

# Age-Related Macular Degeneration: An Update on Nutritional Supplementation

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*Age-related macular degeneration (ARMD) is a progressive disease affecting the central vision of patients older than 55 years. Typically, ARMD patients are classified into dry and wet forms based on clinical characteristics. This has important implications with respect to their clinical presentation, prognosis and management options. Important risk factors in the progression of disease include age, smoking and drusen characteristics. The promising results of a new study on vitamin supplementation provide direction for treatment and prevention, as well as the understanding of the role of antioxidants in ARMD pathogenesis. High-dose vitamins (beta-carotene, vitamins C and E and zinc) should be considered in certain patients with ARMD.*

**Key words:** macular degeneration, vitamins, low vision, supplementation, Amsler grid.

Age-related macular degeneration (ARMD) is the leading cause of vision impairment in North America in people older than 55 years.<sup>1</sup> The visual morbidity associated with this disease can significantly impair the quality of life and impede activities of daily living of our elderly population. This article will review the classification, epidemiology and emerging preventive measures for this disease.

## Clinical Presentation

ARMD is classified clinically into two forms, dry and wet (also known as exudative or neovascular), which are usually distinguished based on characteristic findings on fundoscopy. In the dry form, a dilated retinal exam often reveals the presence of drusen—yellowish deposits in the sub-retinal pigment epithelial space—and/or retinal pigment epithelial (RPE) atrophy in the macular area (Figure 1). Damage and atrophy of the RPE layer leads to overlying photoreceptor dysfunction and, as a result, central vision loss that is gradual in onset (i.e., over many years). The majority of ARMD patients (~85%) have the dry form, and only approximately 10% of these patients progress to develop the wet form. In the clinical differential, one must also consider other causes of gradual visual loss in the elderly, such as

cataract and refractive error, both of which are very treatable conditions.

The wet form of ARMD is defined by the presence of choroidal neovascular membranes (CNVMs). These are neovascular bundles that penetrate into the sub-RPE or sub-retinal space (Figure 1). While these membranes may not always be clinically visible, leakage of lipid, fluid or hemorrhage into the sub-retinal space from these vessels are pathognomonic signs of the presence of a CNVM. Patients with the wet form of ARMD often present initially with complaints of sudden visual loss or metamorphopsia (waviness) of their central vision. Metamorphopsia can be documented clinically with the aid of an Amsler grid (Figure 2). This classic presentation is associated with the rapid leakage of fluid/exudates or hemorrhage of these CNVMs into the sub-retinal space resulting in immediate photoreceptor dysfunction. If left alone, these membranes often lead to scarring and fibrosis resulting in permanent and irreversible central visual loss (Figure 1). Only a minority of ARMD patients (~10%) have the wet form. In the differential diagnosis of sudden visual loss in the elderly, conditions such as retinal vein or artery occlusion, ischemic optic neuropathy, retinal detachment and vitreous hemorrhage should also be considered.

Various risk factors have been iden-

tified that influence the occurrence or progression of ARMD. Perhaps the two most consistent risk factors identified to date are age and cigarette smoking.<sup>2</sup> Certain drusen characteristics, such as large size and soft or confluent morphology, also have been associated with a higher risk of progression to advanced ARMD. While the role of heredity has been supported in many epidemiological studies, the exact genetic understanding is still lacking.<sup>2</sup> The role of other risk factors, such as hypertension, cardiovascular disease, obesity and sunlight exposure, also are not yet clearly understood.<sup>2</sup>

