WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 13, 634-643. Review Article ISSN 2277–7105

A REVIEW OF AGE-RELATED MACULAR DEGENERATION (AMD)

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Article Received on 05 June 2026,
Article Revised on 25 June 2026,
Article Published on 01 July 2026,
https://doi.org/10.5281/zenodo.21027624

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How to cite this Article: [1]*Mehtaj Begum A., [2]Dr. C. Eugine Leo Prakash, [3]Dr. Akilandeswari S. (2026). A Review Of Age-Related Macular Degeneration (Amd). World Journal of Pharmaceutical Research, 15(13), 634–643.

ABSTRACT

Age-related Macular Degeneration (AMD) is a progressive retinal disorder and a major cause of vision loss among individuals over 50 years of age. The disease primarily affects the macula, resulting in gradual impairment of central vision. AMD is generally classified into two forms: dry (non-neovascular) and wet (neovascular). Dry AMD is more common and involves the accumulation of drusen along with degeneration of the retinal pigment epithelium and photoreceptors. In contrast, wet AMD is characterized by abnormal choroidal neovascularization, which can lead to rapid and severe vision loss due to leakage of blood and fluid. Several factors such as aging, smoking, hypertension, genetic susceptibility, and dietary habits contribute to disease development. Diagnosis is supported by clinical evaluation and imaging techniques including fundus examination, optical coherence tomography, and fluorescein angiography. Although there is no definitive cure for dry AMD, disease progression may be slowed through antioxidant supplementation based on the AREDS and AREDS2 formulations. Wet AMD is mainly treated with intravitreal anti-VEGF agents such as ranibizumab, bevacizumab, and aflibercept. Early detection and appropriate management are essential to prevent severe visual impairment and improve patient outcomes.

KEYWORDS: Age-related macular degeneration, retinal pigment epithelium, drusen, choroidal neovascularization, anti-VEGF therapy.

INTRODUCTION

Age-related macular degeneration (AMD) is the leading cause of blindness in people over age 50 worldwide and the third leading cause of blindness overall. As the world population ages, AMD is expected to grow in prevalence, with the number of estimated cases predicted to reach 288 million by 2040. AMD is typically classified into two forms, a non-neovascular or “dry” form and a neovascular “wet” form, but even these simple terms are evolving as we incorporate new information from optical coherence tomography-angiography (OCT-A). All AMD starts as the dry form and is characterized by accumulation of deposits under the retinal pigment epithelium (RPE) and neurosensory retina, as well as degeneration of the RPE, photoreceptors, and even the choroidal vasculature, whereas wet AMD is characterized by the development of new choroidal vessels that are often highly permeable and fragile.[1] This choroidal neovascularization (CNV) extends from the choroid into the subretinal space within Bruch’s membrane, or in the subretinal RPE space. Severe vision loss and impairment of activities of daily living most often occurs in advanced AMD due to two primary causes: 1. central geographic atrophy (GA), in which large sections of RPE and overlying photoreceptor cells are lost; or 2. CNV with its associated leakage of subretinal fluid, lipid deposition, haemorrhage, RPE detachment, and/or fibrotic scarring. AMD is a complex, multifactorial disease and the associations with genetic and environmental factors are well-recognized. While prior research has pointed to and implicated roles for numerous pathways in the pathobiology of AMD, including inflammation, complement, lipids and cell death, our understanding of their precise mechanisms, as well as the relative contributions of these pathways, remains incomplete. The demonstration of the critical role vascular endothelial growth factor (VEGF) plays in ocular neovascularization formed the basis for the development of successful anti-VEGF therapies for the treatment of neovascular AMD and other retinal diseases.[2]

EPIDEMIOLOGY

AMD is one of the leading causes of blindness in older adults globally. The prevalence increases exponentially with age, particularly after 60 years. Both genetic susceptibility and environmental factors contribute to disease development. Smoking has been identified as the

most significant modifiable risk factor, while genetic polymorphisms related to the complement system play a vital role in disease predisposition.[3]

TYPES

1. **Dry**: This type is the most common. About 80% of those with AMD have the dry form. Its exact cause is unknown, although both genetic and environmental factors are thought to play a role. This happens as the light-sensitive cells in the macula slowly break down, generally one eye at a time. The loss of vision in this condition is usually slow and gradual. It is believed that the age-related damage of an important support membrane under the retina contributes to dry age-related macular degeneration.
2. **Wet**: Though this type is less common, it usually leads to more severe vision loss in patients than dry AMD. It is the most common cause of severe loss of vision. Wet AMD happens when abnormal blood vessels start to grow beneath the retina. They leak fluid and blood, hence the name wet AMD, and can create a large blind spot in the center of the visual field.[4]

