QUALITY IN SPORT
eISSN 2450-3118 · Open Access · Peer-reviewed
apcz.umk.pl/QS Nicolaus Copernicus University in Toruń

Cite as: WIEKIERA, Mateusz, WIEKIERA, Adrianna, KOPCIAŁ, Szymon, BUDZIK, Paweł and KORNATOWSKA, Karolina. Age-Related Macular Degeneration: Pathogenesis and Future Therapeutics. Quality in Sport. 2026;56:72001. https://doi.org/10.12775/QS.2026.56.72001

ARTICLE TIMELINE
Received: 17.05.2026 Revised: 20.05.2026
Accepted: 20.05.2026 Published: 25.05.2026

INDEXING & EVALUATION
MEiN points: 20 Unique ID: 201398
Disciplines: Economics & Finance; Management & Quality Sciences

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines: Economics and Finance (Social Sciences); Management and Quality Sciences (Social Sciences).

Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

Age-Related Macular Degeneration: Pathogenesis and Future Therapeutics

Mateusz Wiekiera

Medical University of Łódź

https://orcid.org/0009-0003-9236-2913

Adrianna Wiekiera

The Nicolaus Copernicus Provincial Multispecialty Center for Oncology and Traumatology: Łódź, Poland

https://orcid.org/0009-0001-4829-3768

Szymon Kopciał

The Nicolaus Copernicus Provincial Multispecialty Center for Oncology and Traumatology: Łódź, Poland

https://orcid.org/0009-0008-6647-247X

Paweł Budzik

Norbert Barlicki Memorial Teaching Hospital No. 1 of the Medical University of Lodz: Łódź, Poland

https://orcid.org/0009-0003-3177-5634

Karolina Kornatowska

Dr. Tytus Chałubiński Specialist Hospital: Radom, Poland

https://orcid.org/0009-0008-4622-8285

Abstract

The aging process significantly increases the likelihood of developing ocular diseases, most notably Age-related Macular Degeneration (AMD), which is a leading cause of vision loss both in the US and globally. The development of this disease is directly driven by aging changes occurring in the retina. These include the deposition of specific deposits called drusen, structural remodeling of Bruch's

membrane and the extracellular matrix, as well as inflammation and vascular dysfunction. Additionally, this process is fueled by mitochondrial dysfunction and oxidative stress caused by an excess of free radicals (ROS), which ultimately leads to the degradation of retinal pigment epithelium (RPE) cells. Because current methods for preventing and treating AMD are highly insufficient, researchers are continuously searching for innovative therapeutic strategies and new drug targets.

Keywords: ocular, vision loss

Introduction:

As the foremost cause of permanent central vision impairment in the elderly, age-related macular degeneration (AMD) is a progressive neurodegenerative condition. It specifically damages the macula, which is the central region of the retina essential for clear and focused forward sight [1]. The macula is a round region measuring approximately 5.5 mm across. At its core lies the fovea centralis, a tiny depression in the human eye densely packed with cone photoreceptors. This specific structure is crucial for providing clear, focused central sight. The fovea is structurally encircled by two distinct anatomical zones: the inner parafovea and the outer perifovea [2].

Age-related macular degeneration negatively impacts sharp central sight, making daily tasks like reading, driving, and recognizing faces difficult. Natural aging brings alterations to the retina, notably the formation of small, hard drusen—accumulations of lipids, proteins, and cellular waste. These are typical and found in about 95% of individuals older than 43. However, when these deposits grow, merge, or cause abnormal pigmentation (either too much or too little) in the retinal pigment epithelium

(RPE), leading to vision problems, the condition transitions from normal aging to a pathological state. At this point, it is clinically defined as the early or intermediate stage of AMD [3]. Although dry AMD is more common, the neovascular (wet) form, nAMD, is responsible for the most severe vision loss because it advances much more rapidly and aggressively. Given the substantial impact of these conditions, halting their progression is crucial. There is a pressing demand for innovative and highly effective therapies to preserve patients' eyesight. Furthermore, long-lasting treatments are essential to alleviate the heavy resource strain currently placed on the healthcare system. While the introduction of anti-VEGF drugs over the past twenty years has revolutionized the treatment of wet AMD, the management of dry AMD has unfortunately not seen comparable breakthroughs [4].

