The National Institute for Health and Clinical Excellence (NICE) estimates that there are 26,000 new cases of wet age-related macular degeneration (AMD) in the UK each year and that the condition affects more women than men. This is probably an underestimate according to figures from Owen et al.2 and these numbers are expected to rise because of the long-term nature of the disease and the ageing population. AMD remains the leading cause of irreversible central vision loss in the developed world among individuals older than 50.3-6

Wet AMD accounts for more than half of all severely sight impaired (blind) and sight impaired (partially sighted) registrations. This article discusses the referral of AMD and emphasises the importance of new referral pathways, which have emerged in recent times, in order to reduce sight loss through this devastating disease.

About the author

Chris Steele is consultant optometrist, head of optometry at Sunderland Eye Infirmary (SEI). Over the past 19 years he has developed a wide range of extended roles involving hospital optometrists undertaking cataract, anterior segment, diabetes, glaucoma, paediatrics and medical retina caseloads. He has authored over 50 publications on topics including glaucoma, diabetes, specialist medical contact lenses, refractive surgery and clinical risk management, and has undertaken many presentations, both nationally and internationally. Mr Steele was a member of the NICE Glaucoma Guideline Development Group from 2007 to 2009, which produced the NICE glaucoma guidelines published in 2009.

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Risk factors for AMD
AMD is a complex disease caused by the combination of genetic predisposition16 (involving multiple causative genes) and environmental modifiable risk factors such as smoking, hypertension, nutrition, obesity and excessive exposure to sunlight.17 It is beyond the scope of this article to discuss the presentation and risks of AMD in detail, as this has been discussed previously in OT.15

Dry (non-neovascular) AMD
AMD is characterised by ageing changes at the photoreceptors, retinal pigment epithelium (RPE), Bruch’s membrane and choroid. Dry AMD (non-neovascular) is a form of extensive atrophy (wasting) of cells which usually progresses slowly, with a gradual reduction in central vision (Figure 1). Many patients who have dry AMD may never be referred to have their eyes examined by an ophthalmologist. This is even where an optometrist might have detected a significant progression in dry AMD during a routine eye examination. The reason for this is the current lack of capacity within the Hospital Eye Service (HES) to monitor such patients with a chronic untreatable condition. HES clinic capacity will be squeezed even further in future, unless service provision changes, because of pressures created by new indications for the use of intra-vitreal anti-vascular endothelial growth factor (anti-VEGF) injections for other sight-threatening conditions, such as diabetic macular oedema, and Ozurdex for retinal vein occlusions. Such treatments mean that patients with diseases which can be treated will take priority over patients which cannot be treated.

The area in which a patient lives currently dictates the extent of valuable support which is provided from a low vision clinic or HES counselling services, through an Eye Clinic Liaison Officer (ECLO). OT has previously discussed the benefits of a dry AMD monitoring scheme15 and the importance of regular review is affirmed by the fact that some patients with relatively mild dry AMD often worry about disease progression, not just in developing wet AMD (which can be treated) but also to advanced dry AMD (which cannot be treated but causes profound loss of vision). Some patients would prefer regular monitoring rather than just being told to come back if things get significantly worse, by which time it might be too late for anything to be done.

The change from dry to wet AMD
Patients with intermediate to large soft/confluent drusen, with or without hyper- or hypo-pigmentation areas in the macular region, and no choroidal neovascular membrane (CNV) or geographic atrophy, are considered to have early age-related maculopathy (ARM), (Figure 2). Approximately 10-20% of patients with early ARM will develop the wet form of AMD. Once wet AMD develops, there is a higher risk of subsequent development of CNV in the second eye.16,17 Although an estimated 80% of patients with AMD have the non-neovascular (dry) form of this disease, neovascular (wet) AMD is responsible for almost 90% of cases with severe visual loss (VA of 3/60 or worse).

