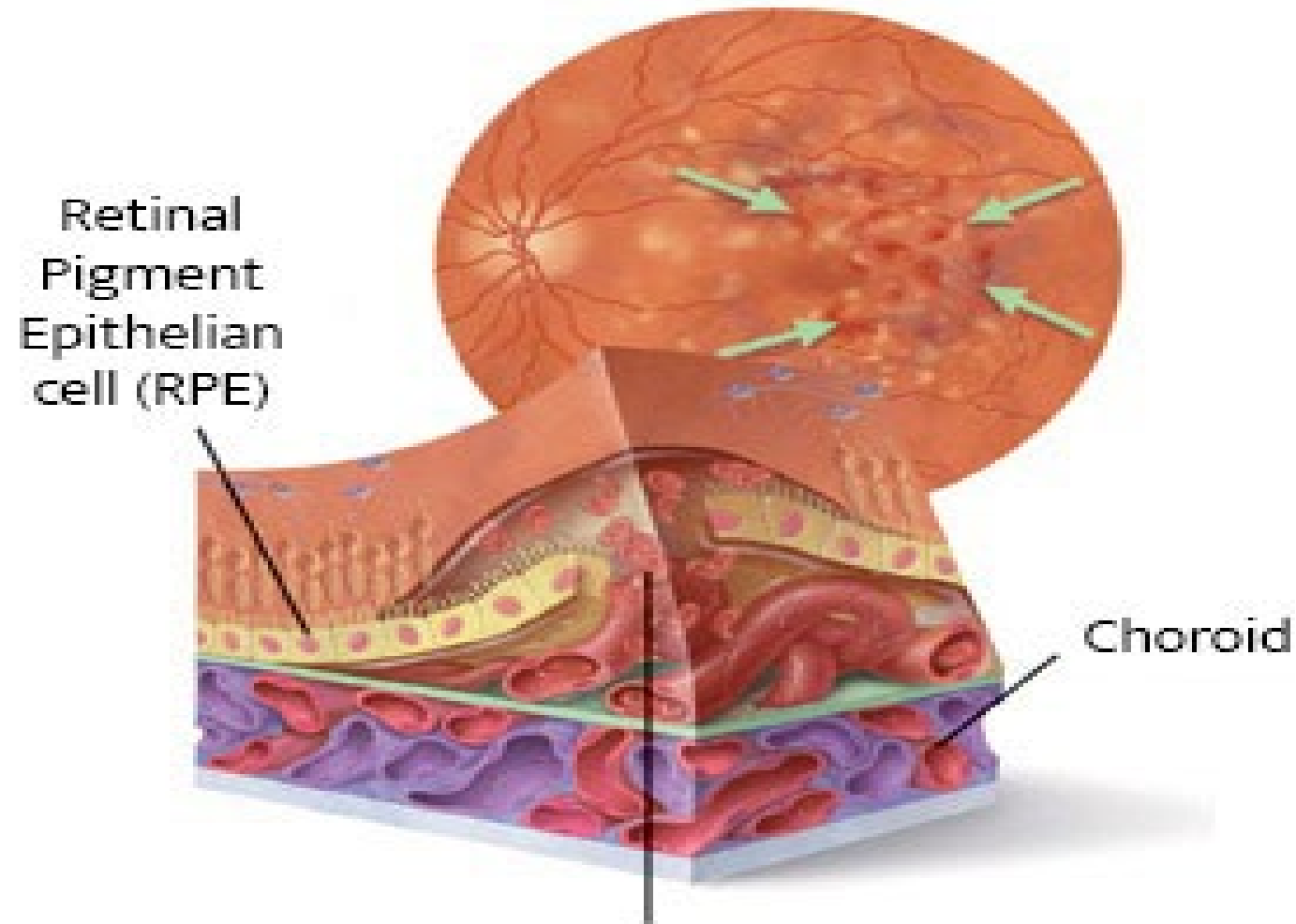
Normal Retina



Early stages of AMD



Wet AMD

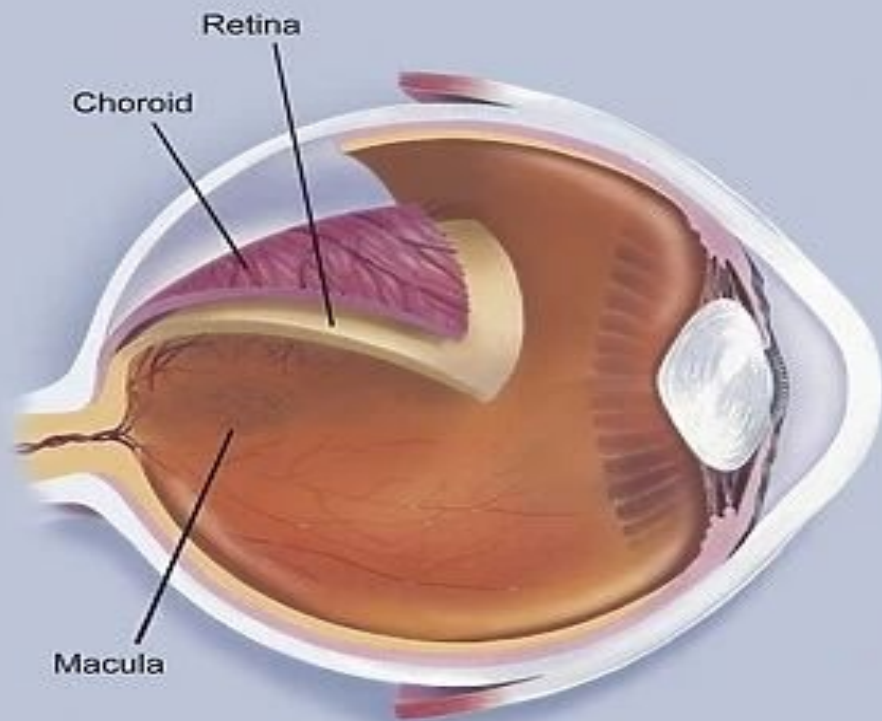


Rapidly growing vessels break through the RPE, leading to leakages and hemorrhage

Macular Degeneration

The word "macula" refers to visual field, and Macular Degeneration, it generally means a deterioration of visual field, a form of visual impairment, usually related to age due to damage of the retina.

Individuals macular degeneration experience problems with the retina and the choroid. While the retina contains nerves for sight communication, the choroid supplies blood to the center of the retina, which is called the macula.



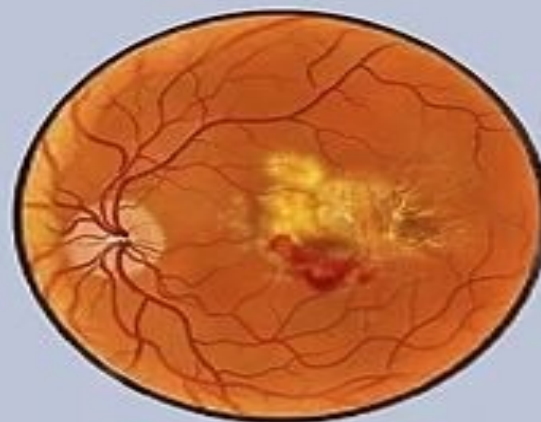
Dry Macular Degeneration,

- gradual onset
- most common
- fatty tissue slowly build up behind the retina causing loss of visual acuity