Epidemiology:

Recent meta-analyses highlight that the annual incidence rates of new late-stage AMD cases vary depending on geography and ethnicity. For white Americans over 50, the yearly incidence of late AMD is about 3.5 per 1,000 individuals, breaking down to 1.9 for geographic atrophy (GA) and 1.8 for the neovascular form. In contrast, European studies show a lower combined annual incidence of 1.4 per 1,000 people. A separate US-based prospective study evaluating ethnic variations reported overall adjusted incidence rates of 4.1% for early AMD and 2.3% for late AMD. When broken down by demographic groups, the rates for early and late AMD, respectively, were highest among white individuals (5.3% and 4.1%), followed by people of Chinese descent (4.5% and 2.2%), those of Latin American descent (3.3% and 0.8%), and lowest among Black individuals (1.6% and 0.4%) [5].

Types of AMD:

Both dry and wet (neovascular) AMD affect the same layers of the retina, with the dry form generally acting as a prelude to the wet form. The process begins when metabolic free radicals and reactive oxygen species subject the RPE to severe oxidative stress. This stress disrupts normal cellular functions—like lipid processing and macrophage activity—leading to the buildup of drusen. These deposits not only physically injure RPE cells but also block the vital exchange of oxygen and nutrients from Bruch's membrane to the photoreceptors. This blockage triggers inflammation, RPE death, and eventually, abnormal blood vessel growth. Specifically, drusen deposits trap IgG antibodies and complement C5a, hindering the macrophages that usually clean up cellular debris. This triggers a vicious cycle: the choroid releases the chemokine CCL2, drawing in more immune factors, which in turn causes the RPE to release VEGF, IL-8, and monocytes. Consequently, the delicate balance

between vessel-promoting (VEGF) and vessel-inhibiting (PEDF) factors is destroyed. As the retina becomes oxygen-starved, it releases more VEGF and inflammatory signals, prompting endothelial cells from the choroid to multiply and form new vessels. Activated macrophages gather near these new vessels, releasing tumor necrosis factor (TNF), which further pushes the RPE to secrete angiogenic factors and promotes cell movement. Aided by proteases and mitochondrial matrix metalloproteinases (MMPs), these fragile, newly formed blood vessels breach Bruch's membrane and invade the subretinal spaces, developing into a disruptive network of arterioles and venules. [11]

Although wet (neovascular) AMD is less common than the dry form, it triggers a much faster and more profound loss of central vision. In this condition, an abnormal network of blood vessels grows beneath the macula (choroidal neovascularization). These fragile vessels leak blood and fluid into the surrounding tissues, eventually causing permanent scarring and central blindness. This harmful vascular expansion is driven by an overabundance of vascular endothelial growth factors (VEGF)—specific cytokines that control vessel formation and permeability. The VEGF family encompasses multiple proteins (including VEGF-A through E, along with placental growth factor) that operate by triggering tyrosine-kinase receptors. Within the eye, VEGF-A is the primary catalyst for new blood vessel creation, pushing endothelial cells to multiply, migrate, and survive. Consequently, the current gold standard for treating nAMD focuses directly on blocking VEGF-A using specific medications like ranibizumab, bevacizumab, or aflibercept. Despite their widespread use, these anti-VEGF treatments have major drawbacks. The reliance on frequent, ongoing eye injections places a heavy burden on patients. This often leads to missed appointments and suboptimal results, while also causing considerable anxiety and physical discomfort. Furthermore, repetitive injections carry localized risks—such as persistent elevated eye pressure, intraocular infections (endophthalmitis), and RPE tearing or atrophy—as well as systemic dangers, including a potentially higher risk of heart attacks and strokes. Concerningly, long-term data from the CATT study revealed that nearly 50% of patients developed retinal scarring within five years of starting therapy. Finally, none of the current medications can fully cure or reverse nAMD; many patients continue to experience fluid leakage from these abnormal vessels even when strictly following their prescribed anti-VEGF regimen. [12]

Angiogenesis and Inflammation:

The creation of blood vessels occurs through two primary mechanisms: vasculogenesis and angiogenesis. Occurring mostly during the embryonic stage, vasculogenesis refers to the de novo formation of the earliest vessels when endothelial cells differentiate from precursor angioblasts.

