Age-related macular degeneration (AMD) is the most common cause of visual disability and blindness in Europe and North America. On the basis of clinical appearance, AMD is classified as dry (non-neovascular) or wet (neovascular). Features of dry AMD include drusen, hyperplasia of the retinal pigment epithelium and geographic atrophy. The hallmark of wet AMD is choroidal neovascularisation (CNV), a pathological process whereby abnormal new vessels arising from the choroidal capillaries grow through the membrane separating the choroid and the retina (Bruch’s membrane) and spread under the retina. The majority of patients who develop CNV will also have features of dry AMD in the affected or contralateral eye. CNV is visualised by fluorescein angiography and is categorised into two main lesion types termed ‘classic’ (well defined) and ‘occult’ (poorly defined), or combinations of these. The position of the CNV in relation to the fovea (the centre of the macula) is also used to classify lesions into subfoveal, juxtafoveal (extending to within 1–199 µm of the fovea) and extrafoveal (extending no closer than 200 µm from the fovea).

There is no specific treatment for dry AMD, but patients should be offered advice on cessation of smoking, the importance of a healthy diet including plenty of fruits and vegetables, the avoidance of ultraviolet and blue light and the potential value of nutritional supplements for prevention of progression to advanced AMD. The Age-Related Eye Disease Study (AREDS) demonstrated that 5 years of supplementation with high doses of antioxidant vitamins (A, C and E) and zinc reduced the risk of developing advanced AMD by about 25% in the contralateral eye of subjects with pre-existing moderate to advanced dry or wet AMD in one (the study) eye [1].

Wet AMD (CNV) represents only 10% of the overall disease prevalence, but is responsible for 90% of the cases for severe visual loss [2]. Treatment for CNV will therefore have maximum impact on reducing the burden of severe visual loss due to this condition. There have been significant advances in the treatment opportunities for wet AMD recently, some of which have attracted considerable media interest. Studies on treatments for CNV have reported their findings using logMAR visual acuity charts, which have five letters on each line and three lines representing a doubling of the visual angle. In other words, the difference between 6/6 and 6/12 Snellen acuity (and 6/12 and 6/24, etc.) is three lines of logMAR acuity or 15 letters. Moderate and severe visual loss is described as the loss of three and six lines of logMAR acuity, respectively.

Argon laser photocoagulation has been used since the 1970s to treat CNV. The aim is to destroy the neovascular membrane by coagulation, but such treatment also destroys the overlying retina, with a resultant scotoma. For this reason, subfoveal and juxtafoveal CNV are rarely treated by laser photocoagulation, as there is usually an immediate post-treatment reduction in central vision. Well defined, extrafoveal CNV can be treated by photocoagulation, with reduction in severe visual loss; however, such lesions represent only 8% of all CNV at presentation [3], and long-term results are limited by high recurrence rates (54% at 5 years) [4].

Photodynamic therapy (PDT) was the next development in the treatment of neovascular AMD, which has been approved in the United States since 2000. PDT utilises a 10-min intravenous infusion of verteporfin (a benzoporphyrin derived photosensitising drug) followed by application of diode laser (689 nm) treatment to the affected area in the retina. Light is absorbed by the verteporfin molecules, which causes an oxidation process in lipid membranes and proteins. Pre-clinical studies in animals showed that light-activated verteporfin could selectively occlude active CNV, with minimal effects on the overlying retina and underlying choroid. It can therefore be used to treat subfoveal and juxtafoveal CNV. In two controlled clinical trials, PDT was shown to be effective in limiting vision loss in patients with predominantly classic (but not minimally classic) subfoveal CNV [5, 6]. Two-year follow-up data for predominantly classic lesions
The mean change in visual acuity at 1 year was a loss of 7 letters in the pegaptanib group and loss of 14 letters in the ranibizumab group. Patients require follow-up at 3-monthly intervals and cost while maintaining the excellent results of 4–6-weekly dosing.

The great advantage of anti-VEGF therapies is that all types of CNV can now benefit from some form of treatment. Treatment with ranibizumab is the first to show an average improvement in vision. The main disadvantages of treatment are the need for repeated intravitreal injections (with a 0.1% risk of endophthalmitis per injection), high cost of the two approved therapies (pegaptanib and ranibizumab) and the requirement of treatment for 2 years or more [14]. In an attempt to address these issues, several studies are currently investigating whether a reduced frequency of dosing (either alone or in combination with PDT) can reduce side effects and cost while maintaining the excellent results of 4–6-weekly dosing.

**Conflicts of interest**

Fraser Imrie and Clare Bailey are both investigators in ongoing commercially sponsored clinical trials of Macugen (manufactured by Pfizer) and Lucentis (manufactured by Novartis). Clare Bailey has received one-off honoraria for sitting on advisory panels to Pfizer and Novartis. Clare Bailey has received travel expenses to attend meetings from Pfizer and Novartis.

**References**


