

# OCULAR PATHOLOGY AND LOW VISION

## PART 1: AGE RELATED MACULAR DEGENERATION

Anne Eyre discusses significant loss of visual acuity.

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Low vision is usually either the result of an inherited disorder, or is acquired later in life due to trauma, disease, toxicity or ageing. There are, therefore a variety of pathological conditions that can result in a significant loss of visual acuity. In basic terms, these can be divided into two distinct groups:

- those affecting the media of the eye
- those affecting the retina

In low vision work the majority of patients present with retinal problems. In order to understand the implications of retinal pathology on visual performance it is necessary to have knowledge of retinal function in the process of seeing.

Essentially the retina can be described as a three-neurone structure comprising photoreceptor, bipolar cells and ganglion

cells. It acts as the primary stage in the image processing system and its complexity is comparable with the intricate nature of the image formation it produces.

### Retinal structure

The retina is a multi-layered structure, bounded by the choroid and the vitreous. With the advent of electron microscopes, it is generally accepted that there are eight identifiable layers in the retina (Figure 1).

There are three areas where this basic structure differs, undergoing modification specific to the task that is undertaken. These comprise the central retina, the ora serrata and the optic nerve head. For those involved in low vision work, it is

the central retina that is of greatest significance.

### The central retina

The central retina is the area surrounding the central axis of the eye, here the retina is organised to provide the highest resolution of acuity. The central retina comprises three structures, the macula, the fovea and the foveola. At the macula the neural retina thickens and then thins to form the fovea, at the centre of this pit displacement of the retinal layers occurs to form a further depression, the foveola (Figure 2).

Considering the diagrams of the fovea (Figures 3 & 4) it is evident that the displacement of the retinal fibres results in a thickening of the retina at the parafoveal region and a thinning of the central area. This means that the photoreceptors in this central region have more direct access to light. This modification of the retinal structure means that there are only the receptor nuclei and their inner fibres between the vitreous and the receptor layer. This results in an area of increased visual sensitivity. The increase in acuity is such that it is believed there is a one-to-one ratio between the cones, midget bipolar cells and midget ganglion cells. The absence of capillaries makes this area avascular.

### Macular pathology

Adverse pathology of the macular region usually results from a defect in the pigment epithelial layer, which, in turn, affects the underlying receptor layer. The pigment epithelial layer (Figure 5) is a single layer of cuboidal cells with distinct functions:

- to absorb stray light
- to provide a pathway for metabolites to the receptor layer via the choriocapillaris
- to remove debris shed by the receptor layer
- to provide mechanical stability to the tips of the rods and cones
- to store and transport Vitamin A to the receptor layer, which is essential for the regeneration of the photosensitive pigment
- maintenance of the integrity of the sub-retinal space by forming part of the blood-retinal barrier and pumping away ions and water

The retinal pigment epithelial cells at the fovea are taller, thinner and contain more melanosomes than anywhere else in the fundus. The adhesion between these cells and the sensory retina is correspondingly weaker than that between the epithelial cells and Bruch's membrane.

### The photoreceptor layer

As with the functional specialisation of the retina, so there is a significant distribution of the receptors across the

retina (Figure 6). The area of highest cone density is the macula; this contains some 146,000 cones per square millimetre, reducing to approximately 10,000 per square millimetre at 10 degrees from the centre.

Rod density, on the other hand, peaks at about 20 degrees from the fovea, falling back to between 30,000 and 80,000 per square millimetre at the extreme temporal and nasal retina. Whilst estimates vary, it is believed there are some 130 million rods and 7 million cones in the human retina.

As with all human tissue, the receptor layer continually regenerates. The discarded rod and cone discs are removed through the pigment epithelium, which breaks them down and recycles them through Bruch's membrane into the choroidal circulation. The process of age affects the epithelial layer resulting in a decrease in the number of pigment cells, thus reducing its efficiency.

The inability of the pigment epithelial layer to remove this debris, results in an accumulation of material at Bruch's membrane. As well as preventing the disposal of debris, the metabolites, which provide the nutriment for the rods and cones, are unable to pass from the Choroidal blood supply to the retina. This, eventually, results in necrosis of the receptor layer.