Wet Macular Degeneration,

- sudden onset
- less common
- leakage of blood and fluid from behind the retina





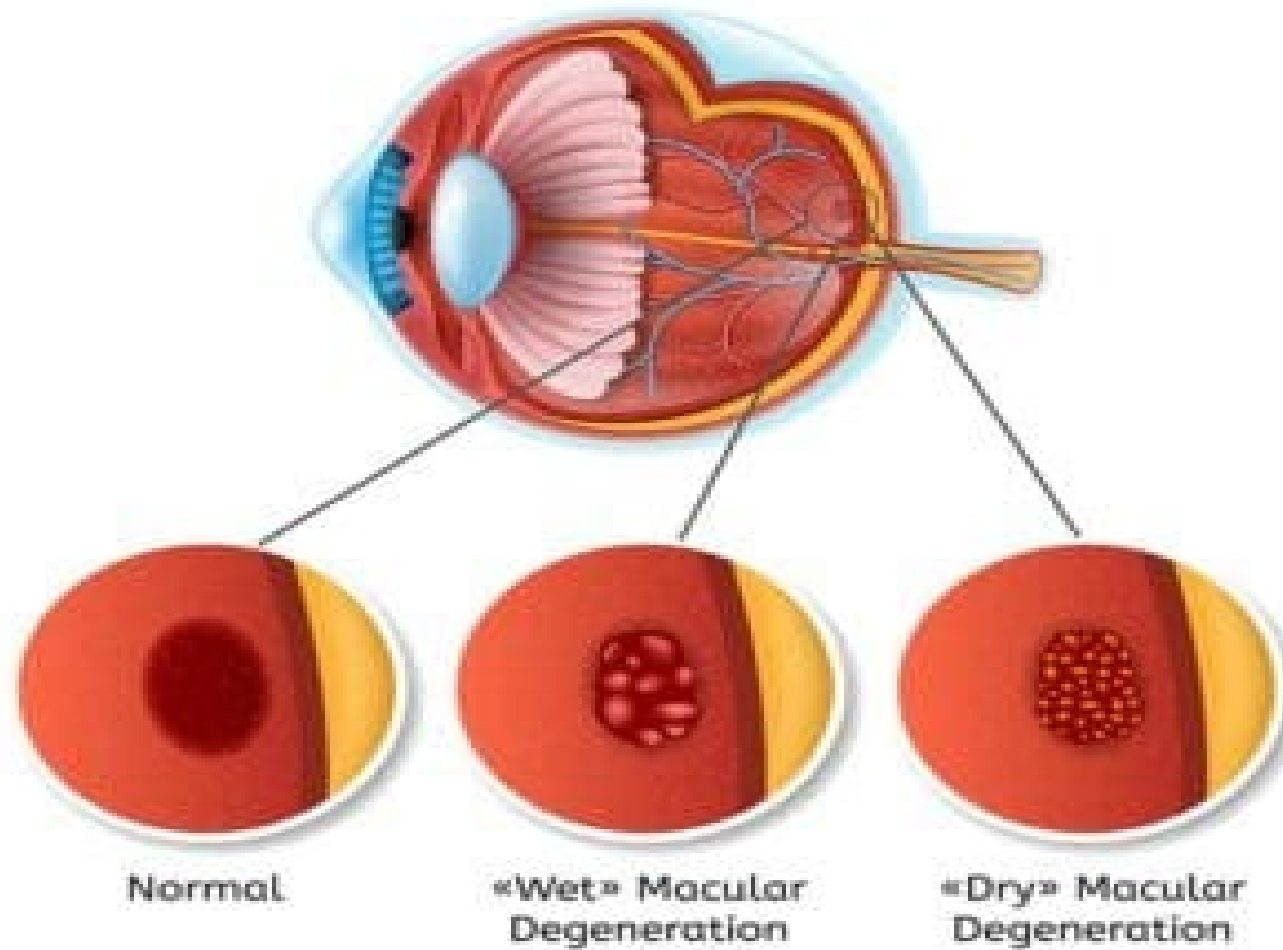

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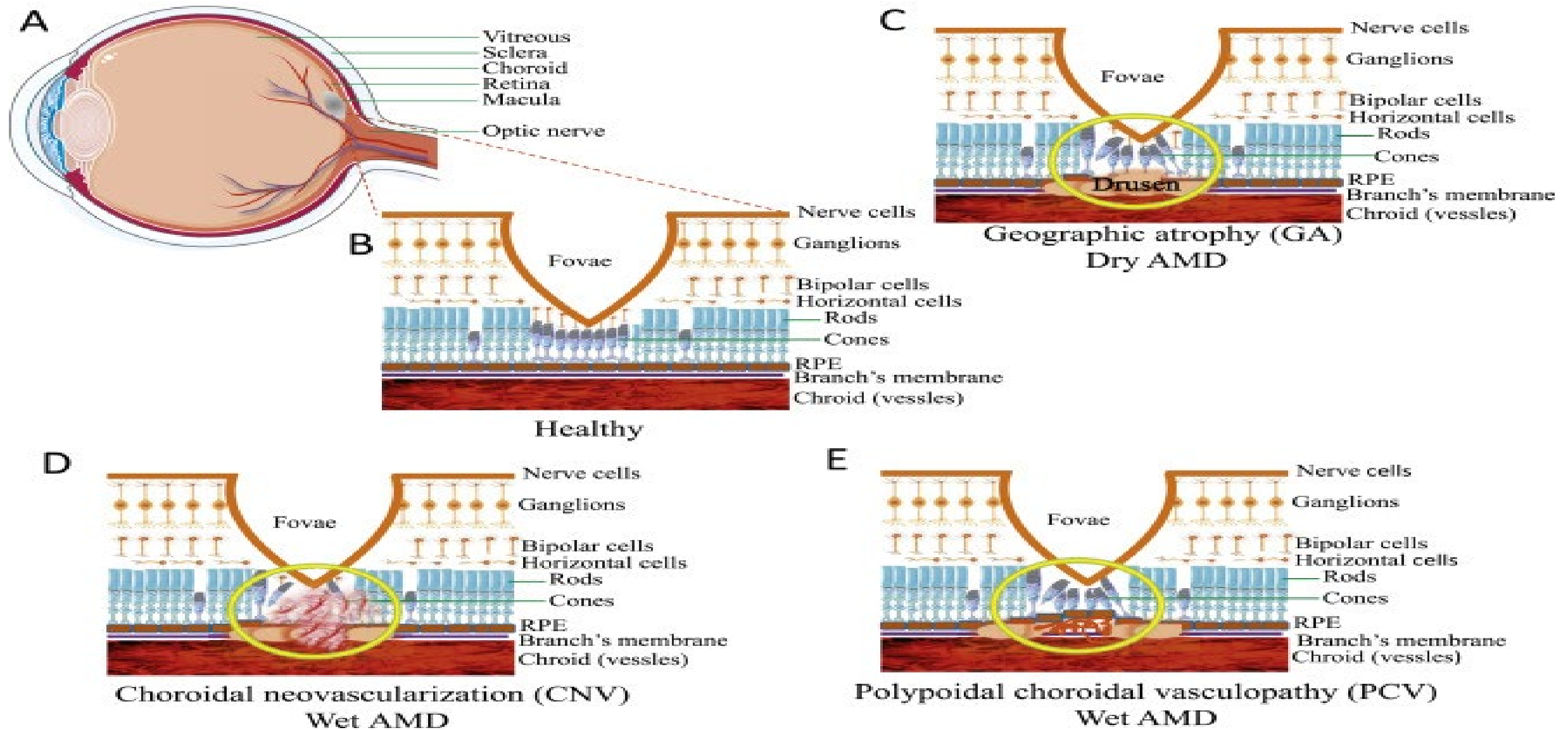
Macular Degeneration



Risk Factors for ARMD

- **Sociodemographic factors:** age, gender, race, socioeconomic status, (women and non Hispanic whites more at risk).
- **Lifestyle:** smoking and alcohol intake.
- **Cardiovascular:** elevated b/p, Atherosclerosis, possible relationship with higher cholesterol. No relationship to Diabetes. HDL may mediate ARMD.
- **Hormonal:** estrogen replacement therapy may be protective.
- **Reproductive risk factor:** HRT and BCP have shown a decrease in ARMD.
- **Inflammatory:** Inflammation plays a role in pathogenesis of drusen(small, yellow or white deposits) that appear in the retina. Made of proteins, lipids, cellular debris. Common in aging, but may indicate early ARMD.
- **Genetic:** Genetic variants associated with ARMD. Y402H in the CFH gene and other variants in factor B/complement component 2, complement component 3, and complement Factor I. Runs in families.
- **Ocular:** Iris color, light colored eyes more likely to develop dry ARMD.

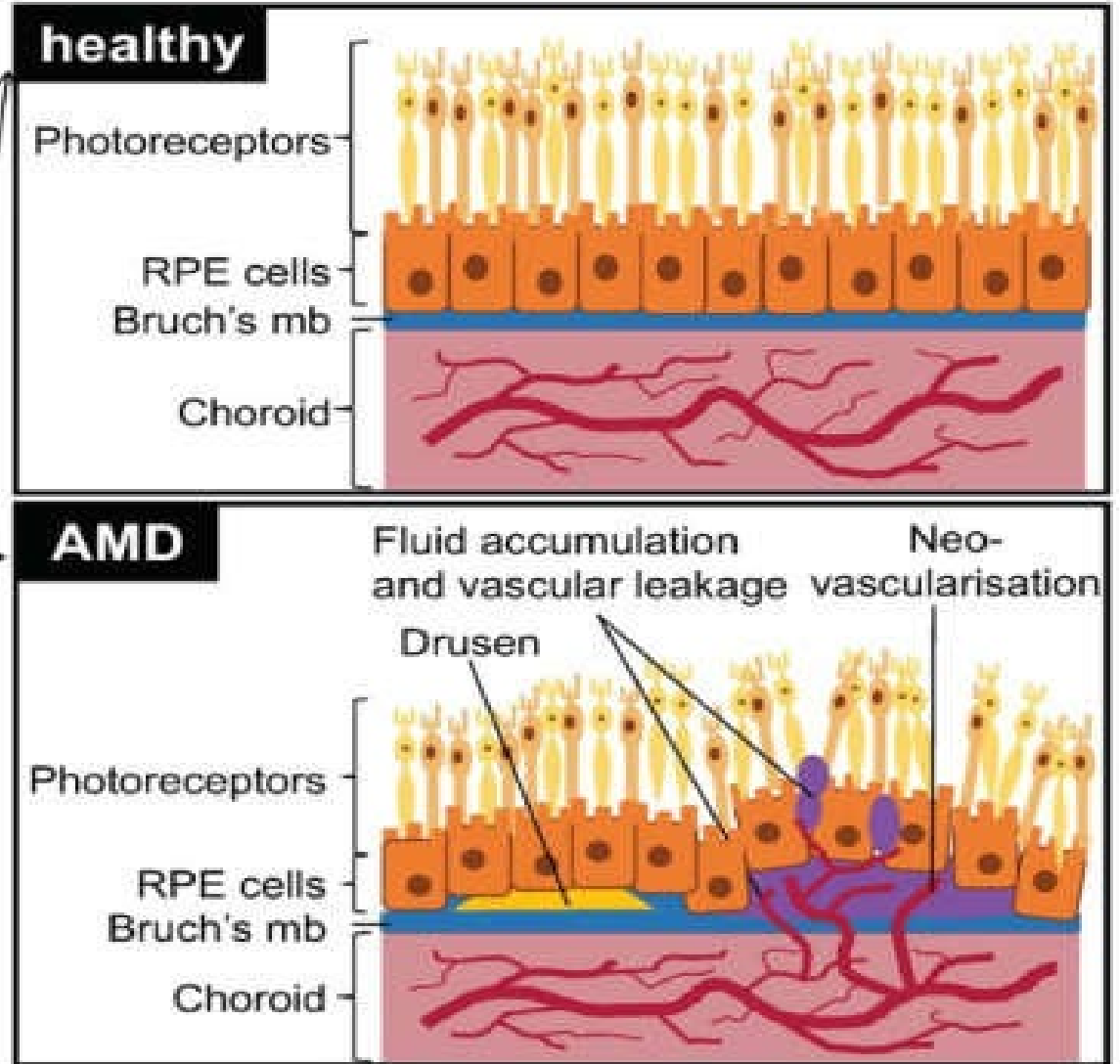
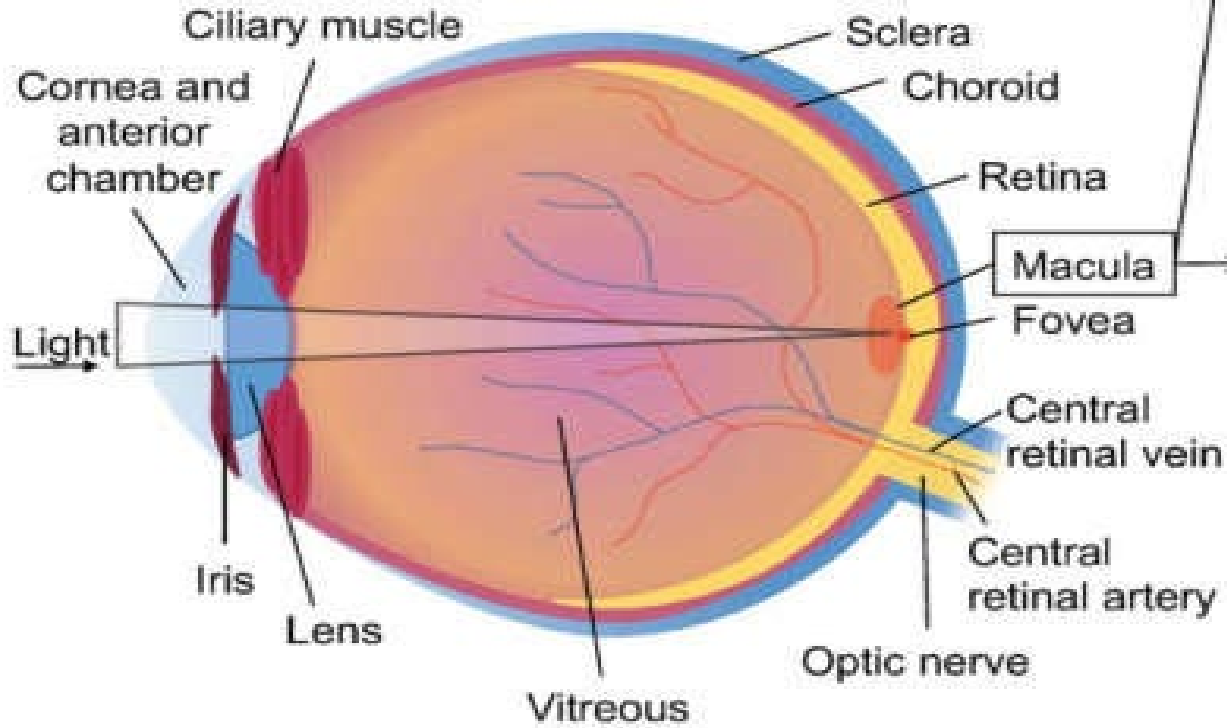
Pathophysiology of ARMD or AMD



