

Macular degeneration

— symptoms and diagnosis

By Kashif Haque, BSc, MRPharmS

Age-related macular degeneration is the most common cause of blindness in the Western world. This article describes the causes and symptoms of the condition, the methods used for diagnosis and the treatments available



Blind spots in the field of vision are a symptom of macular degeneration

Age-related macular degeneration (AMD) is an ophthalmic condition characterised by progressive destruction and dysfunction of the central retina. It is the leading cause of blindness in the Western world and is the most common disease of the macula — the central part of the retina that is particularly important for detailed vision.

In the UK, 220,000 people who are registered blind or partially sighted have AMD. The Royal National Institute of the Blind estimates that the total number of people with AMD is closer to 400,000, with 40 per cent of these being over 75 years old.¹

AMD can be split into two broad types, usually referred to as “wet” and “dry.”² Dry AMD is the most common form, accounting for 80–90 per cent of all cases. Of the two forms, wet AMD is the more severe and accounts for 90 per cent of the cases of severe visual loss in elderly people.³ The estimated annual incidence of wet AMD is between 25,000 and 30,000 cases.⁴ Once wet AMD has developed in one eye, there is a high risk that it will develop in the other — the cumulative estimated incidence of

this is 10 per cent at one year, 28 per cent at three years, and 42 per cent at five years.⁵

— AMD terminology

In dry AMD there are patches of atrophy in the retina overlying the choroid (see Figure 1 for a diagram of the eye), referred to as geographic atrophy. The wet form of AMD is characterised by the development of new blood vessels beneath the retina, a process known as choroidal neovascularisation (CNV). It is subdivided into “classic” and “occult” forms, with the classic form being associated with more rapid progression than the occult form.² Classic and occult CNV can occur within the same lesion. The following terms are generally used to describe the composition of the lesion.

- “Classic with no occult” — lesions that are composed of classic CNV with no evidence of an occult component
- “Predominantly classic with occult” — lesions in which more than half of the lesion is composed of classic CNV but some occult CNV is present
- “Minimally classic” — lesions in which less than half of the lesion is composed of classic CNV

- “Occult only” — lesions in which there is occult CNV with no evidence of classic CNV

It is currently estimated that between 5,000 and 7,500 new cases of “classic with no occult” and “predominantly classic” CNV are diagnosed in England and Wales each year.⁴

CNV lesions are also classified according to their location relative to the fovea (the area at the centre of the macula that is associated with colour vision and perception of fine detail, and where there are no blood vessels to interfere with vision — see Figure 1). Lesions that extend directly under the fovea are described as subfoveal. Those that occur in areas other than the middle of the fovea are described as juxtafoveal and those that occur in areas of the macula other than the fovea are described as extrafoveal. About 10–15 per cent of cases of wet AMD are extrafoveal.¹

— Aetiology

As the name suggests, AMD occurs as people get older and generally affects only those aged over 50 years. The exact cause of AMD is not known, but a number of environmental factors that predispose individuals

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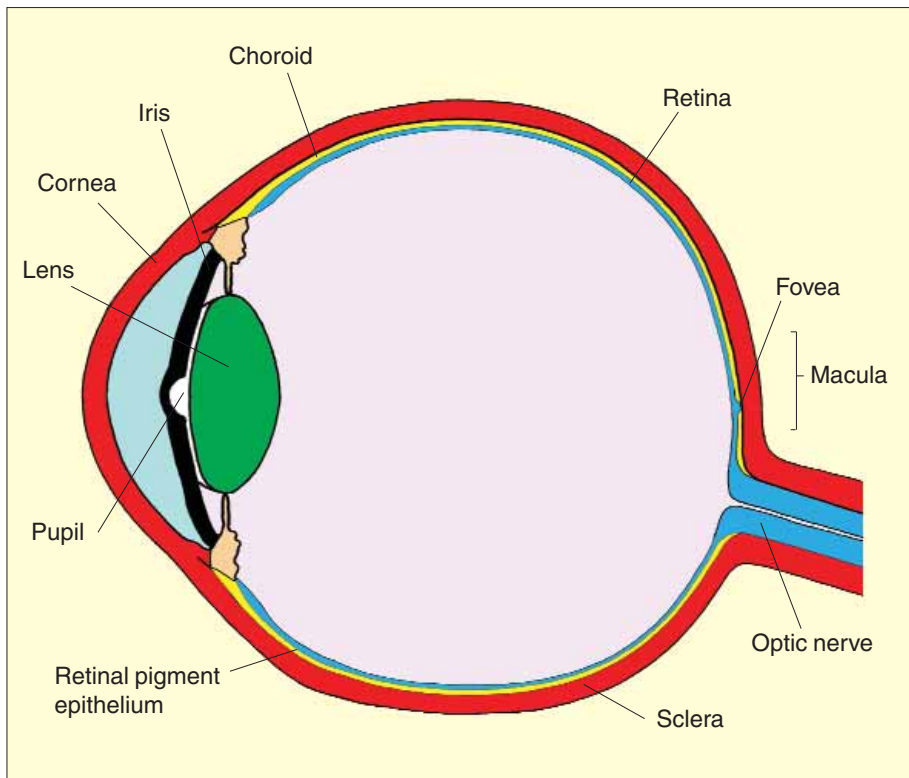


