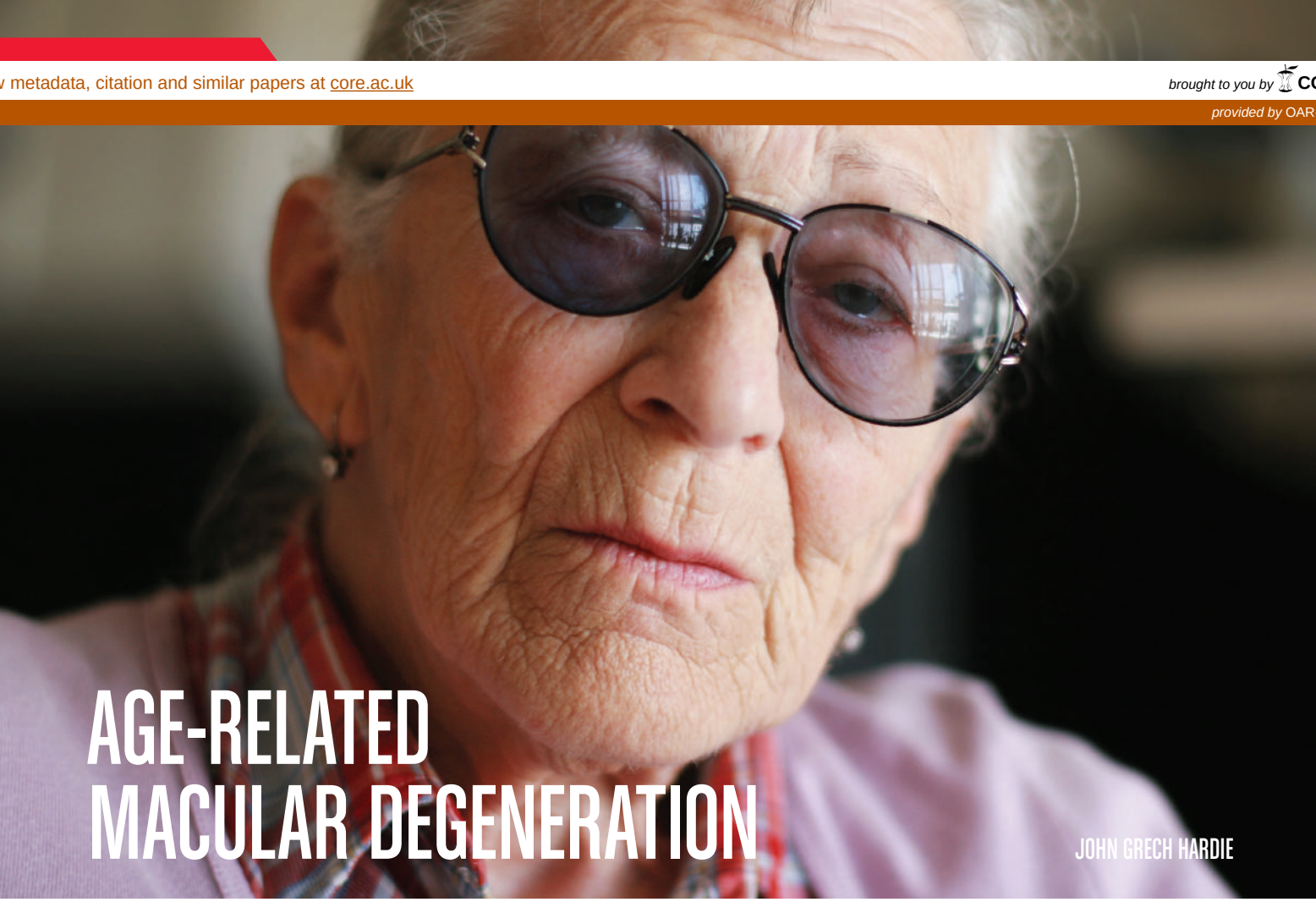


AGE-RELATED MACULAR DEGENERATION

JOHN GRECH HARDIE

Age-related Macular Degeneration (AMD) is a degenerative condition affecting the macular area of the retina. Those affected are usually over the age of 50 years and AMD is the leading cause of blindness over this age in the Western world. It results in distortion or loss of central sharp vision making it difficult to view the object of interest and to carry out close work, to read and write, to recognise faces and to drive although enough peripheral vision remains to allow other activities of daily life. Figure 1 compares a normal vision (a) and the vision in advanced AMD (b).

Figure 1: Comparison between a normal vision (A) and vision in advanced AMD (B)

Source - National Eye Institute, National Institutes of Health

CAUSES AND RISK FACTORS

- Ageing: approximately 10% of people aged 66 to 74 show findings of macular degeneration. The prevalence increases to 30% in the 75 to 85 year age group.
- Family history: the risk of developing macular degeneration is 50% for those with a relative with macular degeneration versus 12% for those with no family history.
- Genetics: changes in several genes, the best studied of which are those involved with the complement system, have been implicated as possible risk factors in AMD.
- Hypertension.
- Cholesterol: elevated cholesterol may increase the risk of AMD.
- Obesity: a risk factor especially among men.
- Race: AMD is more common in Caucasians than in people of African descent.
- Exposure to sunlight especially blue light: there is conflicting evidence about this with some studies showing a relationship and others not.
- Smoking: tobacco smokers show a 2-3 times risk of AMD compared to non-smokers.

AMD is a gradually progressive disease and can pass from early AMD to geographic atrophy and/or neovascular AMD. Early AMD and geographic atrophy are the non-vascular or dry types and account for 90% of AMD while the neovascular or wet type accounts for 90% of blind registrations from AMD.