It is this process which results in the most common ocular pathology seen by the low vision practitioner, that of age related macular degeneration (ARMD).

### Age related macular degeneration

ARMD is the most common cause of blind and partially sighted registration in the Western world. Over thirty per cent of the population over the age of seventy-five exhibit signs of age related problems at the macula.

J.Kanski in *Clinical ophthalmology* gives a definition of the disease: "... the presence of some degree of visual loss in association with Drusen and geographic atrophy of the retinal pigment epithelium, or changes related to sub retinal neovascularization in individuals over the age of 50".

The earliest symptom of the disease is the inability to distinguish fine detail and distortion of straight lines. Measurement of this distortion is undertaken using an Amsler Grid, which evaluates ten percent of the visual field surrounding fixation. The grid comprises 5mm squares, which when viewed at a distance of a third of a metre, subtend an angle of one degree at the fovea. This is the smallest resolution possible in the human eye.

With age related maculopathy the condition often becomes bilateral, although the onset in the second eye is

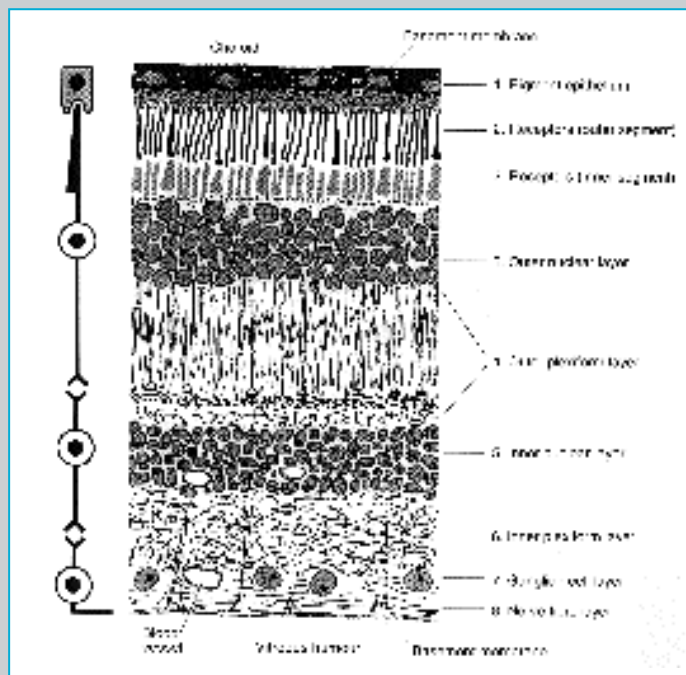


Figure 1: The layers of the retina.

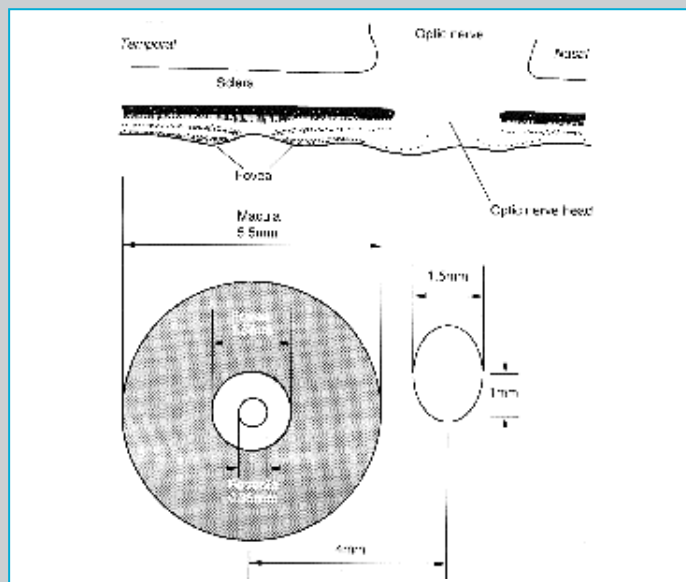


Figure 2: The central retina.