Angiogenesis, in contrast, involves the sprouting of new capillaries from an already established vascular system, serving to expand and reshape the vessel network. This mechanism is essential for both natural physical development and the healing of tissues. The angiogenic process is triggered when tissues suffering from oxygen deprivation (hypoxia), injury, or disease secrete specific chemical signals to stimulate vascular growth. These pro-angiogenic factors prompt the endothelial cells of existing vessels to multiply and migrate. Ultimately, this leads to the assembly of new capillary tubes and the gathering of various supportive cells needed to structurally reinforce and stabilize the newly formed blood vessels [6].

The stability of blood vessels in the eye relies on a delicate equilibrium between factors that promote and inhibit vessel growth. Various disease states, such as oxidative stress, ischemia, or inflammation, can upset this balance by triggering damaged cells to release more pro-angiogenic signals while reducing their anti-angiogenic output. The eye naturally contains several angiogenesis inhibitors, such as angiostatin, endostatin, PEDF, and TSP1. Certain inhibitors, like endostatin, remain inactive until they undergo specific proteolytic cleavage. Both PEDF and TSP1 prevent new vessel formation by specifically triggering programmed cell death (apoptosis) in the endothelial cells (ECs) of developing vessels, leaving the ECs of established, mature vessels largely unharmed. In patients suffering from AMD, analyses of ocular tissues have revealed a reduction in endostatin, PEDF, and TSP1 within the choriocapillaris and Bruch's membrane. Conversely, significant concentrations of PEDF and TSP1 are found within disciform scars, which are classic indicators of choroidal neovascularization [7].

The onset and progression of AMD are heavily driven by immune system dysfunction and inflammation. The signature drusen deposits found in dry AMD are packed with inflammatory markers—like acute-phase proteins, IgG, apolipoprotein E, complement system activators, and coagulation factors-highlighting localized inflammation as a primary trigger for the condition. Multiple lines of research confirm that immune imbalances and inflammatory pathways are essential in both driving drusen buildup and advancing the disease. This leads to the gathering of extracellular debris, localized immune responses, and the influx of macrophages and microglia into the choroid and subretinal areas, which ultimately worsens tissue injury. As the retina ages, it suffers from progressive oxidative stress, evidenced by an increase in oxidized proteins and lipid peroxidation remnants. When faced with this metabolic and oxidative burden, retinal neurons and RPE cells undergo functional and structural decline, sparking a phased immune reaction. At first, the cells try to protect themselves and regain balance by activating autophagy and producing heat shock proteins. Yet, the persistent stress

typical of the aging process eventually defeats these protective measures, forcing the cells into senescence or programmed death (apoptosis) [8].

AMD diagnosing framework:

The framework for diagnosing AMD is built upon three core pillars: gathering datasets, applying image pre-processing methods, and utilizing machine and deep learning (ML/DL) for segmentation and detection. The data acquisition phase highlights essential private and public repositories—including the AREDS, DRIVE, and STARE databases—that provide distinct benefits for AMD research. Following this, the framework details pre-processing steps like noise reduction, contrast improvement, image quality optimization, and segmentation masking. These steps are vital for readying OCT scans and retinal images for AI-driven analysis. Finally, the section on AI diagnostics explores the vast array of machine learning and deep learning strategies used to boost diagnostic accuracy. This includes examining convolutional neural networks (CNNs), recurrent neural networks (RNNs), and ensemble learning, as well as research that leverages transfer learning and manually extracted features for disease classification [9].

AMD and Cardiovascular Disease:

A 2004 joint analysis of the BDES, BMES, and Rotterdam studies found no clear link between AMD and a history of myocardial infarction (MI) across the combined data, despite some localized correlations. Subsequent research—including the WHISE, LALES, Tromsø, and an Israeli study—similarly failed to establish a solid connection between AMD and cardiovascular disease (CVD). Conversely, numerous investigations have demonstrated a positive correlation between various AMD stages and cardiovascular issues across diverse populations. For instance, Hyman et al. and the BMES linked AMD to a history of CVD, while AREDS and later BMES reports associated both early and advanced AMD with higher cardiovascular mortality. Furthermore, studies by Duan and Vassilev connected AMD to a higher risk of MI. Research such as the ARCS, the Cardiovascular Health Study, and MESA highlighted associations between specific AMD stages (early or late) and coronary heart disease (CHD) or CVD, sometimes depending on demographic factors like age or race. A 2014 meta-analysis by Wu et al., along with findings from Thomas et al. in an older veteran population, reinforced the elevated risk of cardiovascular events in patients with macular degeneration. Supporting this, Yang et al. and Wang et al. observed that patients with coronary conditions had a higher prevalence of early AMD, with Wang noting a direct link between CAD severity and AMD rates.