Wet (neovascular) AMD
Wet (neovascular) AMD is characterised by the development of new blood vessels, which grow between the RPE cells and the photoreceptor cells within the macula. At the earliest stages, this presents with sub-retinal fluid (Figure 3) but as new vessels grow, they can easily haemorrhage (Figure 4), leading to visual impairment. VEGF induces new blood vessel formation (angiogenesis), vascular permeability and inflammation and is directly involved in the development and progression of CNV. CNV can be sub-divided into classic and occult forms, according to its appearance on investigation by intravenous fluorescein fundus angiography (IVFA), (Figure 5). A mixture of classic and occult CNV can often occur in the same lesion, with the majority of CNVs occurring sub-foveally.18

Current challenges affecting AMD service delivery
It is clear that long-term medical retina care pathways need to be further developed and rolled out across the UK to meet the growing needs of local populations. The aim is to have robust fast-track patient referral systems in place which ensure patients from primary care, who would benefit from efficacious treatment, receive this promptly and competently with the appropriate long-term follow-up in place, as recommended by NICE and Royal College of Ophthalmologists’ guidelines. Patient safety must be paramount at all times. Unfortunately, many areas around the UK are struggling to treat new patients with wet AMD within the recommended timescales and do not provide sufficiently regular follow-up as recommended. The result is that many patients are needlessly suffering significant sight loss, which could otherwise have been prevented.

There are a number of capacity issues which need to be addressed in order to achieve these aims. Patients who receive intra-vitreal injections for wet AMD currently require regular follow-up (usually monthly, but can be extended in appropriate circumstances) for an indefinite period of time. The main capacity issue is, therefore, dealing with the burgeoning numbers...
of review appointments which patients need according to treat/re-treat protocols.

Another key constraint is access to ‘high tech’ equipment and the ability to undertake, for example, optical coherence tomography (OCT) scans at every visit, to ascertain patient stability, or the need for further treatment. Adequate access to IVFA is also a similar consideration, although less so, considering the huge benefit of performing non-invasive OCT instead now. Even if OCT/IVFA capacity is available, inadequate IT data networks in some units hinder timely access to OCT/IVFA because of the large size of files.

Most HES macular services are bursting at the seams in terms of available accommodation, with insufficient levels of multi-disciplinary, properly trained staff to efficiently and effectively undertake the clinics within the designated time frames. Lack of training and development may well lead to compromised quality of care for patients in a variety of ways, not to mention the pressure, ultimately leading to stress, on staff. Lack of adequate funding and/or resources might also give rise to sub-optimal provision of patient support services, for example, low vision and ECLO services for all patients who require this.

Across the UK, individual macular services providing treatment for wet AMD differ to some extent in the way they are structured in terms of size, staffing, skill mix and variations in population (rural or urban) served. Though no single wet AMD service is ideal, there are many aspects of best practice which can be gleaned from these individual services, which could be used to produce and roll out more efficient and productive care pathways in the future.

**Service models for anti-VEGF treatments**

The Royal College of Ophthalmologists has recommended two main models regarding anti-VEGF service delivery. The regional network model enables a number of local hospitals to work together and share resources and expertise. Each regional network has an administration centre to support all units involved. This option assumes that there is sufficient local wet AMD management expertise and that minimum equipment requirements are met in all included units. Dedicated AMD clinics are undertaken in local hospitals, with facilities similar to those in the network centre. ‘Virtual clinics’ are used where retinal experts at the regional centre report on all OCT images from the peripheral units. This is highly dependent on adequate IT data networks which are capable of sharing high volumes of large image files between different clinic sites. An example of this model is in Sheffield.

The regional macular specialist centre (hub and spoke) is an alternative preferred model for receiving all fast-track referrals (see later) for wet AMD, followed by triage and confirmation of diagnosis after all necessary investigations have been done, prior to prompt treatment. Patients from other hospitals/outreach centres (spoke units) may be re-referred back to the local hospital for subsequent follow-up, provided the appropriate equipment, for example, OCT, is available.

As treatment clinics are run in parallel to triage and follow-up clinics at the regional specialist centre, this enables both ‘one-stop’ (where all examinations, investigations and treatment take place on the same day) and ‘two-stop’ (examinations and investigations take place on one day, followed by treatments on a separate visit) care pathways. Examples include Gloucester, Southampton and Sunderland.