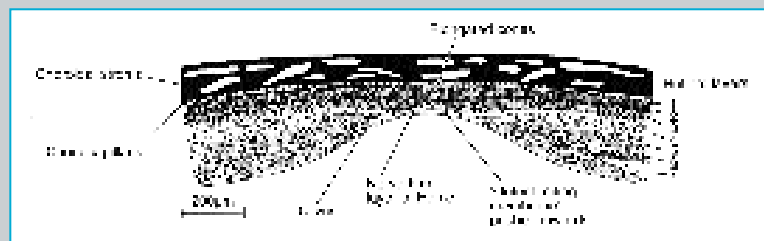


Figure 3: Section through the fovea.



Figure 4: Arrangement of neurones in foveal region.

often delayed. It is perhaps surprising that some patients fail to notice the initial onset and will only present once the second eye begins to fail. This may be due to strong ocular dominance or sometimes to an unwillingness to accept the likelihood of visual problems. The psychological acceptance of visual problems is important and will be addressed in a later article.

Additional symptoms of the disease include metamorphopsia, micropsia and macropsia.

Whilst there may be individual variance, there is a common development pattern for the disease spanning a five-year period. Initial distortion of the central vision in one eye worsens over a two-year period, and is followed by the onset of distortion in the fellow eye. Fine print gradually becomes impossible, although the ability to discern large print may well remain.

The resulting disparity of retinal image size presents problems to the patient in terms of interference, loss of binocular vision and stereopsis and can also make the use of binocular aids unviable.

It is estimated that between 10 and 15 per cent of patients with macular degeneration in one eye, will experience the loss of macula function in the fellow eye within two years. Additionally, some 60 to 70 per cent will qualify for registration as blind within five years of onset.

## Types of macular Degeneration

There are two distinct types of age related maculopathy, Exudative (wet) and Non-Exudative (dry). Less than 10 percent of those affected have exudative maculopathy, but of these 88 per cent are likely to be registered blind. It is a more serious condition, with a poor visual prognosis. Low vision practitioners may observe that often a drop in acuity from 6/12 to counting fingers can occur within a matter of weeks. For those involved, and their relatives, it is a very traumatic experience and needs to be handled sensitively by those professionals involved in the patient's management.

The earliest sign of the likely predisposition towards age related macular degeneration is the presence of asymptomatic yellow deposits beneath the retinal pigment epithelium **Photograph 1**. It is possible to identify five types of drusen through ophthalmoscopy. These are hard, soft, mixed, basal laminar and calcified.

The presence of hard drusen indicates the likelihood of the development of visual loss, whilst soft drusen, which tends to coalesce over a period, is associated with a dysfunction of the retinal pigment epithelium and is indicative of an increased risk of exudative maculopathy.

The two types of age-related maculopathy present a different fundus

picture and visual prognosis. Non-Exudative maculopathy has a slow progression rate. Here there is no leakage of fluid into the sub-retinal space and so a diminished risk of retinal detachment. The degeneration is due to the gradual atrophy of the pigment epithelium and the resultant necrosis of the receptor layer **Photographs 2 & 3**. This produces a dense central scotoma and residual vision of between 3/60 and 6/60. The peripheral field is retained and can be utilised for mobility and in some cases for near vision tasks. There is no active treatment for this type of maculopathy.

Exudative maculopathy is a greater risk to sight because there is often a leakage of fluid into the sub-retinal space, **Photograph 4** this increases the risk of retinal detachment. In untreated exudative maculopathy the loss of central vision is often very rapid. Thereafter the patient will develop a disciform scar and choroidal neovascularization may occur.

## Fluorescein angiography

In exudative maculopathy it is usual to use a fluorescein angiogram to identify the position and extent of the leakage. Here the eye is dilated and 5ml of 10 per cent fluorescein is injected intravenously. Fluorescein enters the eye through the ophthalmic artery, passes into the choroidal circulation via the posterior ciliary arteries and via the retinal artery into the retinal circulation. Fundus photographs are then taken at one-second intervals from between one and twenty five seconds post injection, then ten minutes and twenty-five minutes later.