Interestingly, some data point to an inverse relationship, implying a potentially protective effect. The POLA study found that soft drusen were associated with lower rates of CVD and CHD, while Nguyen-Khao et al. noted fewer strokes and heart attacks in patients with neovascular (wet) AMD. Given these conflicting results, further research into the underlying mechanisms of these conditions is essential. Identifying shared biological risk factors will ultimately enable more effective, unified strategies for treating and managing age-related diseases [10].

Treatment:

Managing AMD effectively requires tailoring the medical approach to the specific phase of the condition. However, regardless of the disease's severity, mitigating known risk factors—most notably quitting smoking—is universally recommended. Numerous large-scale studies indicate that patients who smoke experience a more rapid progression of their AMD compared to non-smokers, even after receiving a clinical diagnosis. Additionally, research from Korea highlights that smokers suffering from wet AMD achieve significantly less improvement in their visual acuity when undergoing anti-VEGF therapy. Consequently, catching AMD in its earliest phases can serve as a crucial catalyst for patients to adopt healthier habits, thereby slowing the disease's advancement [13].

The use of gene therapy in managing dry macular degeneration involves introducing specific genetic material directly into ocular cells. This approach aims to provide a lasting treatment outcome while avoiding adverse immune system reactions. A prime example is HMR59, a therapy created by Hemera Biosciences. It utilizes an AAV2 viral vector to deliver the sCD59 protein, shielding the retinal pigment epithelium (RPE) from the destructive overactivity of the complement system—a hallmark of dry AMD. By naturally residing on RPE cells, the CD59 protein prevents the assembly of the membrane attack complex (MAC), thereby halting the complement cascade and preserving the structural integrity of the retina. The procedure requires an intravitreal injection of HMR59, which subsequently boosts CD59 expression in the RPE. Phase 1 trials (such as HMR-1001) demonstrated that patients tolerated the treatment very well. Notably, after a year and a half of observation, the cohort receiving the highest dosage experienced a 23% decrease in geographic atrophy (GA) progression, with zero cases advancing to the wet, neovascular stage (nAMD). Ongoing research continues to evaluate HMR59's long-term safety and effectiveness [14].

The naturally occurring protein sFLT-1 serves as a powerful inhibitor of VEGF-A. In a joint Phase I/II clinical trial conducted by the Lions Eye Institute and Adverum Biotechnologies, researchers evaluated

AVA-101 (rAAV.sFLT-1), a gene therapy delivered via a single injection beneath the retina. Initially, all eight participants were given supplementary ranibizumab at the start of the study, at week four, and whenever necessary based on strict clinical criteria. Because the treatment proved to be safe, the trial was expanded to include 32 patients, who were randomly assigned to either receive the gene therapy or join a control group. Throughout the study, no severe adverse reactions were reported. Notably, patients receiving the gene therapy required fewer additional ranibizumab injections (a median of two) compared to the control group (a median of four). Although there was no significant enhancement in overall visual acuity, the trial successfully established the therapy's safety and tolerability. These promising results pave the way for future long-acting gene treatments in the ongoing fight against wet AMD (nAMD) [17].

In the early days of AMD treatment, doctors attempted "retinal translocation"—a procedure involving the transfer of healthy retinal cells to damaged areas. Because this surgery was highly invasive and carried substantial risks, scientists shifted their focus toward subretinal RPE allografts. While early experiments using fetal RPE cell suspensions and cultured patches yielded encouraging results, they revealed that successful transplantation heavily depends on proper cell alignment and an intact Bruch's membrane. This realization spurred the creation of patch-based grafting techniques. At the time, however, progress was severely hindered by a shortage of viable fetal donor tissue and the risk of tumor formation associated with alternative cell lines, such as aRPE-19. Fortunately, the emergence of stem cell technology successfully overcame these hurdles. Today, treatments utilizing stem cells stand out as a highly promising strategy for AMD. Preliminary clinical trials demonstrate that these approaches are generally safe and have real therapeutic potential. Nevertheless, optimizing how these cells are manufactured, delivered, and integrated over the long term requires further investigation. The ultimate success of these therapies hinges on overcoming complex obstacles, including immune system rejection, surgical complications, and tumorigenicity. As surgical methods and stem cell technologies continue to evolve, these innovative therapies hold the remarkable potential to completely transform AMD care and help patients regain their lost vision [15].