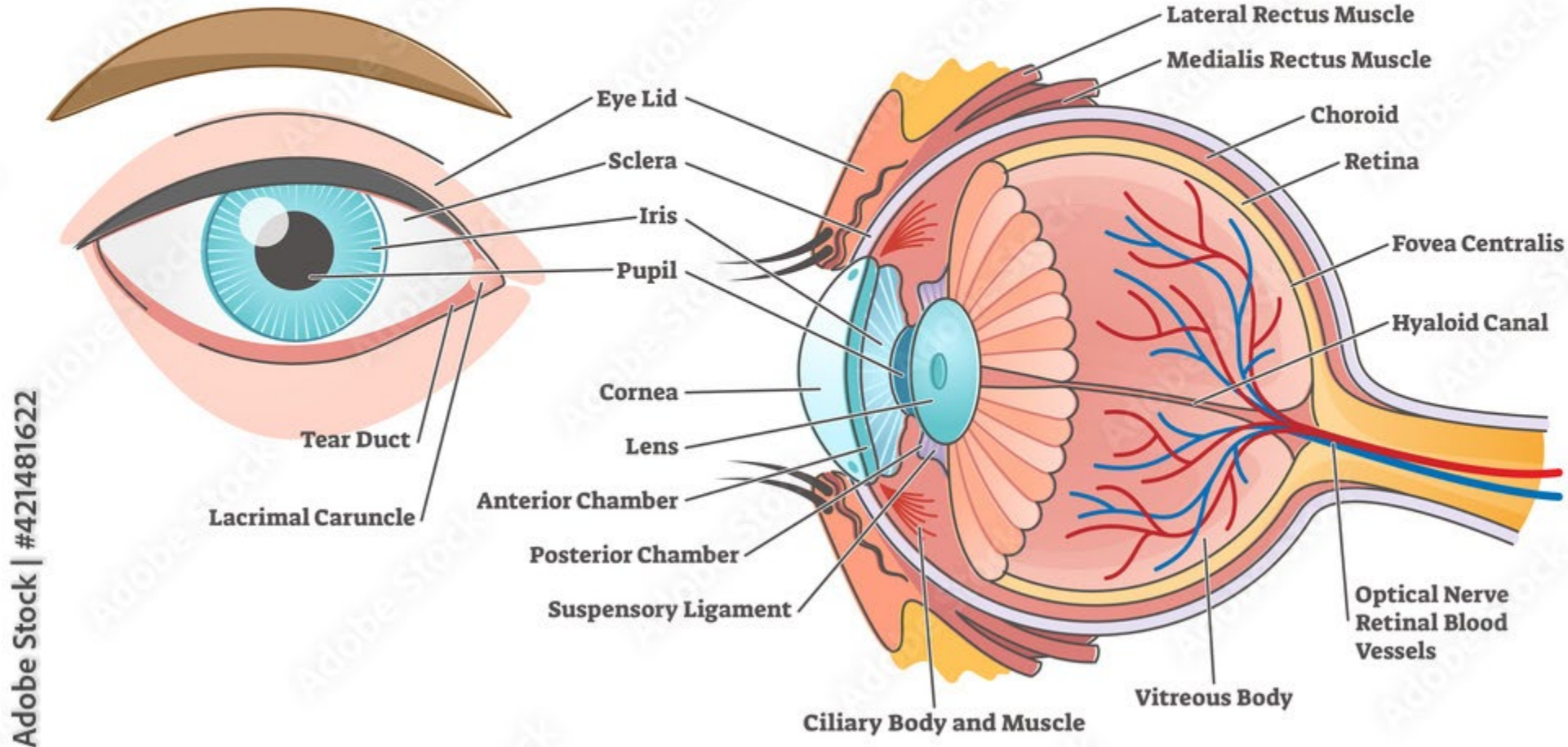
Pathophysiology of ARMD or AMD

- **Figure A. Showing the normal eye with location of the choroid. The macula area is the oval area with a diameter of 1.5 mm near the fovea and is known as the macula.**
- **Figure B. Cross section shows the important structures of the retina in the macular area. Retinal Pigment Epithelium (RPE) cells have the function of removing metabolites produced by photoreceptors. The blood vessels in the choroid can transport nutrients and nourish the outer retina.**
- **Figure C. The formation and location of drusen is shown. Drusen formation will lead to retinal tissue atrophy and Bruch membrane calcification rupture, further leading to ARMD.**
- **Figure D. This picture describes a choroid polypoid lesion.**
- **Figure E. This picture shows the proliferation of new blood vessel.**

Pathophysiology of ARMD Retinal Pigment Epithelium (RPE)



EYE ANATOMY



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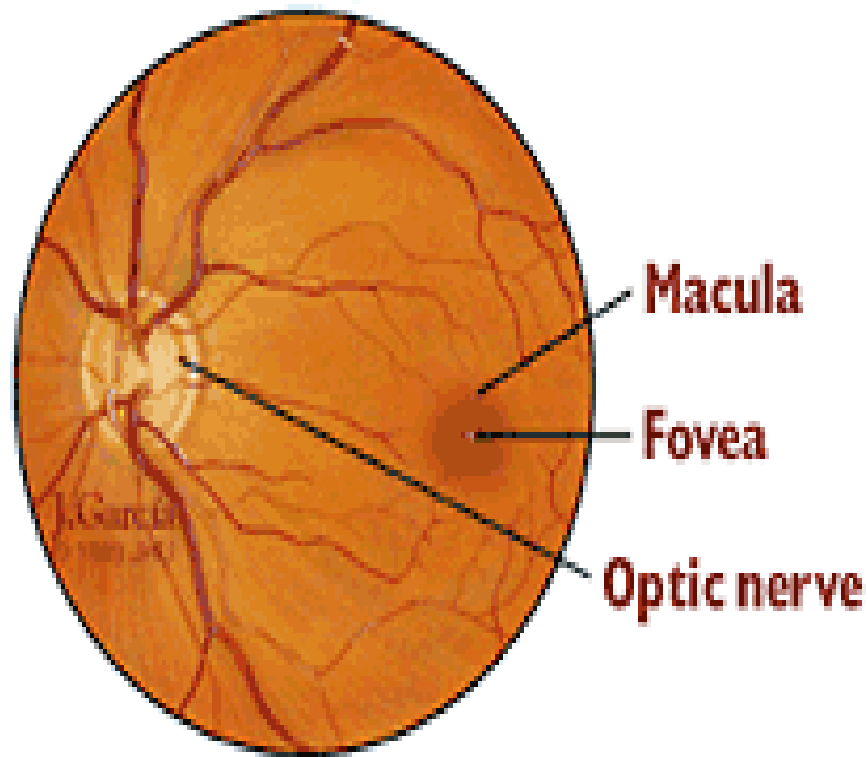


Redefining Retirement Living

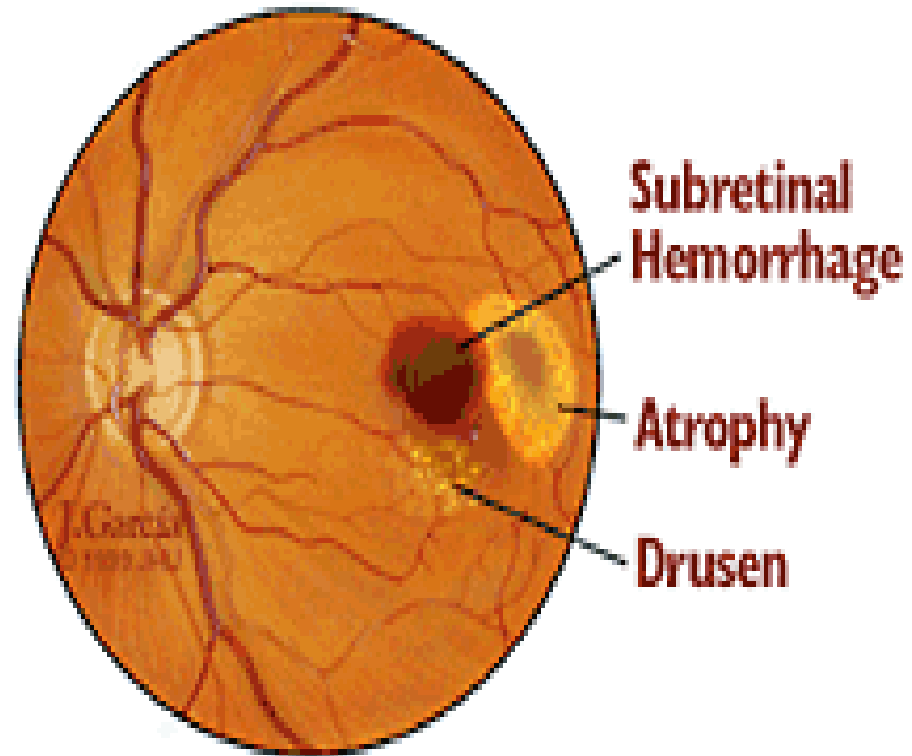
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History and Physical

- **Age-Related macular Degeneration has been classified into two clinical forms:**
- **1. Dry or non-neovascular ARMD.**
- **2. Wet or Neovascular ARMD.**
- **Vision loss is gradual if it occurs in the early or intermediate dry stage of ARMD.**
- **The examination of the Fundus reveals yellowish subretinal deposits or Drusen and Retinol Pigment Epithelium (RPE) hyperpigmentation or hypo-pigmentary changes.**
- **Drusen can be hard (definite boundaries) or soft drusen (indistinct boundaries), or they may confluence into larger drusen and may evolve into a drusenoid, Retinol Pigment Epithelium (RPE) detachments (PED).**
- **Atrophy of the retinol pigment epithelium(RPE) occurs in the advanced stage of the disease known as Geographic Atrophy.**
- **(Kolb H, Fernandez E, Jones B, et al., editors. Webvision: The Organization of the Retina and Visual System).**



