AGE-RELATED MACULAR DEGENERATION

Age-related macular degeneration is a devastating disease that is on the increase in SA.

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Age-related macular degeneration (AMD) is a more advanced, sight-threating stage of age-related maculopathy, characterised by one or more of the following:

- Geographic atrophy of the retinal pigment epithelium with visible underlying choroidal vessels
- Pigment epithelium detachment with or without neurosensory detachment
- Sub-retinal or sub-retinal pigment epithelium choroidal neovascularisation
- Fibroglial scar tissue, haemorrhage and exudates.

WHAT ARE THE RISK FACTORS?

- Age is the main risk factor
- The condition is most prevalent in Caucasians but has been documented in patients of African-decent.
- The patient with ARM that has soft drusen
- A positive family history. The lifetime risk of developing late-stage macular degeneration is 50% for people who have a relative with macular degeneration, versus 10% for people who do not have relatives with macular degeneration.
- Smoking.
- Obesity
- Elevated cholesterol
- Uncontrolled hypertension
- Oxidative stress
- Exposure to sunlight, especially blue light.

PATHOPHYSIOLOGY

The clinical and histopathological features of AMD include a relationship with age and the presence of pigmentary disturbances, drusen, thickening of Bruch's membrane and basal laminar deposits. AMD is an advanced stage of a deteriorative process that takes place in all eyes. The primary lesion in AMD appears to reside in the retinal pigment epithelium, possibly resulting from its high rate of molecular degradation. Beginning early in life, and continuing throughout the lifespan, cells of the retinal pigment epithelium gradually accumulate sacs of molecular debris.

These residual bodies (lipofuscin) are remnants of the incomplete degradation of abnormal molecules, which have been damaged within the retinal pigment epithelium cells or derived from phagocytised rod and cone membranes. Progressive engorgement of retinal pigment epithelium cells with these functionless residues is associated with the extrusion of aberrant materials, which accumulate in Bruch's membrane and aggregate in the form of the death of visual cells due to degeneration of retinal pigment epithelium cells or the effect of leakage from neovascular membranes that invade the region of abnormal extracellular deposits.

WHAT IS DRUSEN?

Drusen (singular, druse) are tiny yellow or white accumulations of extracellular material that build up between Bruch's membrane and the retinal pigment epithelium of the eye. The presence of a few small (hard) drusen is normal with advancing age, and most people over 40 have some hard drusen. However, the presence of larger and more numerous drusen in the macula is a common early sign of AMD.

TESTS FOR AMD

Initial tests for AMD include measurement of the patient's visual acuity and a dilated exam of the retina. While studying the retina, the ophthalmologist looks for specific signs of macular degeneration.

If signs of AMD are found, the ophthalmologist will often take detailed pictures of the retina for future comparison. Tests may also include:

- Angiography: As mentioned above, in this procedure a dye is injected into a vein in the arm. The test identifies vessels that cannot be seen with the naked eye and which may need to be treated.
- Optical coherence tomography. This is a non-invasive exam that produces a cross-sectional image of the retina. This method is helpful in identifying how much the retinal layers are distorted and whether swelling is increasing or decreasing following treatment with injections or laser.
- Microperimetry using a scanning laser ophthalmoscope: This is used to quantify macular sensitivity and fixation pattern.

PROPHYLACTIC TREATMENT (VITAMIN)

There is now substantial evidence, particularly from the AREDS study that the use of high dose multivitamins and antioxidants on a regular basis can decrease the risk of progression of ARM in those with high risk characteristics. These high risk features include visual loss in the contralateral eye from pre-existing AMD, and confluent soft drusen even in the absence of visual loss. Previous studies have suggested that people who have diets rich in green, leafy vegetables have a lower risk for developing AMD. However, the high levels of dietary supplement that were evaluated in this study are difficult to achieve from diet alone. The decreased risk of progression to further visual loss at five years is in the order of 25%.

CURRENT TREATMENT

Dry AMD: No treatment is possible, although low vision aids may be useful in many patients.

WET AMD

Photodynamic therapy (PDT): This was the first revolutionary new drug for AMD but with the newer drugs (discussed later) PDT has taken a back seat.

Verteporfin is a light-activated compound that is preferentially taken up by dividing cells, in this instance neovascular tissue. It is injected intravenously and is then activated locally by illumination with light from a diode laser source at a wavelength (689nm) that corresponds to an absorption peak of the compound. The main advantage of PDT is the ability to selectively damage tissue, attributable to both preferential localisation of photosensitiser to the CNV and irradiation confined to the target tissue.

Anti-angiogenic therapy: Anti-vascular endothelium growth factor (Anti-VEGF) is the most popular treatment for wet AMD at this stage. The products available are bevacizumab and ranibizumab. Bevacizumab is used off label at this stage. The CATT study showed that the side-effect profile was comparable between these two drugs and that ranibizumab was slightly more effective. The drug is injected into the vitreous (posterior pole) through the pars plana. The injections are done every 4 to 8 weeks until the wet AMD has changed to Dry AMD. Most of my patients have ongoing treatment because as soon as I stop, the Wet AMD comes back with a vengeance.

Intravitreal steroids: Triamcinolone acetonide may be used alone but most ophthalmologists will use it as an adjunct to the treatment mentioned above.

TREATMENT AT EXPERIMENTAL STAGE FOR DRY AND WET AMD

- Gene therapy
- Stem cell therapy
- Beta radiation or low-voltage x-ray beams to the macula.

CLASSIFICATION OF MACULAR DEGENERATION

- **Dry (atrophic) AMD**
  - The above is caused by slowly progressive atrophy of the photoreceptor, retinal pigment epithelium and choriocapillaris, although occasionally it may develop after a retinal pigment epithelium detachment (form of wet AMD).
- **Wet (neovascular) AMD**
  - The above is caused by choroidal neovascularisation (CNV) originating from the choriocapillaris, which grows through defects in Bruch's membrane. This is thought to be the result of an imbalance between VEGF, which stimulates vascular growth, and pigment epithelium-derived factor (PEDF) that suppresses growth. The visual loss associated with CNV is caused by leakage of blood and serum under the retina (sub-retinal fluid) into the retina (macular oedema) and under the retinal pigment epithelium (pigment epithelium detachment). Eventually persistent fluid accumulation results in loss of photoreceptors and RPE, the formation of a disciform scar and permanent visual loss.

Dry AMD: Presents with a gradual impairment of vision over months or years. Both eyes are usually affected but often asymmetrically.
Signs in chronological order:

- Focal hyperpigmentation or atrophy of the RPE in association with macular drusen.
- Sharply circumscribed, circular areas of RPE atrophy associated with variable loss of the choriocapillaris.
- Enlargement of the atrophic areas within which the larger choroidal vessels may become visible and pre-existing drusen disappear (geographic atrophy). Visual acuity is severely impaired if the fovea is involved.

Wet AMD: Presents with metamorphopsia, a positive scotoma and blurring central vision due to leakage of fluid from the CNV.

Signs:

- The most frequent signs are caused by leakage from CNV resulting in serous retinal elevation, foveal thickening, cystoid macular oedema, sub-retinal haemorrhage and hard exudates.
- Most CNV membranes can be identified ophthalmoscopically but occasionally they can only be seen on Fluorescein angiography. MC