To alleviate the heavy burden of frequent anti-VEGF eye injections, researchers have developed long-acting drug reservoirs designed to provide continuous treatment. A prominent example is the Port Delivery System (PDS) known as Susvimo. Surgically implanted into the eye's pars plana, this permanent, refillable device steadily releases ranibizumab directly into the vitreous. Extensive Phase 3 clinical trials (Archway, Pagoda, and Pavilion) demonstrated that the PDS is just as effective as

standard monthly injections for managing conditions like nAMD, DME, and diabetic retinopathy. Following these successful trials, the FDA approved the device for nAMD in 2021, with a recommended refill schedule of every six months.

Despite its efficacy, the implant carries a "black box" warning due to a higher risk of severe intraocular infections (endophthalmitis) compared to standard injections. Other surgical complications, such as retinal detachment and bleeding, were also noted, though these are expected to decrease as surgical techniques are refined. In late 2022, a mechanical flaw involving a dislodged septum led to a temporary recall of the device. After redesigning the implant components, Genentech successfully reintroduced it to the market and expanded its FDA approval to include DME. Recent data from the Pagoda and Pavilion trials highlight its remarkable efficiency: between 95% and 98% of patients maintained their vision improvements without needing any supplementary injections between scheduled refills. Ongoing research, such as the Belvedere trial, continues to monitor the long-term safety profile of the implant, specifically its effects on corneal health [16].

Conclusion:

The advent of anti-VEGFA therapies marked a true turning point for wet AMD, transforming a once-untreatable condition. However, these medications rarely offer a definitive cure; instead, they primarily halt disease advancement to stave off severe visual impairment. Furthermore, the standard regimen demands a lifelong commitment to costly intraocular injections—typically administered every two to three months following an initial loading phase—which creates a significant physical and financial strain on patients. Consequently, the push to develop one-time therapeutic alternatives is highly warranted, offering the promise of a vastly improved quality of life for millions affected by the condition.

While improving the patient experience is an important goal in drug development, guaranteeing the treatment's safety and clinical effectiveness must always remain paramount. Crucially, therapies exclusively targeting VEGFA are inherently limited. Although VEGFA plays a central role in driving both healthy and abnormal blood vessel formation, it is merely one of several biological pathways fueling the pathological neovascularization seen in wet AMD [18].

Given that age-related macular degeneration is an intricate condition that places a heavy burden on both healthcare systems and the economy, our grasp of its underlying biology is constantly advancing

to uncover these other driving mechanisms. In light of this, this article examines the potential of non-coding RNAs (ncRNAs) to broaden our knowledge and improve AMD management. In various other medical disciplines, ncRNAs have already proven highly valuable for diagnostics, allowing for premature detection, accurate prognosis, and therapies tailored to specific biomarkers. Furthermore, since targeting ncRNAs has yielded positive results in clinical trials for other illnesses, this approach presents a promising new frontier for AMD research. Moving forward, the successful translation of these findings into clinical practice will depend heavily on access to high-quality diseased tissue samples and thoroughly analyzed patient cohorts (both healthy individuals and those affected by AMD). These resources are essential for discovering reliable ncRNA biomarkers and pinpointing novel targets for future drugs [19].

Alongside these molecular investigations, the role of established clinical markers is also being re-examined. Undeniably, drusen represent a critical early sign of AMD and may play a central role in driving the disease toward its advanced stages. Nevertheless, the recognition of advanced AMD variations that develop without any drusen present—such as polypoidal choroidal vasculopathy (PCV)—raises a compelling question: are drusen actually the root cause of the disease, or simply a byproduct and biomarker?

Laboratory studies currently offer conflicting perspectives. On one hand, disruptions involving typical drusen components, like cholesterol or the complement system, can induce AMD-like characteristics, implying they have a causative role. Conversely, drusen-like formations also appear in knock-out mice targeting the VHL-HIF-VEGF pathway, which is typically a downstream trigger for abnormal blood vessel growth. This suggests that drusen might just be an indicator of underlying pathology rather than the primary trigger. Thus, their exact role remains an open debate.

