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Age-related macular disease

Part 2 – Detection of wet AMD

In the second part of this series, **Dr Frank Eperjesi** looks at the clinical evaluation of suspect maculopathy with particular emphasis on the early detection of the wet form. C7881, one general CET point, suitable for optometrists and DOs

The first article in this three-part series (*Optician*, October 19) looked at the classification of AMD and described the clinical features of dry AMD as: discrete yellow spots at the macula (drusen), hyperpigmentation of the RPE, sharply demarcated areas of RPE depigmentation (hypopigmentation) with focal hyperpigmentation of the RPE a high-risk feature for subsequent wet AMD development. The clinical features of wet AMD were described as geographic atrophy of the RPE with visible underlying choroidal vessels, pigment epithelial detachment (PED) with or without neurosensory detachment, subretinal or sub-RPE neovascularisation, fibroglial scar tissue, haemorrhage and exudates.

While dry AMD is a slowly progressive disease with vision loss taking place over many years, wet AMD is a much more rapidly progressive disease and is the main cause of catastrophic and permanent vision loss, which can occur over a matter of a few days. It is estimated that 18 per cent of patients with intermediate AMD (many medium-sized drusen >63µm but <125µm or one large drusen >125µm – the central retinal vein is about 125µm in diameter at the optic nerve head) in at least one eye and 43 per cent of patients with advanced AMD in one eye only develop choroidal neovascularisation (CNV), in other words wet AMD, within five years.[1] Wet AMD accounts for only 10 per cent of all AMD but accounts for 95 per cent of serious vision loss. This takes the form of a localised loss of vision (scotoma) and or distortion of vision (metamorphopsia). This article will review techniques that can be used in primary care optometric setting in the timely detection of wet AMD.

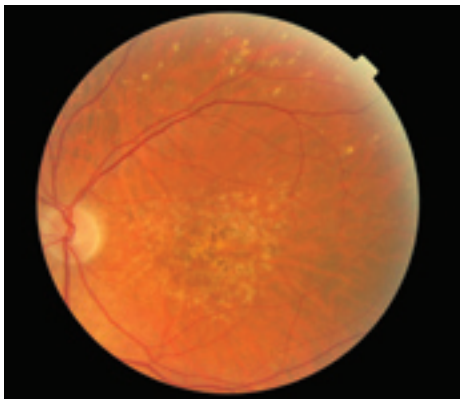

Figure 1 Dry AMD

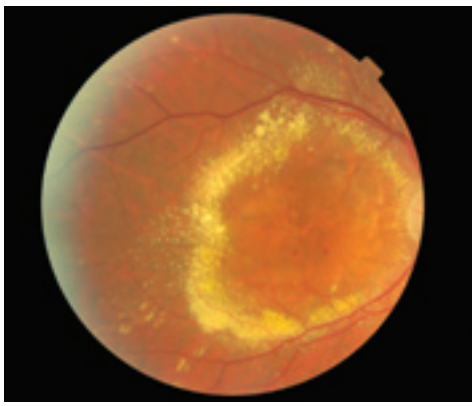

Figure 2 Wet AMD

Early detection of wet AMD

Research has shown that the major current techniques used in the treatment of wet AMD (anti-VEGF and photodynamic therapy) are more likely to be successful and halt vision loss or even reverse vision loss with smaller and less central lesions. According to recent studies investigating the outcome of these treatment modalities, the larger the lesion at baseline the smaller the treatment benefit in terms of the absolute level of visual acuity at two years after the initiation of treatment.

The natural history of CNV is that it gradually increases in size by an average of 10 to 18µm daily[2] and that it grows closer to the foveal centre in about 50 per cent of cases.[3] Therefore, early detection of AMD-related lesions is crucial in the management of these patients. Reeves[4] estimates that in her experience the transition to early wet AMD is not recognised soon enough in approximately 15 per cent of patients. By the time an ophthalmologist sees these patients they have severe, irreversible vision loss for which treatment has minimal impact. She goes onto state that 'ideally, diagnosis and treatment should occur right after conversion to wet AMD before vision loss has occurred'. Recent publications have emphasised the benefits of treating AMD lesions while they are still relatively small.[5,6] Loewenstein[7] reported a case where a patient with a small extrafoveal lesion and visual acuity of 6/12 presented two months later with 6/36 and an extensive subfoveal CNV without treatment.

This reflects the importance of identifying the presence of CNV before the onset of the inevitable and progressive significant visual loss associated with the condition.

