NUTRITION FOR EYE HEALTH

FACT OR FICTION ?

Professor **Alfredo GARCIA LAYANA**

Professor **Angelo Maria MINNELLA**

Théa
let's open our eyes

1. AMD DIAGNOSIS & CLASSIFICATION

1.1 DEFINITION AND DIAGNOSIS

Age-related macular degeneration (AMD) is a progressive degenerative disease of the central part of the retina (the macula) which may result in blurred or no vision in the center of the visual field in one or both eyes. This is a painless pathology with only few symptoms in the early stages. The advanced forms are often symptomatic with loss of contrast sensitivity, visual distortion (metamorphopsia), presence of black or gray spots (scotomata), or blind spot and blurred vision *[AAO, 2015]*. The patient may complain about difficulty with performing normal activities that require good central vision, such as reading and writing, watching television, driving and recognizing faces. AMD may develop unilaterally or bilaterally at the same time or sequentially. Frequently, people are unaware that their disturbed binocular vision is caused by changes in only one eye *[Solomon et al., 2014]*.

Since the early and intermediate stages of AMD usually start without symptoms, only a comprehensive dilated eye exam can detect AMD. According to the disease stage, clinical findings may include drusen, retinal pigment epithelial (RPE) abnormalities, geographic atrophy (GA), RPE detachment, choroidal neovascularization and its consequences (e.g., serous sensory retinal detachment, often accompanied by hard exudates and subretinal hemorrhages), and disciform scar *[AREDS Report No 1, 1999]*.

Fundus photographs are usually used to determine the size and extent of drusen as well as pigmentary abnormalities, and atrophy of the RPE. Reticular pseudodrusen (also called subretinal drusenoid deposits) are often under-recognized *[AAO, 2015]*. They are best imaged using fundus autofluorescence, infrared reflectance, and/or spectral domain – optical coherence tomography (SD-OCT) *[Zweifel et al., 2010; AAO, 2015]*. Fluorescein angiography is the gold standard for detecting and confirming the presence of choroidal neovascularization *[Jia et al., 2014]*. OCT angiography is a recent, non-invasive test , that is rapidly replacing fluorescein angiography in clinical practice for the diagnosis of choroidal neovascularization, as well as useful tool for the follow up of this pathology. Indocyanin angiography is still indicated in selected cases (ie. polypoidal subtype).

1.2 CLASSIFICATION

The current classification is based on the results of the Age-Related Eye Disease Study (AREDS). A simplified severity scale divided into three categories was proposed: early, intermediate, and advanced *[Ferris et al., 2013]* (Table 1). Such a simplified classification is useful to evaluate the relationship between nutritional, medical, and environmental factors and incidence rates of progression from early to intermediate disease to late stages AMD *[Seddon et al., 2006a]* and current treatment recommendations are based on these classifications *[AAO, 2015]*..

Table 1 : Simplified classification of AMD (AREDS)

Stage 1	**No AMD**	No or only few small drusen (< 63 µm)
Stage 2	**Early AMD**	**At least one of the following** • multiple small drusen • few drusen with size between 63 and 125 µm • pigmentary abnormalities
Stage 3	**Intermediate AMD**	**At least one of the following** • multiples drusen with size between 63 et 125 µm and at least one drusen > 125 µm • geographic atrophy outside the fovea.
Stage 4	**Advanced AMD**	Geographic atrophy affecting the fovea and/or exudative AMD

Adapted from AAO, 2015

Subjects with lesions associated with neovascular AMD or geographic atrophy (GA) are considered to have late or advanced late AMD *[Ferris et al., 2013]*. Late AMD is classically divided into 2 categories: dry form (non-exudative) and wet form (exudative).

Geographic atrophy is characterized by the development of uni- or multifocal atrophic patches that involve the RPE, the neurosensory retina and choriocapillaris layer of the choroid without defect in the Bruch's membrane (BM). Dry AMD (i.e. non exudative AMD) is characterized by geographic atrophy of the RPE in the absence of serous or hemorrhagic leakage *[Geltzer et al., 2013]*. Patients with GA, even in the late stage, can maintain a good central vision until the disease progresses to involve the central fovea. Patients with geographic atrophy not necessarily involving the central fovea may have relatively good distance visual acuity, but manifest decreased ability to perform near visual tasks such as reading *[AAO, 2015]*. Individuals with atrophic AMD typically present with a slow and gradual deterioration in visual acuity for which treatment options remain limited. Late stage atrophic AMD involves widespread atrophic loss of retinal tissue and has poor visual outcomes, similar to those seen with untreated neovascular AMD *[Yehoshua et al., 2011, Broadhead et al., 2015, Kolar, 2013]*.