Fluorescein is used because 70-85 per cent of its molecules bind to the serum proteins. The remainder is known as free fluorescein. The major choroidal vessels are impermeable to both bound and free fluorescein. The choriocapillary walls are thin, containing fenestrations through which the free fluorescein molecules can pass into the extravascular space and across Bruch's membrane.

The outer blood-retinal layer comprises tight junction complexes of zonule adherens and zonule ocludens between adjacent epithelial cells, preventing the passage of both bound and free fluorescein. Thus any permeability of this inner barrier must be due to changes in intravascular pressure or changes in the capillary walls.

In a normal angiogram the blood supply will show clearly, but there will be no other areas of fluorescence. An abnormal angiogram **Photographs 5 & 6** will have areas of fluorescence caused by any of the following:

- a** Retinal pigment epithelial window defect, due to atrophy of the underlying cells
- b** Pooling of dye under a detachment of the epithelium or sub-retinal space,

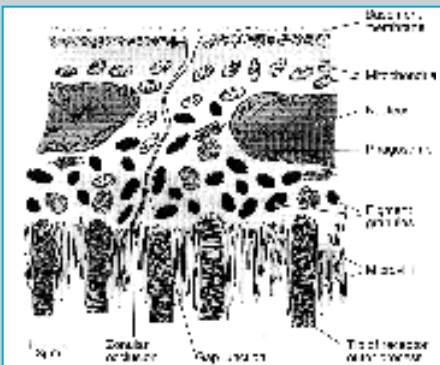
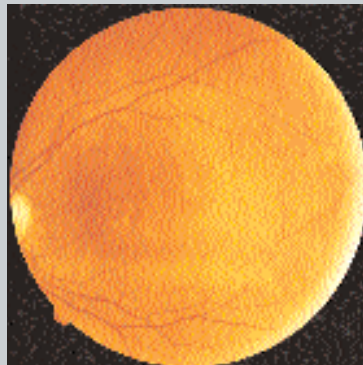


Figure 5: The retinal pigment epithelium.



Photograph 1: Drusen.

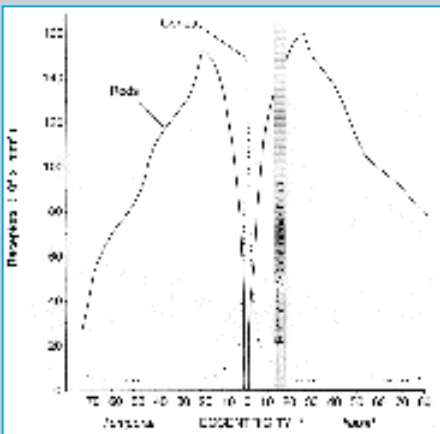
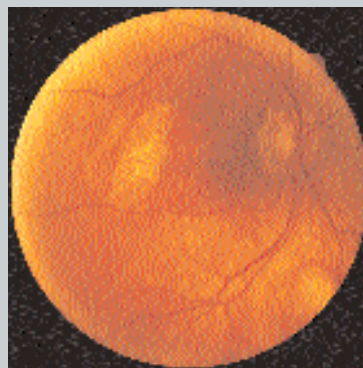
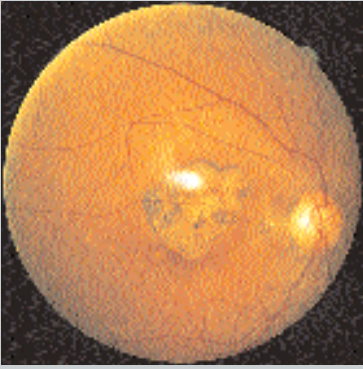


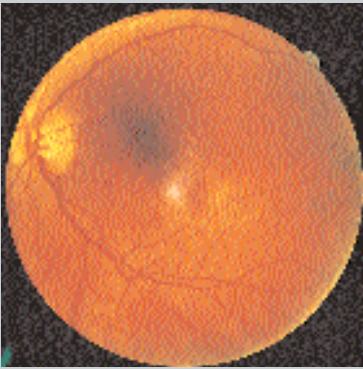
Figure 6: Distribution of rods and cones across the retina.