Using symptoms to detect wet AMD

Detection of wet AMD often involves instructing patients to report symptoms such as distorted lines, blurriness, reduced vision and dark areas in their visual field or use of the Amsler grid and being alert to new symptoms of metamorphopsia, visual field scotoma and blurred vision or micropsia. Many investigators have pointed out that the patients who notice these symptoms or changes in the Amsler grid are detected relatively late in the stage of the disease when a large scotoma is already present.[8,9]

Change in refractive error

In the author's experience it is worth further investigating older patients (especially those with more than one risk factor for AMD – see article three in this series) who present with a reduction in myopia or an increase in hyperopia (hyperopic shift), particularly for those without cortical lens opacities (these have been reported to cause this type of refractive error change).

A hyperopic shift without cortical lens opacities could be due to type 2 diabetes (however, this most commonly causes a myopic shift) or due to CNV elevation

of RPE or neurosensory retina. Further investigation could involve slit-lamp indirect binocular ophthalmoscopy, referral for an ophthalmological opinion or both. Elevation due to a subtle hyperopic shift such as 0.75DS may result in retinal elevation that is too subtle to detect using slit-lamp indirect binocular ophthalmoscopy, so it is useful to ask the patient if they have experienced any metamorphopsia or micropsia to help with the differential diagnosis.

Ophthalmoscopy

Certain types of wet AMD are very easy to detect even when using a direct ophthalmoscope through an undilated pupil (Figure 1 dry AMD and Figure 2 wet AMD). Early CNV changes may not be detectable using a monocular technique and it would be good practice to investigate patients presenting with symptoms of distorted lines, blurriness, reduced vision, dark areas in their visual field, metamorphopsia or micropsia with slit-lamp-based binocular indirect ophthalmoscopy. However, slit-lamp indirect biomicroscopy's clinical utility is variable and depends to a great extent upon the expertise of the examiner and lesions may still be missed.

Using the Amsler grid to detect wet AMD

As the early detection of wet AMD is crucial, patients at risk are encouraged to perform self-monitoring, often using an Amsler grid. The Amsler grid can be used to detect scotomata (missing or blurred lines) and metamorphopsia (bowed or distorted lines) and the likely position of the associated lesion. The basic grid (Amsler chart 1) is printed in white on a dull black background. It is intended for use at 30cm (with the patient fully corrected for that distance) when each square subtends an angle of 1° and the whole chart 20°. Amsler chart 2 has guidelines to help those patients who already have a central scotoma to estimate where the central fixation is located. The original test was intended for use under normal reading illumination conditions. A variation of the standard test is the threshold Amsler test in which the task lighting is reduced by dimming the local illumination or by introducing filters such as those used with the Titmus stereoacuity test or the Mallet unit.[9] Some reports have suggested that this makes the Amsler grid more sensitive to detecting small, recently developed CNV lesions that cause relative but not absolute scotomata.[9] Franklin[10] has also promoted the use of a computer-based test in which the luminance of

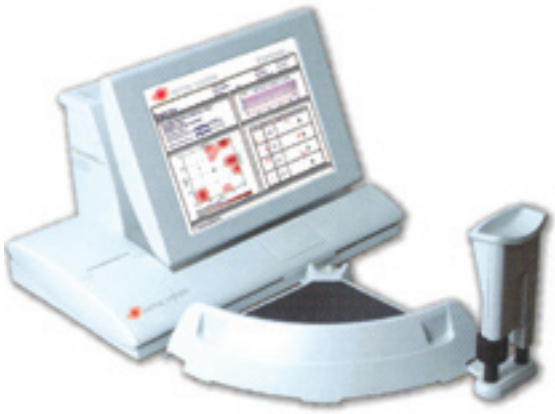

Figure 3 Forsee PHP from Notal Vision

a screen-based Amsler grid is reduced progressively and just before the target disappears altogether relative scotomata become apparent to the patient. With the standard and threshold Amsler tests mydriasis and ophthalmoscopy should be avoided immediately prior to using the Amsler grid especially with suspected AMD.[10] Neither the standard nor threshold versions are as good as conventional perimetry when it comes to detecting scotomata less than 6° (the average optic nerve head is 7°) in diameter.[11] It seems common practice for eye care professionals to supply patients with a copy of the recording sheet (black grid on a white background) for home testing. This may result in spurious results as bright backgrounds with black detail have been shown to result in anomalous illusions of shape and colour akin to the pattern glare described by Wilkins and colleagues in their work on reading problems.[12] It would be better to guide patients or carers to an appropriate website from which they can print a white grid on black background version for themselves or use a screen-based grid for self-testing. Unfortunately, Franklin[10] and others[13] have reported that compliance with self-testing is low. The most common presenting symptom of wet AMD is blurred vision and distortion when reading, rather than changes on the Amsler chart even in patients who are supposed to be self-monitoring.[14]