Figure 1: Diagram of the eye. Light enters the eye through the pupil. Just behind the pupil is the lens, which focuses the light on the retina at the back of the eye. The retina then converts the light into images and sends them to the brain via the optic nerve. The macula is located roughly in the centre of the retina, next to the optic nerve. It is a small and highly sensitive part of the retina that is used to see fine detail, necessary for activities such as reading and writing, as well as the ability to see colour. The fovea is the centre of the macula and is used to form sharp, clear images.

to developing the condition have been identified. These include:

- Poor nutrition. Supplementation with vitamins C and E, beta-carotene and zinc seems to help protect against macular degeneration, whereas a diet high in certain vegetable fats, especially those found in junk foods, may increase the risk of developing AMD⁷
- Smoking
- Hypertension or cardiovascular disease⁸
- Prolonged sun exposure

Genetic factors also predispose a person to developing AMD. In particular, those who have a variant (tyrosine to histidine change) of the complement factor H (CFH) gene at amino acid 402 on chromosome 1 are between two and a half and five and a half times more likely to develop AMD, because the variant CFH gene is less effective at preventing inflammation.⁹ Other genes that have implications for AMD development include HTRA1, which encodes a secreted serine protease.¹⁰ In addition, women are more prone to developing AMD than men.

As AMD develops, initial changes that occur in the retina include alterations to the pigmentation (either an increase or a decrease) of the retinal pigment epithelium (the outermost layer of the retina) and the development of soft drusen (pale yellow, large

deposits with ill-defined margins that form under the retinal pigment epithelium). Soft drusen contain incompletely digested photoreceptor segments, which are then secreted by the retinal pigment epithelium, forming a barrier between the retinal pigment epithelium and its blood supply, the choroid.

In wet AMD, the barrier between the retinal pigment epithelium causes new blood vessels to be formed (ie, CNV), which can leak fluid or bleed, causing lesions to develop and resulting in scarring. Wet AMD usually progresses from a localised lesion to an end stage that involves the entire macula, with complete or near-complete loss of central vision. It has been estimated that 70 per cent of eyes affected with CNV will have severe loss of vision within two years of diagnosis.⁴

When patients have changes to the pigmentation, but still have normal or near normal vision, their condition is referred to as early age-related maculopathy. Patients with early age-related maculopathy can progress to develop dry (ie, geographic atrophy of the retina), wet, or mixed wet and dry AMD.

It should be noted that most people aged over 40 years have some “hard” drusen (round, yellow deposits with defined boundaries) under their retinal pigment epithelium — it is the presence of soft drusen that is the precursor to AMD.

— Symptoms

People suffering from AMD may develop the following symptoms:

- Blurred vision
- Central scotomas (shadows or missing areas of vision)
- Distorted vision (metamorphopsia)
- Slow recovery of visual function after exposure to bright light
- Trouble discerning similar colours
- Difficulty reading or performing tasks that require the ability to see detail

Dry AMD In dry AMD, the most common early symptom is blurred vision. Since fewer light-sensing cells in the macula are able to function, people will see details, such as faces or words in a book, less clearly. Often this blurred vision will go away in brighter lights. If the AMD progresses, people may notice a small, but growing, blind spot in the middle of their visual field.

Wet AMD The first symptoms of wet AMD may be metamorphopsia. This often has the effect of making straight lines appear curved or tilted. Vision deteriorates and eventually central vision may be completely lost, leaving a central scotoma. Central vision loss particularly impairs the perception of fine visual detail and colours, affecting activities such as reading and driving. The ability to read with visual aids depends on the size and density of the central scotoma and the degree to which the person retains sensitivity to contrast (ie, the ability to see less well-defined objects, such as faces, clearly).