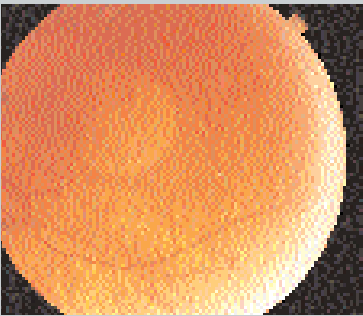
Photograph 2: Non-exudative AMD.



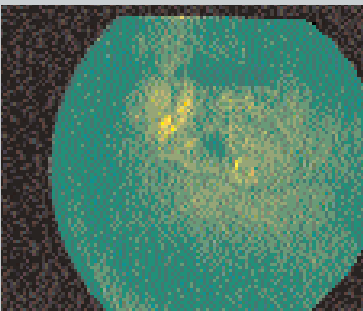
Photograph 3: Atrophy of the retinal pigment epithelium.



Photograph 4: Leakage of fluid in the sub-retinal space.



Photograph 5: Detachment of retinal pigment epithelium.



Photograph 6: Abnormal angiogram.

caused by the breakdown of the outer blood-retinal barrier (Photographs 7).

**c** Leakage into the sensory retina due to the collapse of the inner blood-retinal layer.

**d** Staining of tissue due to prolonged retention of fluorescein.

Once the cause of the leakage is established the ophthalmologist must decide if treatment is possible. To date the only options available are radiation therapy, removal of the foveal membrane, photodynamic therapy and photocoagulation. None of these represent a cure, but at best will slow the rate of progression.

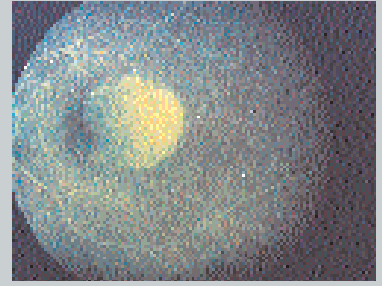
It is clear that there are considerable effects on the visual acuity of the patient with age-related maculopathy, which may include all or some of the following:

- 1 Central field loss
- 2 Scotoma or central blurring where there is an epithelial detachment
- 3 Loss of colour vision
- 4 Distortion of lines and objects
- 5 Poor near visual acuity compared with distance acuity
- 6 Visual hallucination may occur in advanced stages

In the subsequent articles we will look at the current research and its implications and explore ways in which the patients may be helped through low vision assessment and the supply of suitable aids.

### Acknowledgements

- Figures 1-6 reproduced by kind permission from *Ocular anatomy and histology* by DM Pipe and LJ Rapley.
- Photographs courtesy of G Robinson FRCS, Consultant Ophthalmologist, Ysbyty Gwynedd, Bangor, and G Roberts BSc(Hons) FBOA, Ophthalmic Optician, Llandudno.



Photograph 7: Pooling of fluorescein dye under a detachment.

### References

- Kanski J, *Clinical Ophthalmology*, Butterworth and Heinemann.
- Farrall H, *Optometric management of visual handicap*, Blackwell
- Pipe DM & Rapley LJ, *Ocular anatomy and histology*, ABDO.

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### Glossary

**Drusen:** asymptomatic deposits between the basement membrane of the retinal pigment epithelium and the inner collagenous layer of Bruch's membrane.

**Metemorphopsia:** distortion of the perceived image.

**Micropsia:** minification of the perceived image.

**Macropsia:** magnification of the perceived image.

**Zonule adherens:** areas where the membranes of cells on either side of a cell junction are thickened, and an adhesive material is found between.

**Zonule occludens:** areas where the cell membranes are in contact, limiting the passage of materials between the cells.

**Photodynamic therapy:** systemic administration of a photosensitising drug, such as Visudyne, followed by light application to the affected tissue, to incite a localised photochemical reaction

**Photocoagulation:** the stimulation of a reparative retinochoroidal reaction to seal retinal breaks, using laser or Xenon arc sources.

**Hemianopic field loss:** the loss of half of the visual field.