The Amsler grid has been shown to be an unreliable tool for diagnosing central visual field defects in patients with AMD.[9,15] Although the threshold Amsler grid has been reported to show a better performance, 50 per cent of all scotomata in the macular region still remain undetected by either one. This means that one out of every two cases of wet AMD could be missed if the eye care professional were to rely solely on the Amsler grid for detection. Moreover, when scotomata of 6° or less were evaluated the detection rate was even lower.[11]

There are several reasons for the poor performance of the Amsler grid:

- Awareness of visual field defects is limited, with the patient not being cognisant of any defect until the scotoma is considerably large and already includes central vision because of foveal involvement of the lesion. This can be partly explained by cortical completion or the 'filling in' phenomenon.[16] The correlation relation between scotoma size and detection rate has been demonstrated.[11]
- The inability to properly maintain fixation during testing
- The crowding effect caused by the multiple lines that are peripherally presented in the Amsler grid causing low sensitivity of the test and adding to its poor performance
- The non-interactive nature of the Amsler grid, rendering it unsuitable for monitoring patients because factors such as quality of examination performance and reliability measures, such as false positives and false negatives cannot be assessed
- Low compliance to perform the Amsler grid at home.

Preferential hyperacuity perimeter

To try to address some of the shortcomings of the Amsler grid a new method using the hyperacuity function has been developed. This was initially named the 'Macular Computerised Psychophysical Test' and described by Loewenstein and colleagues in 2003[17] but has become known as the 'Preferential Hyperacuity Perimeter' (PHP). The test was originally marketed by Zeiss as the 'Preview PHP' and is now available from Notal Vision (www.notalvision.com) as the Forsee PHP (Figure 3). In this second-generation format it has a number of improvements over its first incarnation in terms of improved speed and ease of interpretation. This system was originally developed to evaluate the central macular visual field and potentially provide early detection of wet AMD. It generates a non-invasive eye exam that allows the detection of elevations in the RPE and the bowing of the photoreceptor layer – both consistent with conversion from intermediate to an advanced stage or wet AMD. Hyperacuity also termed vernier acuity is defined as the ability to perceive a difference in the relative spatial localisation of two or more visual stimuli. Hyperacuity threshold may be as low as 3 to 6 seconds of arc[18] – in other words it is about 10 times more sensitive than standard visual ▶

acuity.[19] Through its use of hyperacuity, the Forsee PHP can overcome the brain's ability to compensate for small defects and may identify CNV lesions prior to the patient experiencing any significant visual loss. Hyperacuity stimuli are highly resistant to retinal image degradation and are suitable for assessing retinal function in patients with lens opacities.[19] Furthermore, there is no decrease in hyperacuity with age between 20 and 85 years.[20] Patients must have better that 6/60 to be able to perform the test.

The patient places their head on a chin rest and views the monitor with one eye occluded. Task-orientated fixation was incorporated to try to eliminate the need for continuous fixation of a central located target. This means that the patient can move their eye to fix the stimulus without the results being affected, which is unlike the majority of visual field analysers, were central and maintained fixation is paramount to the successful application of the test. The patient is presented with a pattern of dotted lines projected for 160msec to the central 14° of the visual field (Figure 4). Each line contains an artificial distortion at a different magnitude and the distortion serves as a competitive stimulus to any retinal disease-related distortion (hyperacuity defect) that might appear on the presented pattern. The patient uses a stylus pen to touch the screen where the distortion was located (Figure 5). When there is a CNV lesion, attention competition between the artificial distortion and the pathologic distortion takes place in the patient's brain.

In general, the brain ignores the smaller of two stimuli and this phenomenon is exploited in PHP testing to assess the magnitude of the retinal disturbance (Figure 6). Varying sizes of artificial distortion are presented, allowing a quantification of the retinal distortion by analysing the patient's response. Based on these responses a visual field map is constructed, analysed and compared to normative data, thereby determining the likelihood of this defect being CNV (Figure 7). The fast flash time and use of hyperacuity allow the device to overcome brain compensation mechanisms to better capture visual defects. The PHP has been shown to detect recent onset CNV with high sensitivity (82 per cent) and differentiate these patients from those with intermediate AMD with high specificity (88 per cent). PHP was also shown to be more sensitivite than slit-lamp indirect binocular biomicroscopy.[21] The same group has shown that the PHP had a greater positive predictive value and sensitivity compared with the Amsler grid for detecting wet AMD-related lesions. Of 32 patients with CNV, 30 (94 per cent) were detected by the PHP and only 11 (34 per cent) with the Amsler grid.[17]

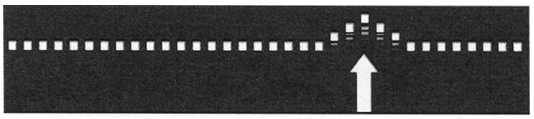

Figure 4 Patient is shown a dotted line with some dots deviating from the line (artificial distortion). The artificial elevation is made progressively smaller