RISK FACTORS FOR AGE-RELATED MACULAR DEGENERATION [5]

- Being 50 and older
- Eating a diet high in saturated fat
- Smoking
- High blood pressure or hypertension

CLASSIFICATION

- **Early AMD**: Defined by the presence of numerous small (<63 microns, “hard”) or intermediate (≥63 microns but <125 microns, “soft”) drusen. Small drusen often appear in people aged 50 and above as a normal aging change, whereas intermediate drusen are more strongly linked with AMD.
- **Intermediate AMD:** Macular disease characterized by either extensive drusen of small or intermediate size, or any drusen of large size (≥125 microns) Note: 124 microns is the average diameter of the retinal vein at the optic disc margin.
- **Advanced AMD:** Defined by the presence of either geographic atrophy or choroidal neovascular membrane (along with its sequelae, such as subretinal or sub-RPE hemorrhage or serous fluid and subretinal fibrosis).[6]

SIGNS

- Drusen
- Geographic atrophy
- Subretinal fibrosis
- RPE changes
- Subretinal fluid or haemorrhage/hard exudate.[7]

SYMPTOMS

- Decreased visual acuity, insidious or sudden onset
- Dry AMD constitutes 85%-90% cases of AMD and usually does not cause severe vision loss.
- Wet AMD constitutes 10%-15% of AMD cases and is the major cause of severe vision loss.
- Blurred vision
- Distorted near vision
- Scotoma
- Visual distortion, metamorphopsia, micropsia
- Vague visual complaints.[8]

PATHOPHYSIOLOGY

Dry AMD (Non-neovascular AMD): Dry AMD occurs due to progressive degeneration of the retinal pigment epithelium (RPE), photoreceptors and the underlying Bruch's membrane. The condition is characterized by the accumulation of extracellular deposits known as drusen, which contain lipids, proteins and cellular debris between the RPE and Bruch's membrane. These deposits interfere with nutrient and oxygen transport to retinal cells, leading to oxidative stress and chronic inflammation. Over time, this results in gradual atrophy of the RPE and photoreceptors, causing slow and progressive loss of central vision. In advanced stages, it may lead to geographic atrophy, where large areas of the retina lose functional cells.

Wet AMD (Neovascular AMD): Wet AMD develops when abnormal blood vessels grow from the choroid through Bruch's membrane into the subretinal space, a process known as choroidal neovascularization (CNV). This abnormal vessel growth is mainly stimulated by increased levels of vascular endothelial growth factor (VEGF) in response to retinal hypoxia and inflammation. The newly formed vessels are fragile and highly permeable, leading to

leakage of blood, fluid and lipids beneath the retina. This causes retinal swelling, haemorrhage, and scar formation, which rapidly damages photoreceptors and leads to sudden and severe central vision loss if left untreated.[9]

DIAGNOSTIC INVESTIGATIONS

- **Amsler Grid Test**: Screening tool for central visual distortion
- **Fundus Examination**: Detection of drusen and retinal changes
- **Optical Coherence Tomography (OCT)**: Evaluation of retinal thickness and fluid accumulation
- **Fluorescein Angiography**: Identification of choroidal neovascularization
- **Autofluorescence**: Assessment of RPE integrity. [10]

GENERAL SUPPORTIVE TREATMENT MEASURES

- **Smoking cessation:** Smoking cessation is recommended because smoking increases the risk of progression to advanced AMD. Also, no vaping with nicotine-containing products, as nicotine may exacerbate neovascularization.
- **Blood pressure control**: There is association of hypertension and neovascular AMD. Monitoring and control of BP should be done.
- **Diet**
- **Antioxidant, Vitamins and Zinc**: Patients with extensive intermediate-size drusen, at least one large drusen or noncentral geographic atrophy in one or both eyes should be treated with a daily oral eye vitamin supplement (eg, Ocuvite, PreserVision).