Normal

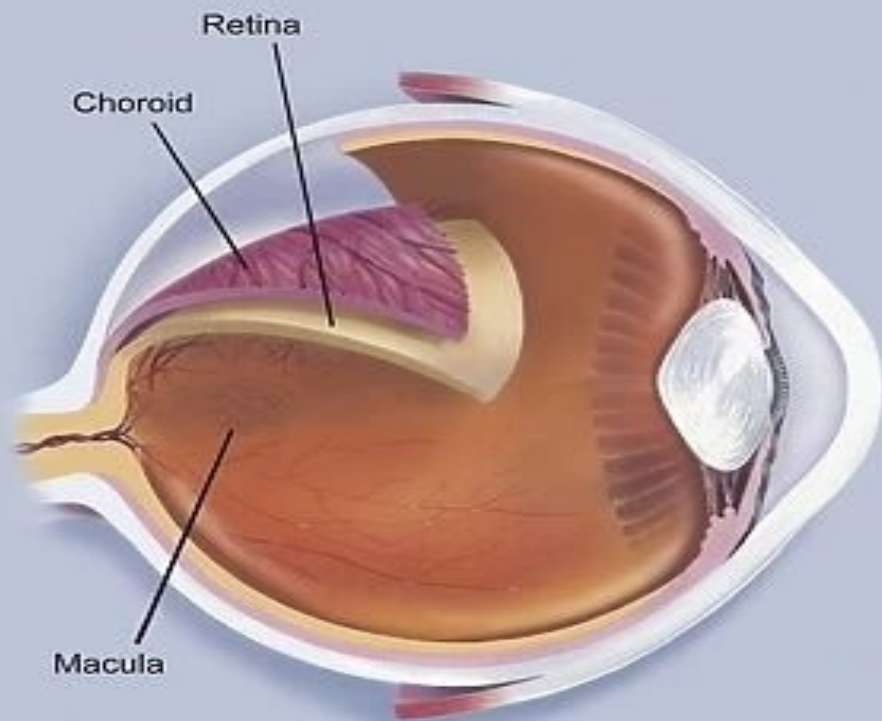


**Macular
degeneration**

Macular Degeneration

The word "macula" refers to visual field, and Macular Degeneration, it generally means a deterioration of visual field, a form of visual impairment, usually related to age due to damage of the retina.

Individuals macular degeneration experience problems with the retina and the choroid. While the retina contains nerves for sight communication, the choroid supplies blood to the center of the retina, which is called the macula.



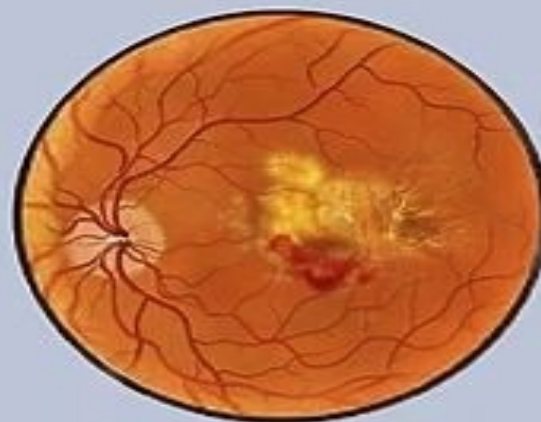
Dry Macular Degeneration,

- gradual onset
- most common
- fatty tissue slowly build up behind the retina causing loss of visual acuity



Wet Macular Degeneration,

- sudden onset
- less common
- leakage of blood and fluid from behind the retina



NORMAL EYE



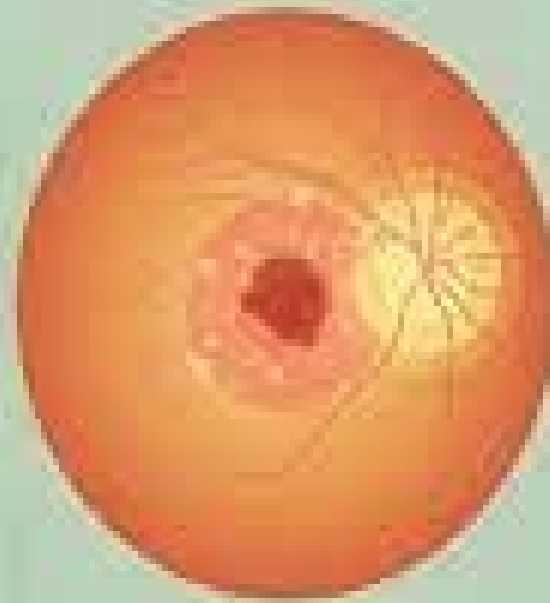
Clear vision of normal eye

DRY MD



Unusually blurry or distorted vision

WET MD



Blind spot in center of field of vision

ARMD has been staged into 4 Groups based on the clinical examination of the Macula.

- **Group 1 (no ARMD):** no drusen or 5-15 small drusen (<63 microns in diameter) in the absence of any other stage of ARMD.
- **Group 2 (Early stage ARMD):** more than 15 small drusen or less than 20 medium sized (63-124 micron in diameter) indistinct soft drusen or pigment abnormalities but not geographic atrophy.
- **Group 3 (intermediate stage):** the presence of at least one large drusen (>125 microns in diameter), or presence of numerous medium sized drusen (approximately 20 or more with indistinct boundaries and 65 or more drusen with distinct boundaries) or presence of non-central geographic atrophy i.e., atrophy not involving the fovea.
- **Group 4 (advanced stage):** Central geographic atrophy that involves the fovea or presence of neovascular ARMD.

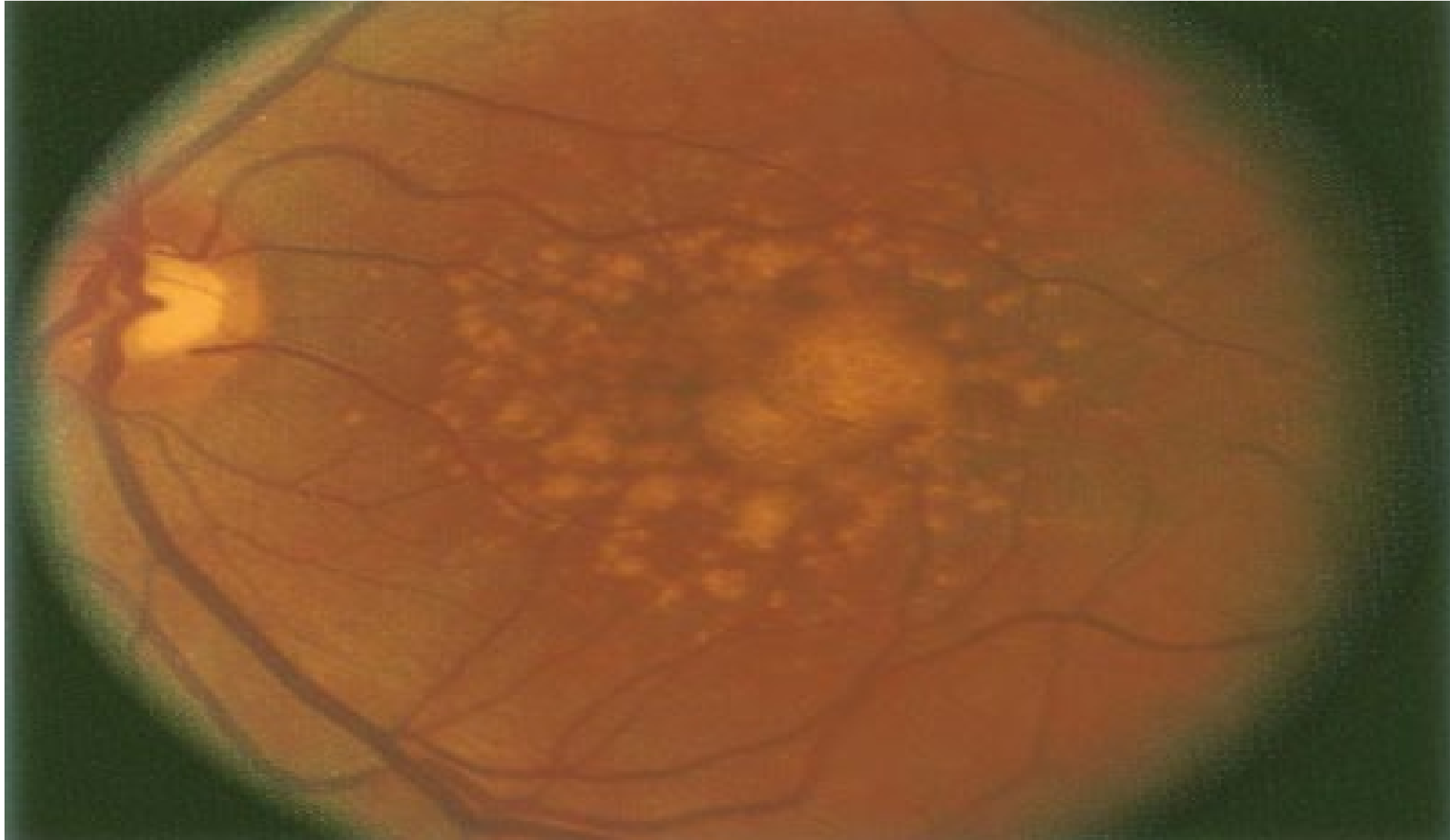
There is no treatment for drusen. However people with lots of drusen or serious vision loss might benefit from taking a certain combination of nutritional supplements. A large study (AREDS 1 and the later AREDS 2 study) found people with certain drusen may slow their dry ARMD by taking these vitamins and minerals daily:

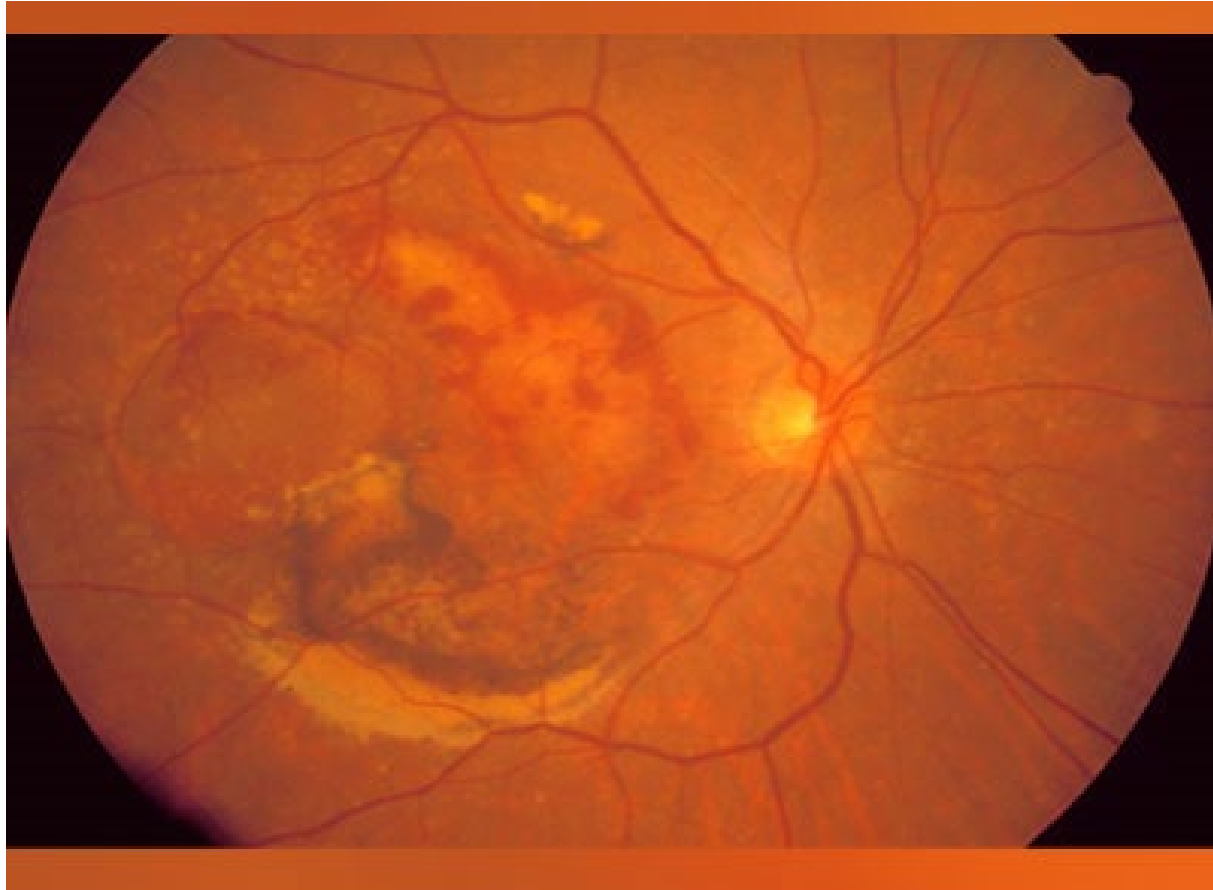
- Vitamin C (500 mg)**
- Vitamin E (400 IU)**
- Lutein (10 mg)**
- Zeaxanthin (2 mg)**
- Zinc (80 mg)**
- Copper (2 mg)**

Your ophthalmologist can tell you if vitamins and minerals are recommended for your dry ARMD, as not all forms will benefit from the AREDS supplements.

Beta carotene should not be used by smokers as it raised the risk of lung cancer.

Dry ARMD with soft drusen





Wet ARMD Fundus Photographs

With wet ARMD, abnormal blood vessels grow under the retina, leak blood or other fluids, and cause scarring. This can damage your vision quickly.

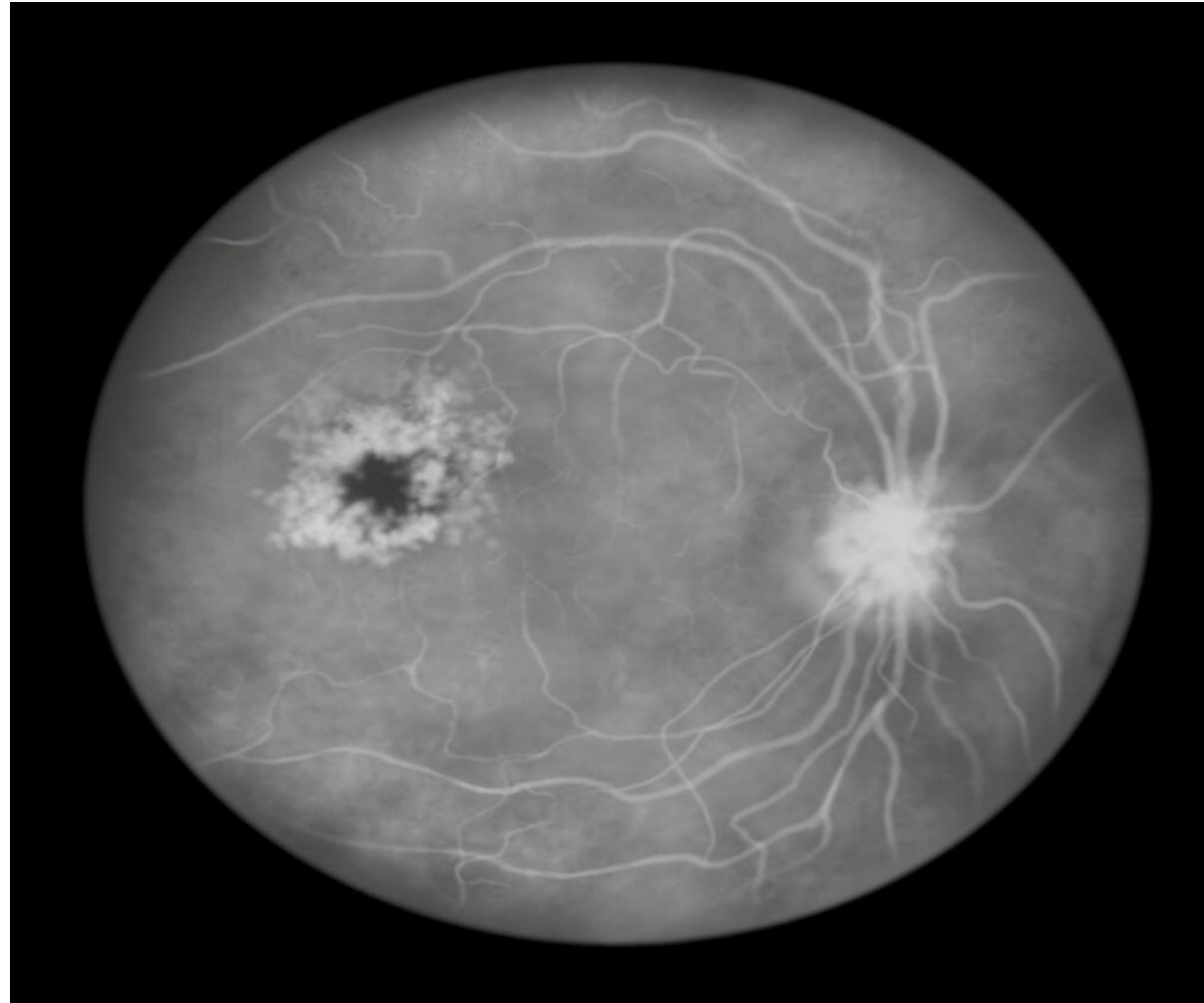
This is what wet ARMD looks like using fundus photography.

Wet macular degeneration photo

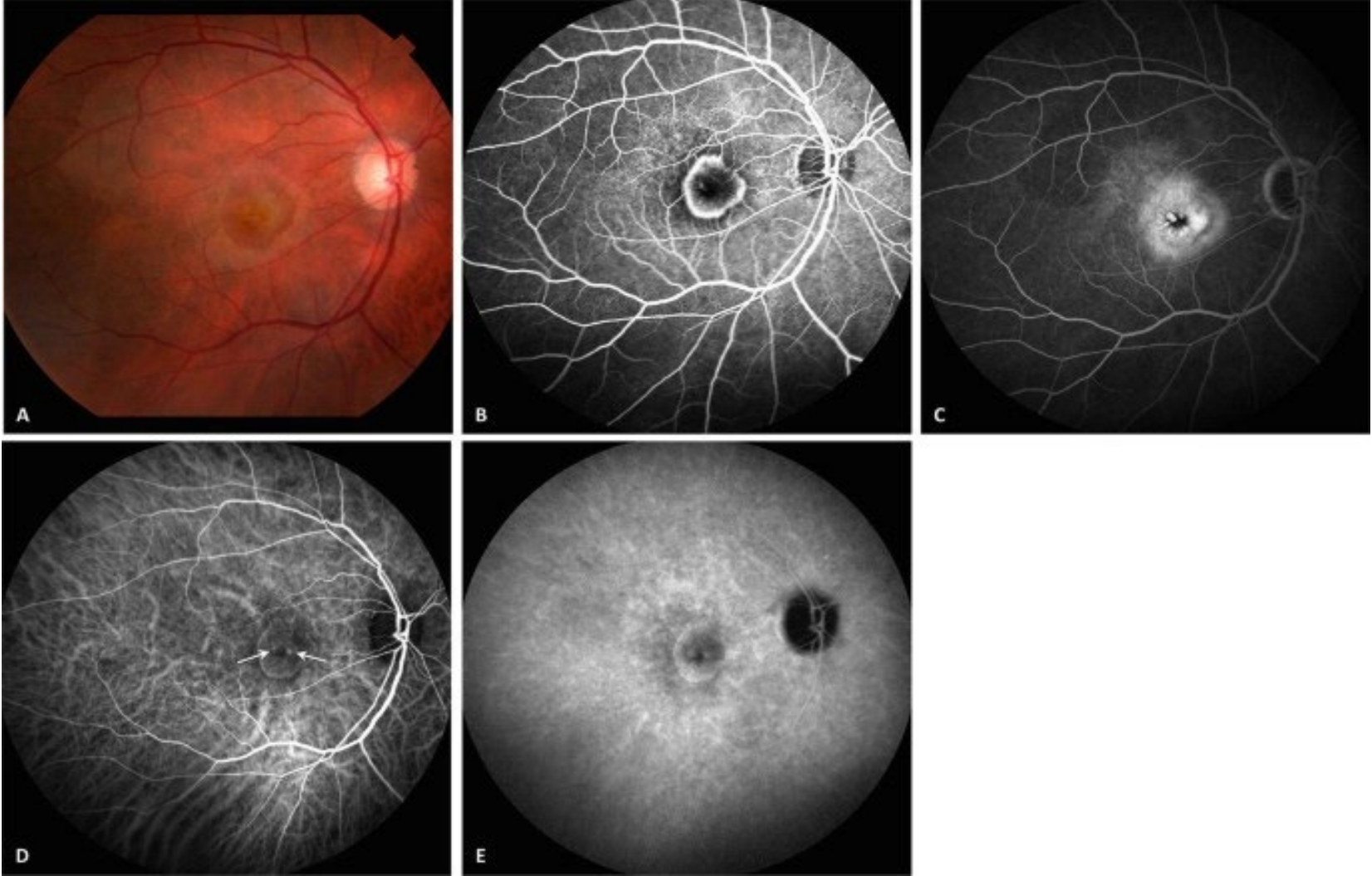
Evaluation of Dry ARMD

- **Imaging of DRY ARMD:**
 - **1. Fundus fluorescein angiography (FFA) :** Hyperfluorescence seen with hydrophilic drusen.
 - **2. Indocyanine Green angiography (ICGA)** The hard drusen becomes hyperfluorescent 2-3 minutes after dye administration. Soft drusen appears hypo fluorescent or iso fluorescent.
 - **3. Autofluorescence:** Evaluates Retinol Pigment Epithelium (RPE) activity. Helps define the area of geographic atrophy. Picks up progression of geographic atrophy.
 - **4. Optical coherence tomography (OCT)** Drusen are seen as a nodular elevation of Retinol Pigment Epithelium (RPE). Shows geographic atrophy, photoreceptors, the RPE, and Bruch's membrane complex.