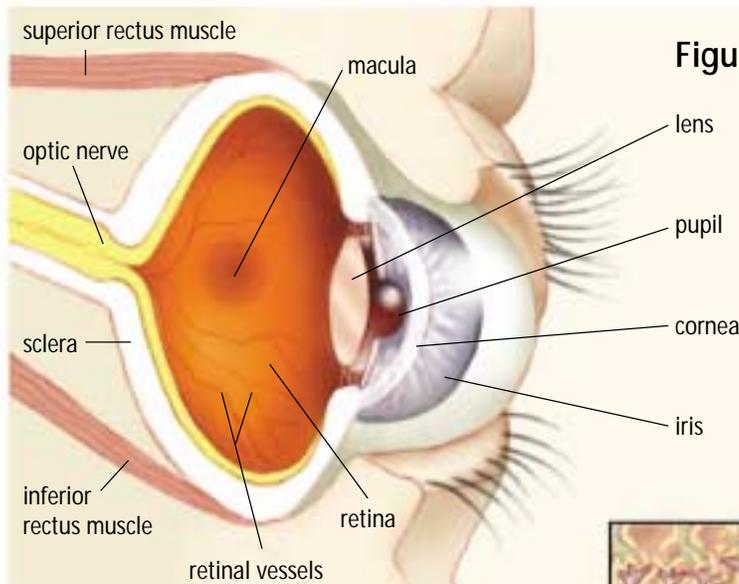
## Management

### Dry Form

While there is no treatment available to cure the dry form of ARMD, there are various helpful management options one could offer the patient. As was previously mentioned, the only consistent modifiable risk factor identified thus far is cigarette smoking, and as such, smoking cessation is one preventive strategy. Perhaps the most significant advancement in the management of patients with the dry form of ARMD has been in the area of vitamin supplementation. The rationale for vitamin supplementation was that long-term chronic oxidative damage might play a role in the pathogenesis and mechanism of this disease. This was supported, albeit inconsistently, by various small studies which showed that vitamins may provide modest protective properties with respect to ARMD progression.<sup>3,4</sup>

This lack of convincing evidence led to a recent multicentre, randomised trial published by the Age-Related Eye Disease Study group (AREDS) looking at high-dose antioxidant therapy for slowing the progression of ARMD.<sup>5</sup> In the AREDS study, more than 3,500 patients (age range 55–80 years) were enrolled, having met the inclusion criteria of drusen and/or RPE changes in one or

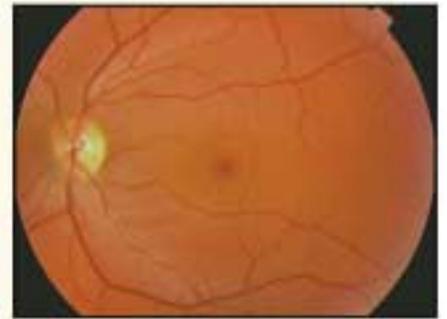
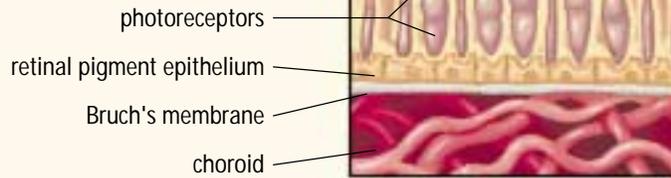
# Age-Related Macular Degeneration



**Figure 1: Age-Related Macular Degeneration**

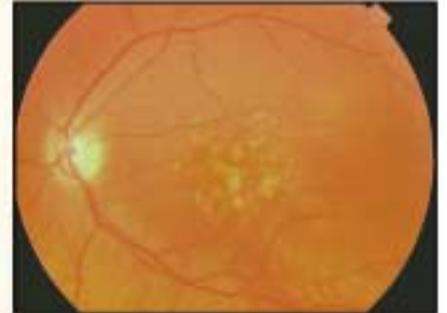
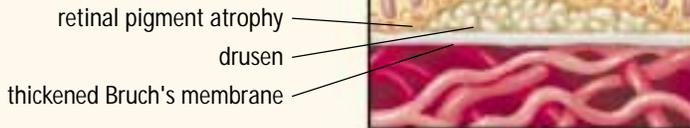
ARMD is classified clinically into two forms, dry and wet, which are usually distinguished based on characteristic findings on funduscopy. In the dry form, a dilated retinal exam often reveals the presence of drusen (yellowish deposits in the sub-retinal pigment epithelial space) and/or RPE atrophy in the macular area. The wet form is defined by the presence of choroidal neovascular membranes (CNVMs), neovascular bundles that penetrate into the sub-RPE or sub-retinal space. If left untreated, CNVMs can lead to scarring and fibrosis, resulting in permanent and irreversible central vision loss.