Rapidly deteriorating vision has an impact on emotional well-being, and individuals are likely to suffer depression and anxiety due to their loss of vision and reduction in independence. However, there is a great deal of individual variation in the ability to cope with loss of vision.

— Diagnosis

Various methods and tests are useful in the diagnosis of AMD, including:

- The visual acuity test
- The dilated eye examination
- The Amsler grid test
- Fluorescein angiography

Visual acuity test This eye chart test measures a person’s vision at various distances. (See Panel 1, p155, for more information about visual acuity.)

Dilated eye examination The dilated eye examination involves viewing the macula for signs of AMD. Measurement of intraocular pressure is carried out at the time as this routine ophthalmological assessment.

Panel 1: Visual acuity

Visual acuity (VA) is a quantitative measure of the ability to identify black symbols on a white background at a standardised distance. The VA score represents the smallest size that can be reliably identified. VA is the most common clinical measurement of visual function and is typically performed using a Snellen chart. A VA of 20/20 is frequently described as "normal" vision and means that a person can see the same detail from a distance of 20 feet as a person with normal eyesight would see.

In North America and most of Europe, legal blindness is defined as a VA of 20/200 or less in the better eye, while wearing the best correction possible. This means that a legally blind individual would have to stand 20 feet from an object to see it with the same degree of clarity as a normally sighted person would from 200 feet.¹¹

Amsler grid test An Amsler grid consists of horizontal or vertical black lines on a white background with a dot in the centre. Patients with AMD generally see distorted grid lines and a blurred dot.

Fluorescein angiography Photographs of the macula are taken after an intravenous fluorescein dye injection. Any CNV lesions will hyperfluoresce (grey/green appearance) and leak fluorescein so the lesion size, position and characteristics can be assessed. In the classic form, the lesion is well-defined in the early stages of the angiogram and then the margins blur as the fluorescein leaks. In the occult form, the CNV lesion leaks late in the angiogram and has poorly defined margins.⁶ In dry AMD, atrophic areas of the retina will have a pale appearance.

Management

For patients with dry AMD, there is currently no treatment available. Management consists of "best supportive care". This

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generally involves the teaching of skills and the provision of equipment to facilitate reading and other activities of daily living, to help people make the most of their remaining vision. However, the availability of these services is limited, and not everyone with AMD has access to high quality visual rehabilitation.

For patients with wet AMD, various treatments are available, including:

- Laser treatment
- Photodynamic therapy
- Macular translocation
- Transpupillary thermotherapy

Laser treatment In "classic with no occult" AMD, burning the abnormal vessels with a thermal laser can prevent the growth of the lesion, and this may help delay or prevent visual deterioration.² However, this treatment also damages the overlying retina, and so is not usually suitable when the CNV lesion is subfoveal.

Photodynamic therapy (PDT) The aim of PDT is to destroy CNV lesions without damaging the overlying retina, thereby slowing or halting the progression of vision loss. PDT involves the intravenous infusion of a light-sensitive agent, followed by localised light activation of the drug. At present only verteporfin, a benzoporphyrin derivative, is licensed in the UK for this indication, but other agents are in development. This therapy will be discussed in more detail in the next article in this special feature (p155).

Macular translocation Macular translocation involves surgically moving the macula so that the fovea lies over a healthier part of the choroid. This may involve detaching and rotating the retina (macular translocation with 360° retinotomy), or making an incision in the retina, folding the outer layers of the eye, making the sclera shorter and moving the choroid slightly in relation to the macula (limited macular translocation). Few cases have responded well, and some have responded badly. National Institute for Health and Clinical Excellence guidance on this procedure comments that there is particular concern that the vision of some patients can deteriorate after the procedure. It was also noted that the evidence base for this procedure is poor.¹²

Transpupillary thermotherapy (TTT) TTT uses laser energy (at a lower power and with a more diffuse beam than standard laser treatment) to coagulate vessels. It can be used to treat patients with occult new vessels. NICE guidance on the use of TTT for the treatment of wet AMD states that current evidence on the safety and efficacy of this treatment does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research.¹³

Conclusion

AMD is the leading cause of blindness in the Western world. Wet AMD is the least common form of the condition, and is also the most severe. However, it is also the most treatable form. Drugs used to treat wet AMD are described in the next article (p155).

ACKNOWLEDGEMENTS I thank all those who were involved in the production of this article, especially Paul Bishop, consultant ophthalmologist and Selwa El-Beik, medicines information manager, both at Central Manchester and Manchester Children's Hospitals NHSTrust.

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