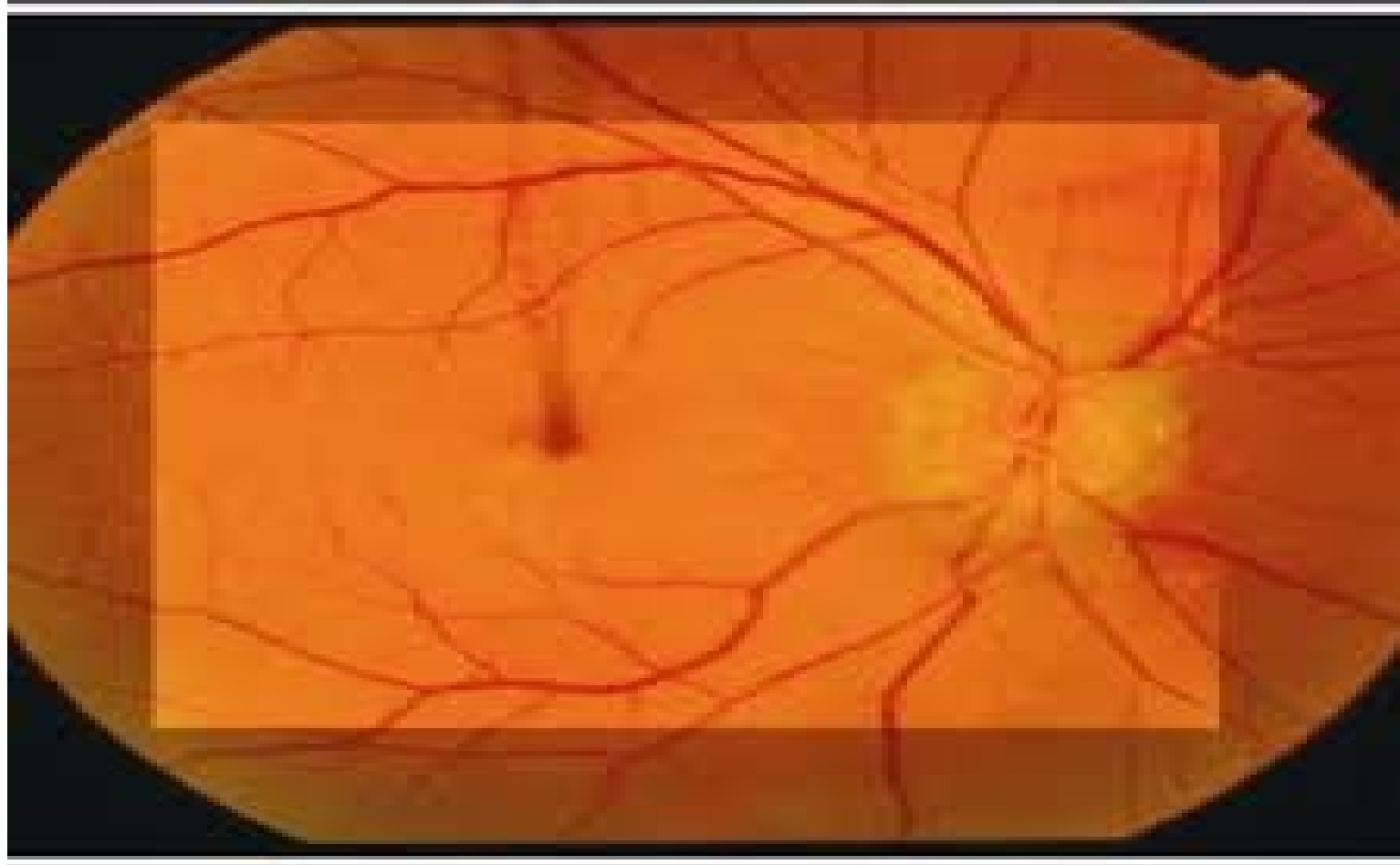
Fundus Fluorescein Angiography (FFA)



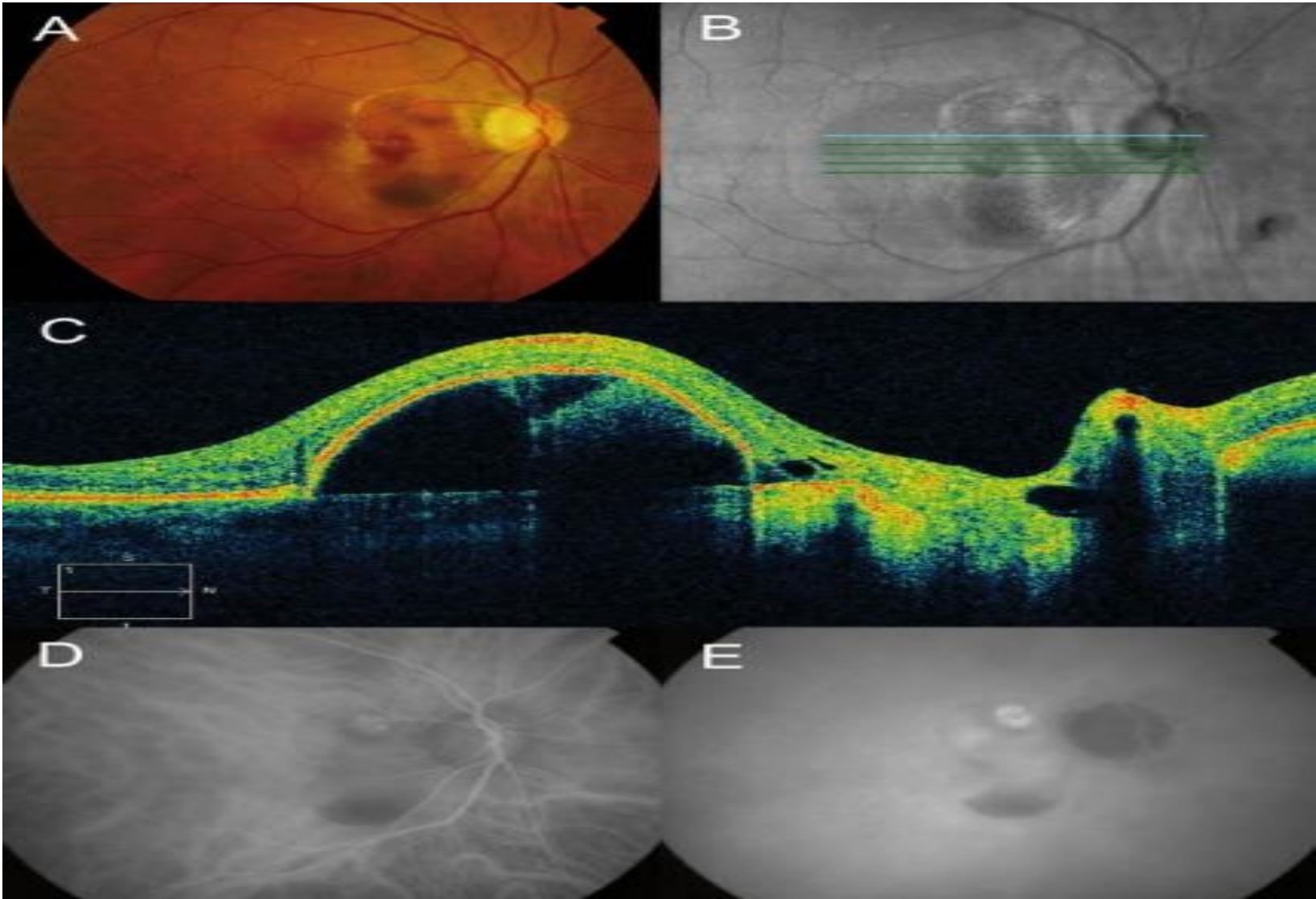
Indocyanine green angiography (ICGA)



Autofluorescence



Optical coherence tomography (OCT)



Imaging of Neovascular ARMD (WET ARMD)

- **1. Fundus Fluorescein Angiography (FFA):** helpful in identifying the type of PED (Retinol Pigment Epithelium Detachment).
- **2. Indocyanine Green Angiography (ICGA):** Better visualization of the choroidal vessels. It is more sensitive tool for identifying CNVM (choroidal neovascular membrane) associated with serous, drusenoid or hemorrhagic PED(Retinol Pigment Epithelium detachments).
- **3. Optical coherence tomography (OCY):** The four variants of PED can be differentiated on OCT. It is useful in defining the type of choroidal neovascular membrane (hyperreflective lesion) based on its location beneath the RPE (type 1) or above the RPE (type2).
- (Kolb H, Fernandez E, Jones, B, et al., editors Webvision).

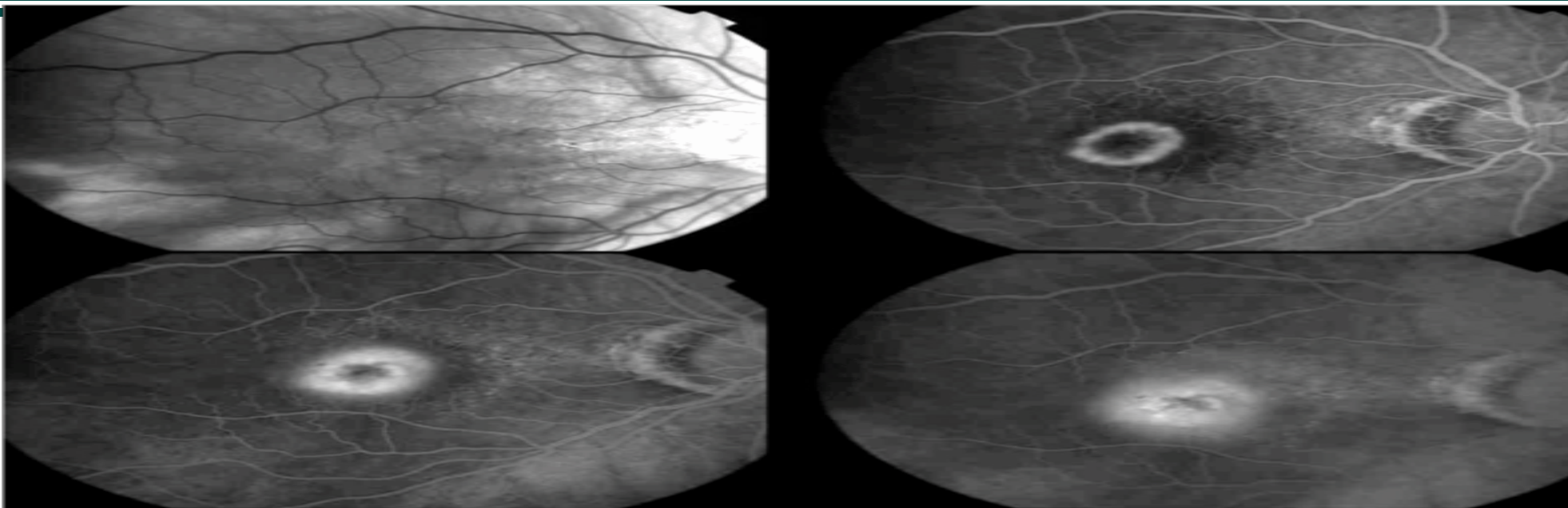


Figure 2. Classic choroidal neovascularization. Early hyperfluorescence of lacy network with central hypofluorescence, intense progressive leakage.