Neovascular AMD (i.e. choroidal neovascularization) occurs less frequently but is far more aggressive when compared with dry AMD *[Kolar, 2013]*. Neovascular AMD is caused by abnormal growth of new blood vessels into retinal tissues. Endothelial cells from the choriocapillaris of the choroid migrate to and across the RPE monolayer and into the sensory retina. Neovascular AMD is characterized by occurrence of RPE detachment, choroidal neovascularization (CNV), leakage of blood and serum into the surrounding retina (subretinal hemorrhage). RPE detachment can be divided into 4 categories:

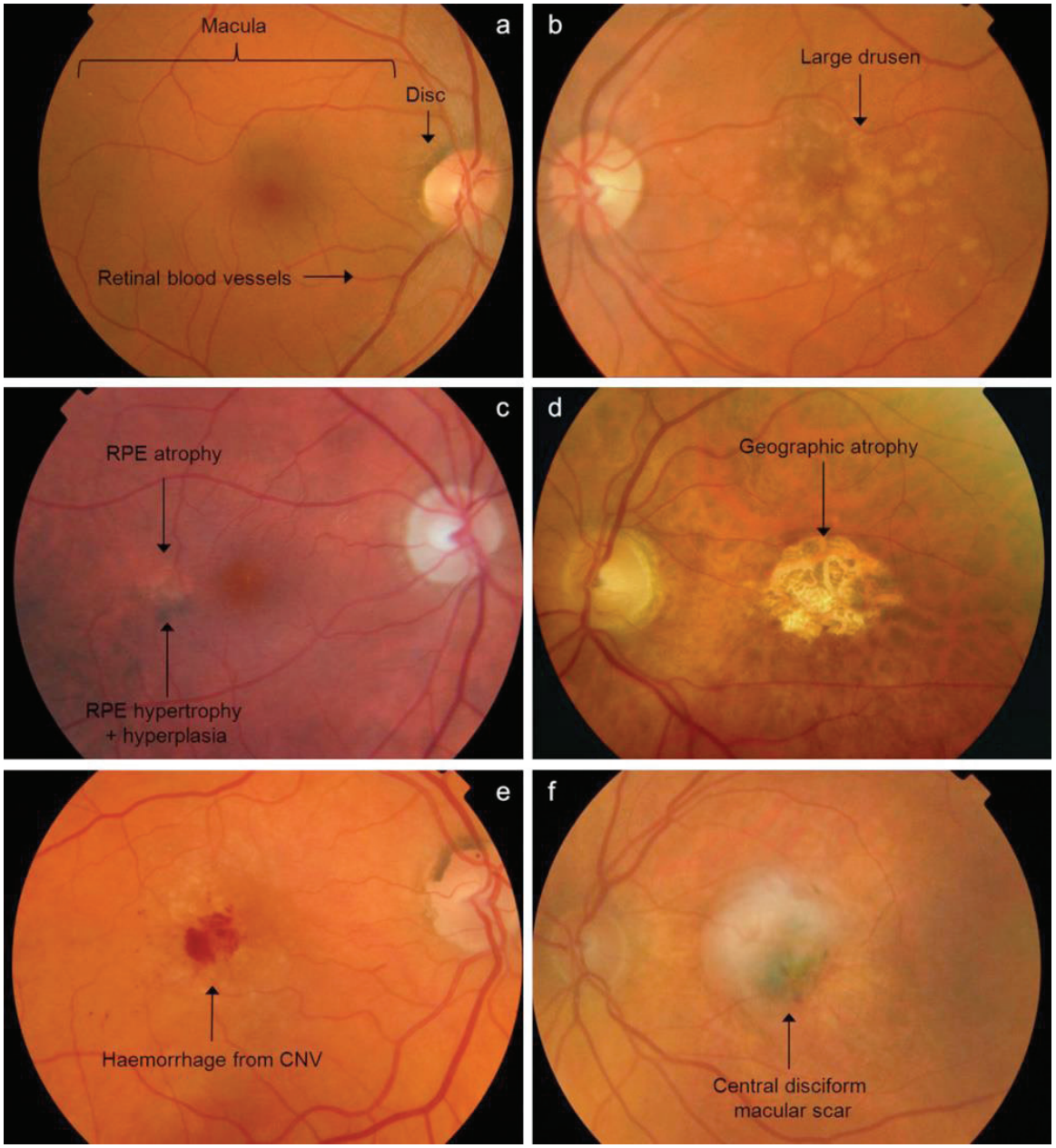
1) drusenoid RPE detachment,

2) serous RPE detachment,

3) hemorrhagic RPE detachment, and

4) fibrovascular detachment. *[AAO, 2015]*. This initially leads to central blurring or visual distortion and subsequently to more significant loss of vision caused by scarring and extensive leakage.

Figure 1 : Fundus photographs of various stages of age-related macular degeneration



(a) Normal eye. Photograph of the fundus (back) of the right eye. The optic disc, where nerve fibers come out of the eye, can be seen as a white spot, due to myelinization of the nerve fibers when they leave the globe. Radiating out from the optic disc in 4 quadrants are the retinal blood vessels. The macula is the area just temporal to the optic disc. It usually appears darker due to increased pigment, xanthopill and lutein (herein the latin term "macula lutea"), and its centre is marked by an absence of visible blood vessels the foveal avascular zone (FAZ). **(b) Early AMD-drusen.** Large drusen can be seen as multiple yellowish clumps. **(c) Early AMD-pigmentary irregularities.** An area of hyperpigmentation (due to RPE cell hypertrophy and hyperplasia) and hypopigmentation (RPE atrophy) can be seen just temporal to the centre of the macula. **(d) Late AMD-GA.** This patient has an extensive area of sharply demarcated RPE atrophy. The underlying choroidal vessels are atrophic and central vision is affected. **(e) Late AMD-CNV.** Blood vessels have grown from the choroid (the vascular layer posterior to the retina) to form a choroidal neovascular membrane. This has caused a haemorrhage within the retina, causing sudden loss of central vision. **(f) Late AMD-scar.** Untreated CNV may result in a permanent macular scar. The central vision is permanently poor *[Adapted from Khandhadia et al., 2012]*.

2. EPIDEMIOLOGY & RISK FACTORS