In some areas, repeat injections of anti-VEGF may be undertaken at spoke units, as it will significantly reduce travelling time for patients who need re-evaluation and treatment every four to six weeks, for a minimum of two years. Alternatively, all patients may be re-evaluated at the regional macular centre. A good example of a regional macular centre model is Sunderland Eye Infirmary (SEI). To the author’s knowledge, the involvement of hospital optometrists in this service is unique at the time of writing. All new patient referrals (mainly from community optometrists) are directed by rapid access referral to a named ‘on take’ medical retinal consultant who allocates the patient, either to triage or directly to an AMD specialist.

Fast-track triage clinics are undertaken by highly trained hospital optometrists to identify any false positive wet AMD referrals and redirect patients appropriately. The optometrists involved in these triage referral
clinics hold Independent Prescriber (IP) status
and the Foundation Trust has authorised special dispensation for them (as well as an A&E nurse consultant) to prescribe fluorescein for intravenous use, for the purpose of undertaking urgent diagnostic IVFA. This enables optometrists to independently instigate and interpret IVFAs, depending on other clinical findings and OCT results, with the minimum of delay. If necessary, indocyanine green (ICG) may be used instead, to help visualise the choroidal circulation where differential diagnosis is required for other conditions which can mimic wet AMD. Results from patients in whom wet AMD is confirmed or suspected by the optometrist are discussed with a medical retinal consultant, and those requiring intravitreal treatment have the choice of immediate (one-stop) treatment or joining a dedicated intra-vitreal injection list (two-stop).

Currently patients are offered Lucentis (Ranibizumab) treatment, which is injected monthly after an initial loading phase of three consecutive injections spaced one month apart, then further injections on a monthly basis as clinically required (which depend on OCT and VA results). Avastin (bevacizumab) may be equally as effective and is much cheaper than ranibizumab. Eylea (aflibercept) is now being offered to new patients as it has the advantage of only needing bi-monthly injections beyond the loading phase, thus requiring fewer follow-ups. These changes in treatment options not only affect frequency of patient follow-up but also reduce costs of treatment. In future, these factors will ultimately have significant effects on how emerging treatment pathways will develop and will strongly influence how the skills of optometrists will be best utilised.

To the author’s knowledge, SEI is also one of the first few centres in the UK where an innovative nurse-led intravitreal injection service has been successfully established. This has enhanced productivity while maintaining quality and preventing vision loss through timely treatment. All OCT review clinics (eight per week) are undertaken by nursing staff and the OCT images are reviewed by optometrists in three virtual clinics throughout each week. Optometrists decide on whether treatment is required for each patient. Those requiring further injections are listed by the optometrists. For patients developing wet AMD in their second eye, the optometrist will independently instigate IVFAs on which to base treatment decisions. Some ‘stable’ patients (who have not needed an intravitreal injection for at least six months) are seen at satellite OCT review clinics, undertaken by nurses closer to their home, for which a mobile OCT scanner is used.

An ECLO undertakes sessions simultaneously to these specialist clinics so that patients requiring support can undergo disability assessment and visual rehabilitation during the same visit to the hospital. Low vision assessments (LVA) by the optometry department are also offered to all patients, where appropriate.

**AMD fast track referral pathways**

For an AMD referral pathway to be maximally effective, there needs to be rapid access to retinal specialists with expertise in the management of wet AMD for all patients, irrespective of geographic location. Patients should be seen within one week of diagnosis, and there should be no more than one week between evaluation and treatment.