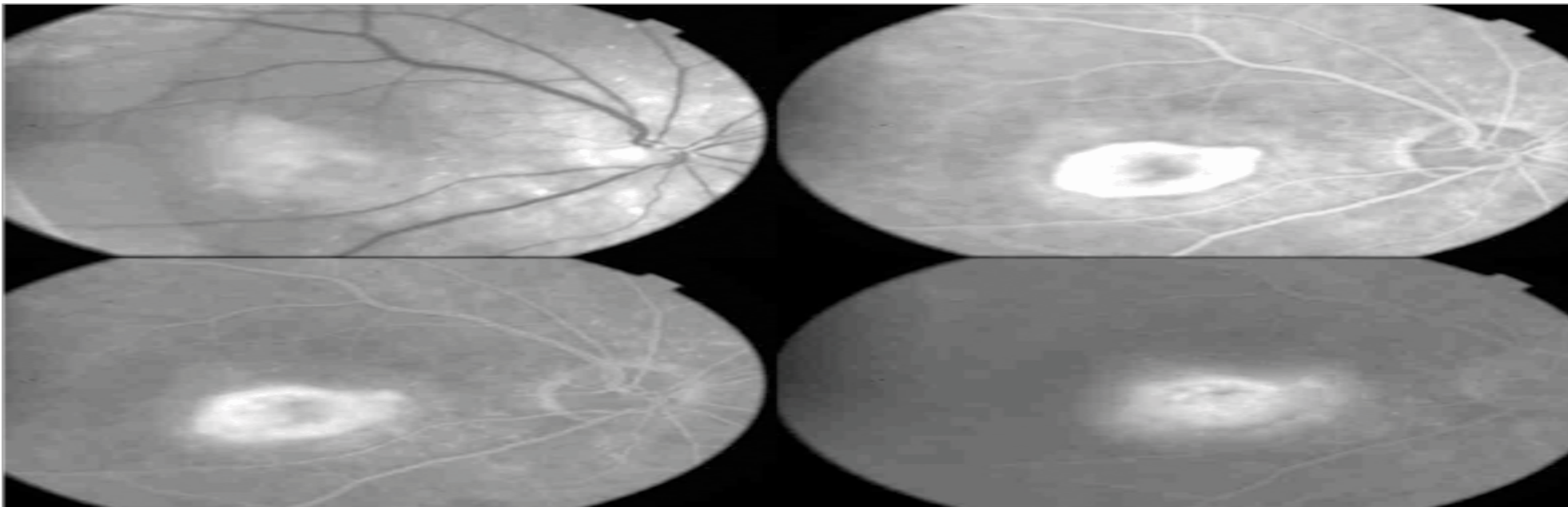


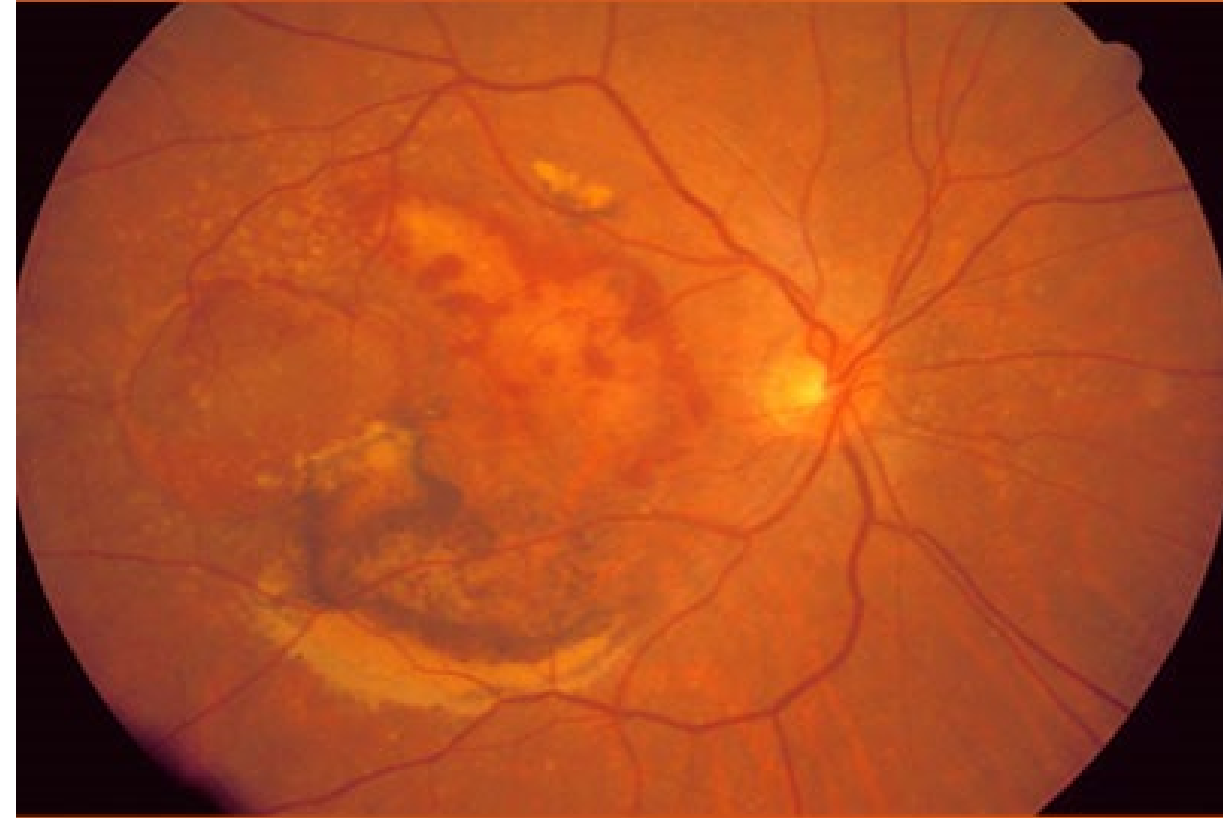
Figure 3. Atypical classic choroidal neovascularization. Early hyperfluorescence with less intense leakage.

Wet ARMD Fundus Photographs

With wet ARMD, abnormal blood vessels grow under the retina, leak blood or other fluids, and cause scarring. This can damage your vision quickly.

This is what wet ARMD looks like using fundus photography.

Wet macular degeneration photo



Treatment and Management for Dry ARMD

- **Requires regular follow up to identify early signs of progressions**
- **Early ARMD in both eyes requires no interventions.**
- **There is no evidence to suggest that using early dietary supplements of antioxidants and minerals will reduce the risk of progression to advanced ARMD or intermediate ARMD.**
- **Individuals with intermediate ARMD or advanced ARMD in at least one eye, should be started on the dietary supplement as suggested by the AREDS Reports.**
- **Individuals with advanced ARMD in both eyes may consider this supplement if the individual has a visual acuity of 20/100 in at least one eye.**

Treatment for Intermediate or Advanced Neovascular ARMD (Wet)

- **The formulation suggested by AREDS 1 is the following:**
- **Daily dose 500 mg vitamin C**
- **Vitamin E 400 IU daily**
- **Beta Carotene 15 mg daily (do not take if smoker increases risk of lung cancer)**
- **Zinc Oxide 80 mg daily**
- **Cupric oxide 2 mg daily (reduce risk of copper-deficiency anemia)**
- **Lutein 10 mg (Macular pigments)**
- **Zeaxanthin 2 mg (Macular pigments)**
- **Omega -3 fatty acids 1 GM**
- **(Check with your eye doctor)**

Treatment for Neovascular ARMD: WET ARMD

- **LASER PHOTOCOAGULATION:** Lesions sufficiently peripheral to the fovea that presents minimal risk of iatrogenic damage is the one that can undergo laser treatment. Rarely used today, high recurrence rates.
- **PHOTODYNAMIC THERAPY (PDT):** introduced in 2000 as less destructive phototherapy in treating CNV. Involves light of a specific wavelength to the CNVA after administering a drug verteporfin. Progression slowed for CNVM but visual prognosis poor. Used sparingly.
- **ANTIANGIOGENIC THERAPY:** Both grow-promoting and growth inhibiting factors, contributes to angiogenesis. Activates Vascular endothelial growth factor (VEGF) , fibroblast growth factor. Several forms approved by FDA over the years. Ranibizumab current form used once monthly found to improve visual acuity and macula remains dry.
- **INTRAVITREAL INJECTIONS:** has reduced the need for laser or surgery with ARMD. Has its own set of side effects.

Surgery Indicated for Some Cases of ARMD

- **Surgery is required in a few cases of ARMD, where patients present with submacular hemorrhage.**
- **Submacular surgery involving the removal of the CNVM and macular translocation surgeries have been abandoned nowadays.**
- **Many patients improve with the use of intravitreal agents. Cost burden to patient.**

Other treatments and future procedures

- **Retinal Pigment Epithelium (RPE) Transplantation**: Because ARMD is mainly related to damage RPE cells which are easy to cultivate and independent of synaptic connections, RPE Cells can be transplanted to repair or replace RPE cells in patients.
- RPE transplantation mainly includes macular translocation, autologous RPE-choroidal transplantation, and RPE cell suspension injection.
- **Stem Cell Therapy**: new potential method for dry ARMD treatment. In 2012, researchers first reported the transplantation of human embryonic stem cells (hESC), derived RPE (Retinal Pigment Epithelium) cells into elderly patients with dry ARMD.
- They successfully transplanted the cells hSEC cells into the patients and no pathological conditions such as teratoma, which are abnormal proliferation of hESC-RPE cells were found.
- Patients best –corrected visual acuity was obtained and tolerated.

Other Treatments and Future Developments for ARMD

- **Biological Patch** consisting of RPE monolayer derived from hESC.
- In their clinical trials, the vision of two ARMD patients with severe visual impairment was stabilized and improved. This was a new treatment for dry ARMD. One disadvantage of this technique is that local immunosuppression is necessary for hESC-RPE. There is no evidence of adverse proliferation, tumorigenicity, or other ocular or systemic safety problems.
- Mandai et al studied the feasibility of transplantation of RPE cells derived from Pluripotent stem cells (IPSC) for the treatment of ARMD. ISPC was generated from skin fibroblasts of patients. Subretinal injection.
- (Yanhui Deng, Lifeng Qiao, Mingyan Du, Chao Qu, et al., Age-Related Macular Degeneration: Epidemiology, genetics, pathophysiology, diagnosis, and targeted therapy. Genes and Diseases, January 2022.