Our understanding of this complex dynamic continues to grow thanks to cutting-edge imaging technologies, such as OCT and OCT angiography, used alongside traditional fundus imaging and advanced genetically modified animal models. Furthermore, emerging diagnostic frameworks—including pachychoroid neovasculopathy and new disease classifications based on choroidal thickness versus drusen presence—will undoubtedly provoke deeper discussions about what drusen actually do. Ultimately, successfully bridging clinical observations with fundamental science holds the promise of fully unraveling AMD's mechanisms and paving the way for innovative therapies [20].

In conclusion, the future of AMD management lies in a multifaceted and highly personalized approach. As we move beyond the era of strictly anti-VEGF monotherapy, the integration of artificial intelligence and deep learning in early diagnostics will be crucial for identifying at-risk patients long before irreversible macular damage occurs. Furthermore, acknowledging the systemic nature of AMD—particularly its intricate ties to cardiovascular health and lifestyle factors like smoking—underscores the critical need for comprehensive, holistic patient care rather than an isolated focus on the eye. The ongoing evolution of sustained drug delivery systems, coupled with the revolutionary potential of gene editing and stem cell replacement therapies, signals a profound paradigm shift: moving from merely halting disease progression to actively restoring lost vision. By uniting advanced AI diagnostics, holistic risk management, and cutting-edge molecular therapeutics, the medical community is steadily approaching a future where blindness caused by macular degeneration may become a fully preventable and reversible condition. Achieving this ambitious goal will require sustained, multidisciplinary collaboration among geneticists, ophthalmologists, and biotechnological innovators. Ultimately, alleviating the overwhelming economic and logistical strain currently placed on global healthcare infrastructures will depend on these continuous scientific breakthroughs. By transforming our therapeutic arsenal from reactive, generalized interventions into proactive, precision medicine, we can ensure that the aging global population retains not just their sight, but their independence and overall quality of life for years to come.

DISCLOSURE

Author's contribution

Conceptualization: Mateusz Wiekiera, Szymon Kopciał, Adrianna Wiekiera, Paweł Budzik, Karolina Kornatowska, methodology: Mateusz Wiekiera, Szymon Kopciał, Paweł Budzik, Adrianna Wiekiera, Karolina Kornatowska, software: Mateusz Wiekiera, Adrianna Wiekiera, Szymon Kopciał, Paweł Budzik formal analysis: Mateusz Wiekiera, Szymon Kopciał, Paweł Budzik investigation: Mateusz Wiekiera, Adrianna Wiekiera, Szymon Kopciał, Paweł Budzik resources: Adrianna Wiekiera, Karolina Kornatowska, Paweł Budzik data curation: Adrianna Wiekiera, Karolina Kornatowska, Szymon Kopciał riting - rough preparation: Mateusz Wiekiera, Karolina Kornatowska writing - review and editing: Mateusz Wiekiera, Adrianna Wiekiera, Szymon Kopciał, Paweł Budzik, Karolina

Kornatowska, visualization: Mateusz Wiekiera supervision: Mateusz Wiekiera, Adrianna Wiekiera, Szymon Kopciał, Paweł Budzik project administration: Mateusz Wiekiera

All authors have read and agreed with the published version of the manuscript.

Funding Statement

This research received no external funding.

Institutional Review Board Statement

Not applicable

Informed Consent Statement

Not applicable

Data Availability Statement

Not applicable

Conflict of Interest Statement

The authors declare no conflict of interest.

REFERENCES

[1] Marchesi N, Capierri M, Pascale A, Barbieri A. Different Therapeutic Approaches for Dry and Wet AMD. Int J Mol Sci. 2024;25(23):13053. Published 2024 Dec 4. doi:10.3390/ijms252313053

[2] Deng Y, Qiao L, Du M, et al. Age-related macular degeneration: Epidemiology, genetics, pathophysiology, diagnosis, and targeted therapy. Genes Dis. 2021;9(1):62-79. Published 2021 Feb 27. doi:10.1016/j.gendis.2021.02.009

[3] DeAngelis MM, Owen LA, Morrison MA, et al. Genetics of age-related macular degeneration (AMD). Hum Mol Genet. 2017;26(R1):R45-R50. doi:10.1093/hmg/ddx228

[4] Heloterä H, Kaarniranta K. A Linkage between Angiogenesis and Inflammation in Neovascular Age-Related Macular Degeneration. Cells. 2022;11(21):3453. Published 2022 Nov 1. doi:10.3390/cells11213453