The AREDS2 formulation contains vitamin C (500 mg), vitamin E (400 IU), lutein (10 mg), zeaxanthin (2 mg), zinc (80 mg as zinc oxide) and copper (2 mg as cupric oxide). The earlier AREDS formula included beta-carotene, which is associated with increased lung cancer risk in smokers; therefore, it is mainly recommended only for nonsmokers or those at low risk.[11]

SPECIFIC TREATMENT: WET AMD

- Intra-vitreous injection of a vascular endothelial growth factor (VEGF) inhibitor like Ranibizumab, Bevacizumab and Aflibercept.
- Frequency: For Ranibizumab (0.5 mg) and bevacizumab (1.25 mg) monthly injections for 3-6 months and then as needed determined by further assessment of disease activity. For

aflibercept: administer three doses (2 mg) at four-week intervals, followed by 2 mg every eight weeks.

- Adverse effects: Endophthalmitis (0.6-1.3%), increased IOP and light sensitivity.[12]

AGE-RELATED MACULAR DEGENERATION: INSIGHTS AND CLINICAL FINDINGS

Nutritional Supplementation (AREDS / AREDS2)

There is no definitive curative pharmacotherapy for dry AMD. However, disease progression can be slowed through antioxidant and micronutrient supplementation based on AREDS and AREDS2 recommendations.

AREDS2 formulation includes

- Vitamin C
- Vitamin E
- Zinc
- Copper
- Lutein
- Zeaxanthin

Beta-carotene is excluded in AREDS2 due to the increased risk of lung cancer in smokers.[13]

Mechanism of Action

- Reduces oxidative stress
- Protects retinal pigment epithelium (RPE)
- Slows progression from intermediate to advanced AMD.[14]

THERAPY FOR WET (EXUDATIVE) AMD

Anti-VEGF Therapy (Gold Standard)

Anti-vascular endothelial growth factor (anti-VEGF) agents are the first-line treatment for wet AMD.

Table 1: Types of Anti-VEGF Agents Used for Wet AMD Treatment.[15,16]

Drug	Type
Ranibizumab	Monoclonal antibody fragment
Bevacizumab	Monoclonal antibody
Aflibercept	VEGF-trap fusion protein
Brolucizumab	Humanized antibody

Mechanism of Action

- Inhibition of VEGF-mediated angiogenesis
- Reduction of vascular permeability and macular edema.[17,18]

Route of Administration: Intravitreal injection.[19]

Adverse Effects

- Endophthalmitis
- Increased intraocular pressure
- Intraocular inflammation.[20,21]

Emerging and Investigational Therapies

- Complement pathway inhibitors for dry AMD
- Gene therapy for sustained anti-VEGF expression
- Long-acting drug delivery systems to improve compliance.[22,23]

Photodynamic Therapy

- IV injection of the photosensitizing dye verteporfin just prior to treatment with a photo-activating laser applied through the eye with a specific contact lens.
- The activated dye forms reactive free radicals that damage the vascular endothelium and result in thrombosis of the neovascular tissue that retains dye more avidly than normal vessels. However, these vessels often reopen.[24,25]

Role of Pharmacists

Pharmacists play a vital role in AMD management by educating patients, promoting lifestyle modification, guiding appropriate nutritional supplementation, monitoring anti-VEGF therapy and ensuring medication safety. Their involvement enhances treatment adherence, pharmacovigilance and interdisciplinary care.[26]

CONCLUSION

Age-Related Macular Degeneration is a major cause of visual impairment among the elderly, with complex pathophysiology and varied clinical presentation. Advances in diagnostic imaging and pharmacological therapies have improved disease management, especially for wet AMD. However, preventive strategies and early detection remain essential to reduce disease burden. Pharmacists play a pivotal role in the comprehensive management of Age-Related Macular Degeneration by supporting both preventive and therapeutic strategies. Their

responsibilities include patient education on disease progression, counselling on lifestyle modification and smoking cessation, and guidance on evidence-based nutritional supplementation such as AREDS/AREDS2 formulations. In patients receiving anti-VEGF therapy, pharmacists contribute to safe handling of biologics, dosing schedule optimization and pharmacovigilance through monitoring and reporting adverse drug reactions. Pharmacists also aid in improving medication adherence, identifying drug–drug and drug–nutrient interactions and collaborating with ophthalmologists and other healthcare professionals to optimize patient outcomes. As emerging therapies evolve, the pharmacist's role in clinical decision support and patient-entered care will remain essential in reducing the burden of AMD.

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