Enhancing Healthcare Team Outcomes

- **ARMD is the leading cause of blindness in the elderly population.**
- **Interprofessional communication and coordination are important in screening for the disease.**
- **People above the age of 50 should undergo an eye evaluation by an ophthalmologist to rule out the presence of ARMD.**
- **Early ARMD patients are often asymptomatic so annual eye exams are important.**
- **Timely intervention should be discussed.**
- **Physicians may refer patients with poor vision to an ophthalmologist for low vision aides.**
- **Patients with ARMD and poor vision can wear wrist bands so others can protect them from falling and other accidents.**
- **ATMD can be managed appropriately if recognized timely and treated sincerely.**
- **Intravitreal injections are the standard of care for these patients.**
- **The cause-effect relationship of systemic side effects and these drugs is not well established, therefore, the risk-benefit ratio is favorable.**

Some of the best visual aids for patients with ARMD include:

1. Magnifiers

Magnifiers enlarge fine print or small objects, making them easier to see. Handheld magnifiers are portable and can be used for reading, crafting and other hobbies, but they must be held by hand. In contrast, stand magnifiers can be placed on top of a book or newspaper and are always focused for the correct distance.

2. Closed-Circuit Television (CCTV) Systems

These systems use a digital camera to magnify print or objects and display them on a screen. They can be adjusted to suit the individual's needs and can be used for a variety of tasks, such as reading, writing and crafting.

3. Electronic Reading Aids

These devices use text-to-speech technology to read aloud printed materials such as books, newspapers and labels. They can be portable or desktop-based and can be adjusted to suit the individual's reading speed and preferences.

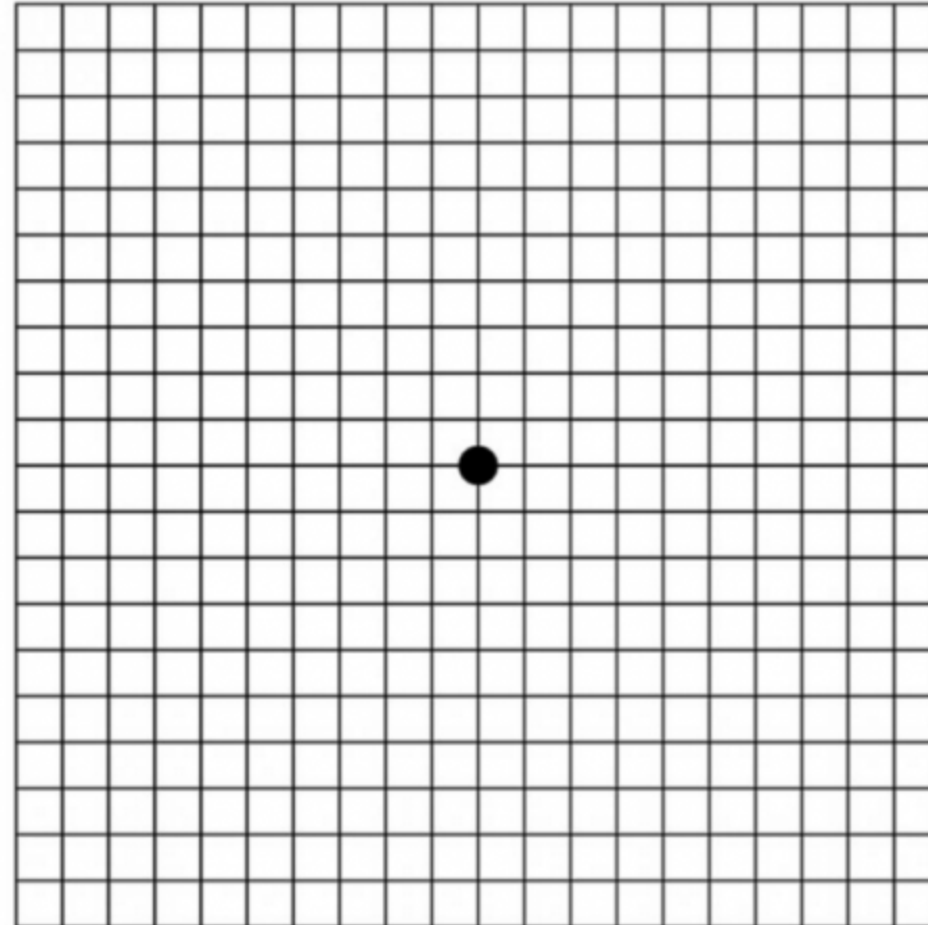
4. Talking Watches and Other Appliances

Talking watches and clocks verbally announce the time, so they're useful for patients who have difficulty reading a traditional clock or watch. Other household appliances, such as microwaves, kitchen scales and thermometers, can also come with a "talking" feature that is low-vision friendly.

5. Low Vision Optical Lenses

Your low vision optometrist can prescribe a wide range of optical lenses and glasses to help broaden your vision. Some examples include E-Scoop glasses, prismatic glasses, binocular or telescope glasses, and bioptic glasses. You can also get customized glasses to suit your specific needs.

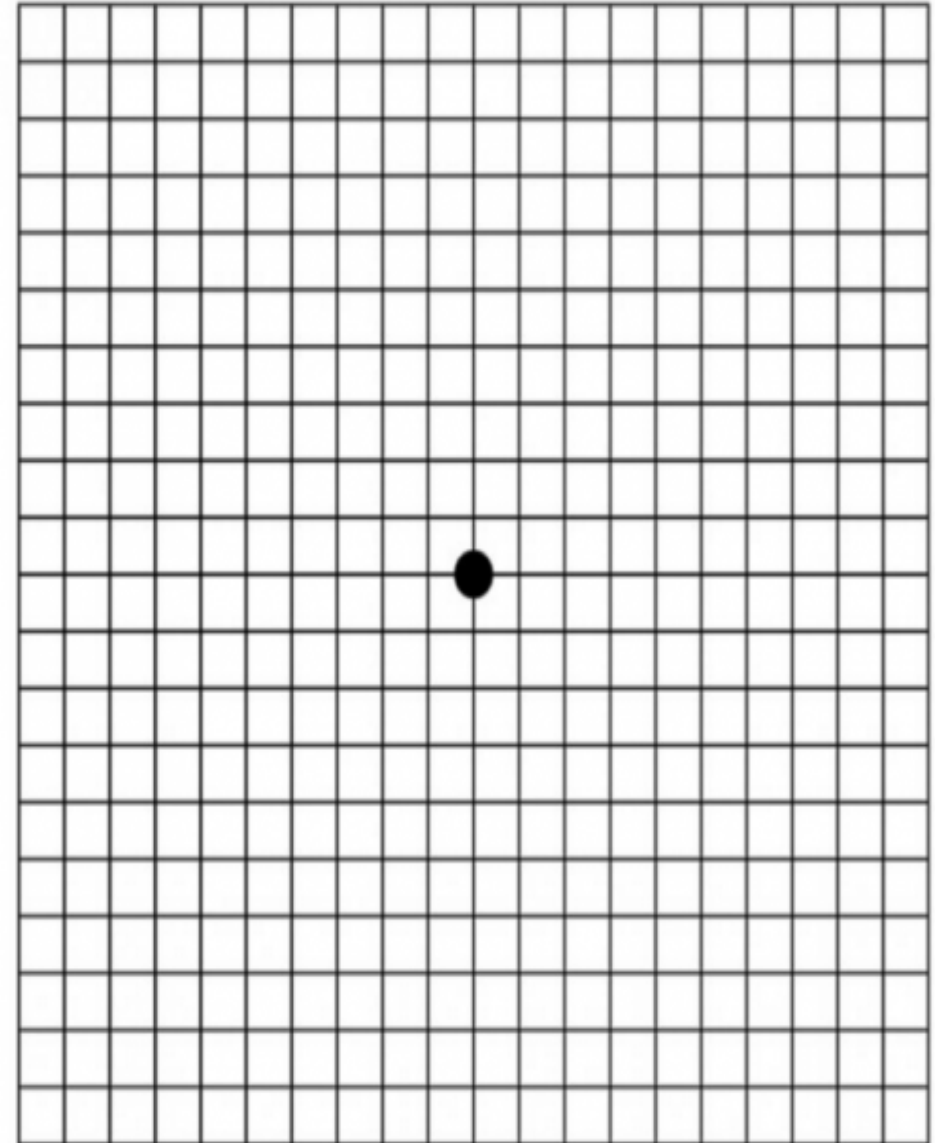
Amsler Grid Tool: At home Eye exam for people to use to check for vision changes.



Amsler Grid Tool: At home Eye exam for people to use to check for vision changes.

How to Use the Amsler Grid

1. Use the Amsler grid pictured here. Or, download and print this [free Amsler grid eye test](#) on plain white paper.
2. With reading glasses on, hold the grid at a distance that allows you to get most of the lines in focus; it will probably be about 12-14 inches away, the same as book reading distance.
3. Cover one eye and focus on the black dot in the middle of the grid.
4. Cover the other eye and repeat the test. If the lines appear to be wavy, dim, irregular, or fuzzy, schedule an eye exam immediately.
5. Repeat the test once a week. Call us at 1-855-345-6637 to request a magnetic version of the Amsler grid so you can put it on your refrigerator.



Summary

- Today we discussed:
- Age-Related Macular Degeneration, it's forms and classifications.
- We discussed Dry ARMD and Wet ARMD.
- We reviewed the anatomy and physiology of the human eye.
- We discussed risk factors and healthy life-style changes we can make to protect our eyes.
- Pathophysiology of ARMD was discussed.
- Treatments for ARMD were listed.
- Discussion of the Healthcare Team and how they must communicate and coordinate services to improve the patients understanding and compliance with annual eye exams and early treatment for ARMD.
- Thank you for sharing your day with me.

References

- **Monika Fleckenstein, MD; Steffen Schmitz-Valckenberg, MD; Usha Chakravarthy, MD, PhD, Age-Related Macular Degeneration, A Review. JAMA. 2024;331(2):147-157.**
- **Surabhi, Ruia: Evan J. Kaufman: Macular Degeneration; NCBI Bookshelf Stat Pearls Publishing: 2024. January.**
- **Yanhui Deng, Lifeng Qiano, Mingyan Du, Et al: Genes and Diseases, Science direct, Volume 9, Issue 1, January 2022, Pages 62-79. Age-related Macular degeneration: epidemiology, genetics, pathophysiology, diagnosis, and targeted therapy.**
- **Kolb H, Fernandez E. Jones, B, er al., editors. Webvision: The Organization of the Retina and visual System. Gross Anatomy of the Eye. May 1, 2024.'**
- **The role of the gut microbiome in eye diseases, 2023, Progress in Retinal and eye Research.**
- **Interpaly between Aging and other factors of the pathogenesis of age-related macular degeneration. 2022, Aging Research Reviews.**