**1. Normal Retina and Fundus (left eye)**



**2. Dry ARMD (left eye)**

Extensive soft, confluent drusen throughout the macula with subtle RPE drop-out.



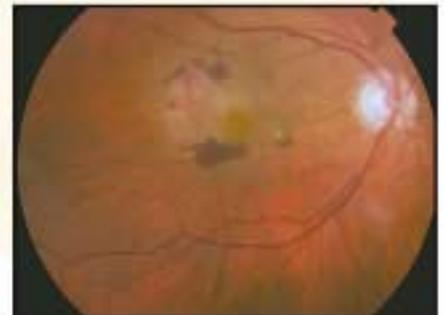
**3. Early Wet ARMD (left eye)**

Acute sub-retinal blood (red lesions) in macular area with subtle sub-retinal fluid; choroidal neovascular membrane (CNVM) is not clearly visualized.



**4. Late Wet ARMD (right eye)**

Sub-retinal blood (red lesions), CNVM (greenish lesion) and sub-retinal fibrosis with RPE atrophy (central whitish lesion) in macular area.



Photographs courtesy of Cynthia Vanderhoven, ophthalmic photographer, Hospital for Sick Children, Toronto, ON.

both eyes or advanced vision loss in one eye already from ARMD, and at least one eye with better than 20/32 vision. Participants were randomised to receive daily oral tablets containing one of the following:

- 1) antioxidants (beta-carotene 15mg, vitamin C 500mg, vitamin E 400 IU);
- 2) zinc (zinc 80mg, as zinc oxide; and copper 2mg, as cupric oxide);
- 3) antioxidants plus zinc; or
- 4) placebo.

Outcome measures included both photographic progression and visual acuity loss and the follow-up period was over six years. The study group found a statistically significant odds reduction for the development of advanced ARMD in the group given both antioxidants and zinc compared with the placebo group. The group of patients that benefited most had certain drusen characteristics—specifically, extensive intermediate or large drusen size. The combination of antioxidants and zinc was more effective than either supplement alone, with a demonstrated risk reduction of 25% in this higher risk group of patients. Patients with small drusen had a very low progression rate to begin with, and the benefit of vitamin supplementation could not be demonstrated adequately in this group.

While the doses of vitamins used in this study were 5–15 times the recommended dietary allowances, there were no significant adverse outcomes. However, smoking was considered a contraindication to concomitant beta-carotene use due to the increased risk of lung cancer. Certain issues that were not addressed in this study were the role of vitamin supplementation in patients who already have advanced or wet ARMD, and the role of another vitamin, lutein, that is currently available in many commercial formulations. The AREDS study was, however, able to conclude that ARMD patients older than 55 years with extensive intermediate or large drusen on dilated funduscopy, and who are non-smokers, should consider vitamin supplementation with antioxidants and zinc. It is interesting to note that despite the AREDS study being well publicized, a recent Canadian survey demonstrated that while approximately 80% of ARMD patients were on some form of vitamin supplementation, none met the recommended dosages for all four ingredients.<sup>6</sup> A possible explanation for this discrepancy may be the slow transition of commercial formulations to match the exact AREDS dosing.