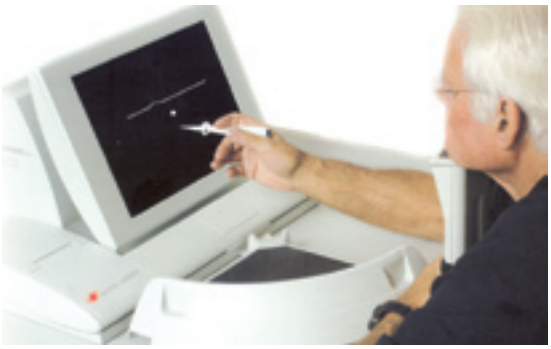

Figure 5 The patient use a stylus pen to touch the screen where the distortion was located

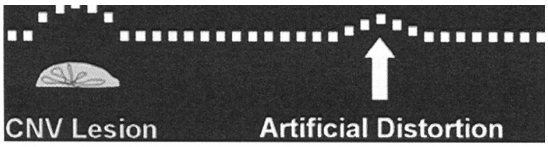

Figure 6 Competition occurs in the presence of a CNV. When the CNV causes a larger elevation than the artificial one, the patient will pick the spot of true distortion

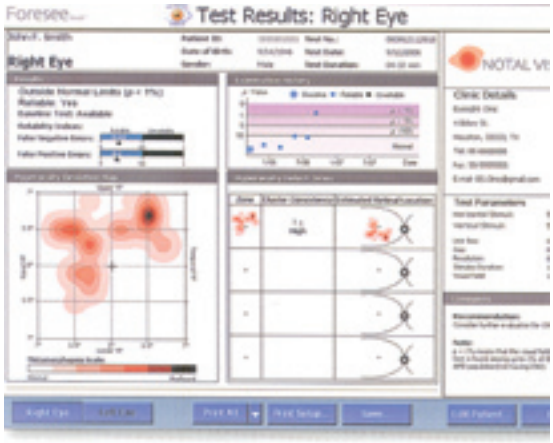

Figure 7 Test results from the Forsee PHP

Previous tests can be retrieved from memory and therefore long-term tracking of retinal changes is easily achievable. In the US, the PHP has FDA approval for monitoring the progression of AMD and detecting the conversion of dry to wet AMD signalled by the onset of CNV.

Reeves[4] has advocated that all AMD patients should have a baseline PHP. Then, depending on the absence or presence of high-risk features for CNV, repeat testing may be performed anywhere from two to four times a year. Interestingly, Reeves[4] has suggested that PHP in conjunction with OCT may also help minimise the use of angiography (not without its risks) during follow up.

Conclusion

It is important for eye care professionals to be aware that the Amsler grid will only detect half of those patients with early wet AMD and before new techniques such as the PHP become ▶

more widely available it is important to use a combination of patient symptoms (especially blurred, missing or distorted lines), reduced distance and near visual acuity, hyperopic shift and slit-lamp indirect binocular microscopy to detect the presence of new CNV. The newly emerging treatment options for wet AMD and in particular anti-VEGF therapies have made it incumbent on eye care professionals to upgrade monitoring techniques for earliest possible detection of CNV. The use of PHP has been shown to be more accurate than slit-lamp indirect binocular biomicroscopy and twice as accurate as the Amsler grid and could significantly enhance the rate of early detection of CNV development leading to earlier treatment and better final visual acuity. The use of PHP for home monitoring is currently being investigated by its developers. ●

● The author has no commercial interest in any of the equipment described.

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MULTIPLE-CHOICE QUESTIONS – take part at opticianonline.net

1 What percentage of patients with intermediate AMD will develop a CNV after five years?
A 10
B 15
C 18
D 20

2 The standard Amsler grid cannot detect lesions smaller than which of the following?
A 64µm
B 125µm
C 14° of arc
D 6° of arc

3 The threshold Amsler test involves which of the following?
A Preferential hyperacuity perimetry
B Standard Amsler testing and reduced illumination
C Carrying out standard Amsler testing immediately after direct ophthalmoscopy
D Standard Amsler testing and very high levels of illumination

4 Hyperacuity has a resolution of approximately which of the following?
A 6°
B 7°
C 125µm
D 5 secs of arc

5 The Forsee PHP analyses which of the following?
A 7° around the fovea
B 14° around the optic nerve head
C At the level of the internal limiting membrane
D. 3 to 6 seconds of arc around the fovea

6 Which one of the following is correct?
A Compared to the Amsler grid the PHP is about eight times better at detecting CNV lesions
B The Amsler grid will detect about 80 per cent of cases with early CNV
C Slit lamp indirect binocular microscopy is better at detecting early CNV than PHP
D The PHP can provide information on levels of hyperopic shift in dioptres

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