(A) EARLY AMD

Early AMD is usually asymptomatic with the appearance of Drusen of variable size and shape and focal hypo-pigmentation/ hyper-pigmentation of the macular area (figure 2). Drusen

Figure 2: Early AMD

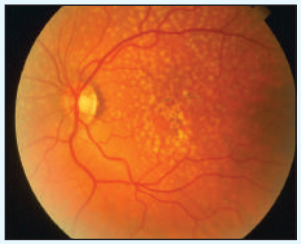


Figure 3: Amsler grid chart in advanced AMD

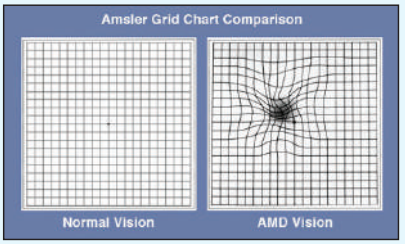


Figure 4: Geographic Atrophy

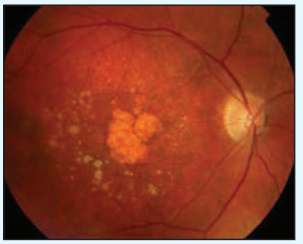
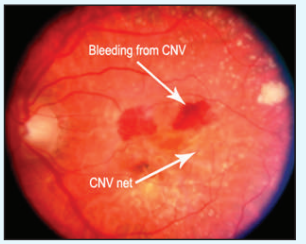


Figure 5: Neovascular AMD



Source - chicagoretinavitreous.com

are yellowish deposits or accumulations of PAS-positive amorphous material in Bruch's membrane under the retina while the pigmentary changes correspond to retinal pigment epithelium and photoreceptor loss.

Treatment at this stage involves:

- Stopping smoking: this is probably the most important modifiable factor.
- Diet and anti-oxidant vitamin supplementation: the Age-related Eye Disease studies (AREDS and AREDS2) showed that an anti-oxidant vitamin combination (500mg Vit C, 400IU Vit E, 15 mg beta-carotene, 80mg Zinc and 2mg Copper) had a moderate protective effect (25% decrease in the risk of developing late AMD) on the fellow eye of patients with vision loss from moderate to late AMD. Beta-carotene is contra-indicated in smokers as it increases the risk of lung cancer. AREDS2 showed that it can be substituted with 10mg lutein and 2mg zeaxanthin with no loss of effect and modern drug formulations make use of this fact. Many ophthalmologists place patients on these supplements even at an early stage of the disease.
- Monitoring of vision using an Amsler grid chart and yearly, or as required, ophthalmic review. An Amsler grid examines a person's central visual field. In the test, done serially at home, the subject looks at the small dot at the centre of the grid with each eye separately. The appearance of wavy or missing lines is indicative of macular disease and should prompt the patient to seek ophthalmic review. The test is particularly useful in monitoring the fellow unaffected eye of a patient with advanced AMD in the other eye. The chart can be easily downloaded from the Internet. Figure 3 depicts an Amsler grid chart in advanced AMD.

(B) GEOGRAPHIC ATROPHY

Together with Drusen, this shows slowly enlarging sharply demarcated areas of atrophy of the retina with exposure of the underlying choroidal vessels (figure 4).

Treatment at this stage is the same as for early AMD as well as the use of low-vision aides such as magnifying lenses and computer screen readers which enlarge reading material.

(C) NEOVASCULAR OR EXUDATIVE AMD

This typically presents with an acute change in central vision such as distortion (metamorphopsia) or a blind spot. The responsible lesion is a growth of choroidal neovascularisation (CNV) from the choroid through Bruch's membrane to a sub-RPE/retinal location. Clinically this appears as a greyish-green elevated lesion with associated leakage of blood (haemorrhage) and/or exudation (figure 5). The CNV grows and ultimately forms a central scar. Definitive diagnosis is achieved with intravenous fluorescein angiography. This defines the size and location of the lesion and any associated pigment epithelial detachment. Although invasive, the test is quick and quite harmless; apart from the remote possibility of allergy to the fluorescein dye. It is done on an out-patient basis and is also useful in follow-up after treatment.

Until recently treatment of neovascular AMD was not very effective in controlling the disease and preventing loss of vision. Previous treatments, now less commonly used, include:

- Laser treatment to ablate compact lesions away from the centre of the macula. This also destroys some surrounding healthy tissue leading to a blind spot.
- Photodynamic therapy which involves the intravenous injection of a drug, verteporfin, which selectively binds to growing new vessels in the eye. A specific laser is then shined into the eye to activate the drug which then causes the blood vessels to close off and regress.

With the introduction of **Anti-VEGF injection therapy** there is now hope in a previously hopeless situation. In neovascular AMD, abnormally high levels of vascular endothelial growth factor (VEGF) are secreted. This protein promotes the growth of abnormal new blood vessels. Anti-VEGF agents bind VEGF causing regression of the new vessels. This helps stabilise vision and in some cases restore some of the vision lost. The agents are injected directly into the vitreous of the eye and the injection is repeated monthly or bimonthly. The commonly used drugs are the approved but expensive ranibizumab (Lucentis®) and aflibercept (Eylea®) and the more commonly used and cheaper bevacizumab (Avastin®) used off-label. The duration of treatment varies in each case and may need to be long-term. This treatment is not a cure and the condition may progress in spite of this treatment. Ongoing stem cell research is beginning to show some promising results in the restoration of at least some of the vision lost in advanced cases of AMD.