[5] Fleckenstein M, Keenan TDL, Guymer RH, et al. Age-related macular degeneration. Nat Rev Dis Primers. 2021;7(1):31. Published 2021 May 6. doi:10.1038/s41572-021-00265-2

[6] Heloterä H, Kaarniranta K. A Linkage between Angiogenesis and Inflammation in Neovascular Age-Related Macular Degeneration. Cells. 2022;11(21):3453. Published 2022 Nov 1. doi:10.3390/cells11213453

[7] Farnoodian M, Wang S, Dietz J, Nickells RW, Sorenson CM, Sheibani N. Negative regulators of angiogenesis: important targets for treatment of exudative AMD. Clin Sci (Lond). 2017;131(15):1763-1780. Published 2017 Jul 5. doi:10.1042/CS20170066

[8] Jiang F, Ma J, Lei C, Zhang Y, Zhang M. Age-Related Macular Degeneration: Cellular and Molecular Signaling Mechanisms. Int J Mol Sci. 2025;26(13):6174. Published 2025 Jun 26. doi:10.3390/ijms26136174

[9] Abd El-Khalek AA, Balaha HM, Sewelam A, et al. A Comprehensive Review of AI Diagnosis Strategies for Age-Related Macular Degeneration (AMD). Bioengineering (Basel). 2024;11(7):711. Published 2024 Jul 13. doi:10.3390/bioengineering11070711

[10] Pennington KL, DeAngelis MM. Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors. Eye Vis (Lond). 2016;3:34. Published 2016 Dec 22. doi:10.1186/s40662-016-0063-5

[11] Śpiewak D, Drzyzga Ł, Dorecka M, Wyględowska-Promieńska D. Summary of the Therapeutic Options for Patients with Dry and Neovascular AMD. J Clin Med. 2024;13(14):4227. Published 2024 Jul 19. doi:10.3390/jcm13144227

[12] Wolf AT, Harris A, Oddone F, Siesky B, Verticchio Vercellin A, Ciulla TA. Disease progression pathways of wet AMD: opportunities for new target discovery. Expert Opin Ther Targets. 2022;26(1):5-12. doi:10.1080/14728222.2022.2030706

[13] Stahl A. The Diagnosis and Treatment of Age-Related Macular Degeneration. Dtsch Arztebl Int. 2020;117(29-30):513-520. doi:10.3238/arztebl.2020.0513

[14] Ciszewski P, Drelichowska A, Pikor D, Wiśniewska E, Azierski M. Innovative technologies for the treatment of dry age-related macular degeneration (AMD) - modern therapeutic perspectives and their future. Rom J Ophthalmol. 2025;69(1):10-16. doi:10.22336/rjo.2025.03

[15] Giacalone JC, Parkinson DH, Balikov DA, Rao RC. AMD and Stem Cell-Based Therapies. Int Ophthalmol Clin. 2024;64(1):21-33. doi:10.1097/IIO.0000000000000510

[16] Rowe LW, Akotoye C, Harris A, Ciulla TA. Beyond the injection: delivery systems reshaping retinal disease management. Expert Opin Pharmacother. 2025;26(8):939-952. doi:10.1080/14656566.2025.2496424

[17] Guimaraes TAC, Georgiou M, Bainbridge JWB, Michaelides M. Gene therapy for neovascular age-related macular degeneration: rationale, clinical trials and future directions. Br J Ophthalmol. 2021;105(2):151-157. doi:10.1136/bjophthalmol-2020-316195

[18] Blasiak J, Pawlowska E, Ciupińska J, Derwich M, Szczepanska J, Kaarniranta K. A New Generation of Gene Therapies as the Future of Wet AMD Treatment. Int J Mol Sci. 2024;25(4):2386. Published 2024 Feb 17. doi:10.3390/ijms25042386

[19] Zhang C, Owen LA, Lillvis JH, Zhang SX, Kim IK, DeAngelis MM. AMD Genomics: Non-Coding RNAs as Biomarkers and Therapeutic Targets. J Clin Med. 2022;11(6):1484. Published 2022 Mar 9. doi:10.3390/jcm11061484

[20] Ban N, Shinojima A, Negishi K, Kurihara T. Drusen in AMD from the Perspective of Cholesterol Metabolism and Hypoxic Response. J Clin Med. 2024;13(9):2608. Published 2024 Apr 29. doi:10.3390/jcm13092608