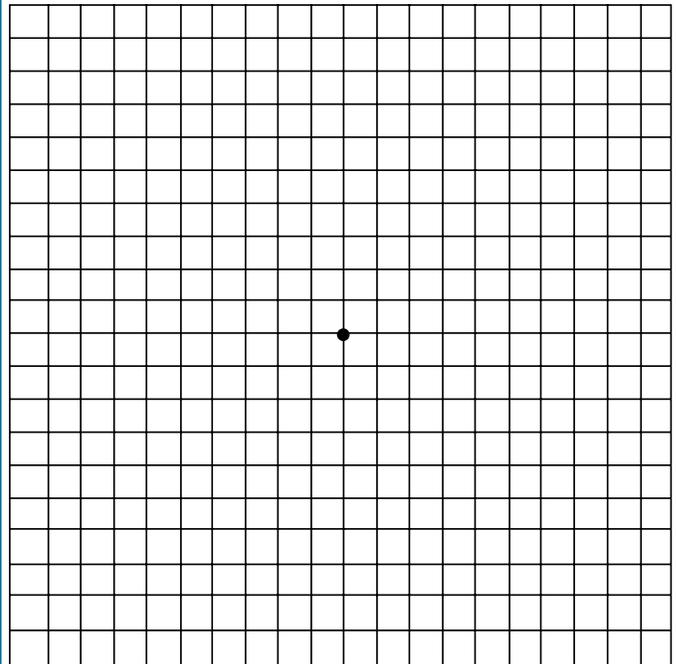
Another management option in patients with dry ARMD is educating the patient to monitor for progression. These patients should be given an Amsler grid to take home and instructed to check each eye individually on a frequent basis. They should report for immediate ophthalmologic assessment at the first sign of metamorphopsia or central visual loss (Figure 2). These acute changes may be the first indications of the development of wet ARMD from leakage or hemorrhage from a CNVM. Once the gradual vision loss progresses in the dry form to impact on activities of daily living, low

Figure 2

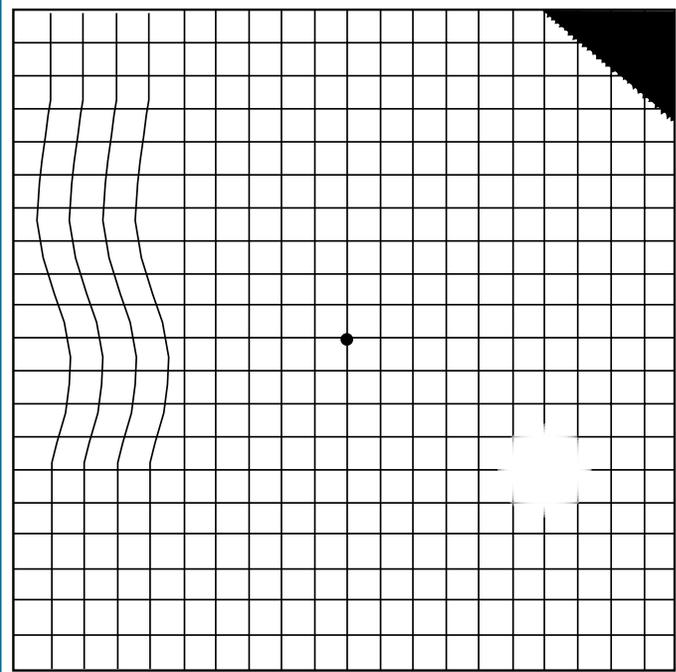
## Amsler Grid Test

a: While focusing on the dot in the centre of the grid, with one eye covered, patients should ask themselves:

1. Am I able to see the corners and sides of the square?
2. Do I see any wavy lines?
3. Are there any holes or missing areas?



b: Possible distortions, such as metamorphopsia, develop as macular degeneration progresses.



vision rehabilitation services also should be considered. These services use various optical and non-optical means of enhancing what little visual function remains in an otherwise diseased macula.

### Wet Form

The wet form of ARMD provides unique management challenges. These patients often have significant visual morbidity from the sequelae of their CNVMs. While their visual acuity may not return, eliminating their CNVMs often prevents further visual loss and irreversible scarring. Current strategies are aimed at destroying CNVMs, either with conventional laser photocoagulation or with photodynamic therapy. The advantage of photodynamic therapy is that it targets vascular tissue over neurosensory retina. Naturally, those membranes that are small or far away from the centre of the fovea have

a better prognosis. A fluorescein angiogram would help elucidate which, if any, therapy may be indicated in these patients. Other options include submacular intra-ocular surgery, which is currently under investigation. Finally, for those patients with irreversible visual loss, low vision assessment and low vision aids may offer some benefit.

### Conclusion

In conclusion, while ARMD can evolve into a significantly blinding disease that may be untreatable, there is evidence for preventive strategies. Specifically, vitamin supplementation is now considered to be helpful in preventing and slowing an otherwise progressive disease. As a result, high-dose vitamin supplementation (beta-carotene, vitamins C and E, and zinc) should be considered in certain ARMD patients. ◆

No competing financial interests declared.

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