All patients suspected of having wet AMD by their community optometrist, GP or other practitioner should be referred directly to the nearest AMD Centre. In this regard, community

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**Figure 4** Topcon OCT demonstrating intra-retinal fluid associated with a large macular haemorrhage in wet AMD

**Figure 5** (a) Spectralis OCT showing intra-retinal (IRF) and sub-retinal fluid (SRF) associated with an occult neovascular membrane (b) Fluorescein angiogram demonstrating the same occult sub-retinal neovascular membrane lesion

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optometrists should send all suspect wet AMD referrals directly to an ophthalmology department, not via the GP, as delays could seriously undermine the effectiveness of timely treatment. Referrals should be via fax or secure e-referral, including OCT images where available, to the AMD centre. Once received, the referral is allocated to an “on take” medical retina specialist who prioritises clinic appointment requests, instigates necessary investigations and books an AMD triage appointment or specialist AMD clinic, as required. If patients allocated to a triage clinic are subsequently confirmed to have wet AMD, they are referred into the consultant AMD specialist clinic for appropriate treatment.

Optometrists should always advise patients accordingly and strongly encourage patients to self refer or present themselves to eye casualty or an AMD centre if they notice any sudden reduction in their vision and/or distortion. As discussed earlier, this is just as important for patients currently diagnosed only with ARM or dry AMD, as a significant proportion will go on to develop wet AMD. This is vitally important in patients with wet AMD who have second eye involvement. Table 1 provides a useful guide which can be used to help clinical decision-making.

The use of community-based referral refinement schemes by optometrists with a special interest have been demonstrated to work well for conditions such as glaucoma. However, for patients with suspected wet AMD, such pathways will introduce unnecessary delays which could adversely affect outcomes of treatment and/or result in misdiagnoses where full, immediate access to OCT and IVFA may not be available.

**Conclusion**

The success of any eye care pathway relies on appropriate referrals and good communication between primary and secondary care teams.

Fast-track wet AMD care pathways require strong clinical leadership from ophthalmologists, with expertise in the management of wet AMD, who are supported by appropriately trained multi-disciplinary staff (including community-based optometrists), adequate ‘high tech’ equipment, combined with up-to-date IT data networks and sufficient clinical space from which to operate the service. In future, greater use of optometrists should be considered. This would range from hospital optometrists extending their specialist clinical roles to transferring patients with ‘stable’ wet AMD and certain patients with dry AMD into community review clinics, in order to free up secondary care capacity. This would require a significant expansion of OCT equipment availability in the community which is linked by secure IT networks capable of rapidly transmitting high volumes of patient data containing large image files between hub and spoke sites.

### Table 1 Features of AMD that require referral

<table>
<thead>
<tr>
<th>Vision/VA</th>
<th>Untreatable AMD Routine referral recommended for LVA/ECLO assessments and/or CVI registrations</th>
<th>Advanced wet (disciform) AMD Routine referral recommended for LVA/ECLO assessments and/or CVI registrations</th>
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<tbody>
<tr>
<td>6/96 or better, although patients with poorer vision with recent symptoms may be referred for assessment</td>
<td>Any</td>
<td>Less than 6/96</td>
</tr>
<tr>
<td>Sudden loss of central vision (&lt;3 months)</td>
<td>Slow loss of vision Sometimes mild distortion</td>
<td>Extensive loss of central vision and/or distortion Onset of missing patch/blurring in central vision</td>
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<tr>
<td>Sudden onset of central visual distortion (&lt;3 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset of missing patch / blurring in central vision</td>
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<tr>
<th>Symptoms</th>
<th>RET atrophy or disturbance Pigment clumping in the centre of the macula Hard or soft drusen</th>
<th>Extensive sub-retinal fibrosis and pigmentation change at the macula Central macular elevation with/without sub-retinal fluid, hard exudate and fibrosis</th>
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</thead>
<tbody>
<tr>
<td>Retinal elevation/swelling or pigment epithelial detachment</td>
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<td>Sub-retinal and retinal haemorrhage</td>
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<td>Exudates associated with sub-retinal fluid or thickening</td>
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<td>Visible ‘greyish’ sub-retinal membrane</td>
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**Macular Signs**

**Symptoms**

- Sudden loss of central vision (<3 months)
- Sudden onset of central visual distortion (<3 months)
- Onset of missing patch / blurring in central vision

**Table 1 Features of AMD that require referral**

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