### AMD phenotype and distinguishing clinical features

<table>
<thead>
<tr>
<th>Normal aging changes</th>
<th>Optical coherence tomography (OCT)</th>
<th>Fundus autofluorescence (FAF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Drupelets only (&lt;63µm diameter, up to approximately half the width of a large vein at the disc margin)</td>
<td>• Drupelets appear as just detectable discrete irregularities or elevations of the RPE with variable internal reflectivity</td>
<td>• Drupelets may colocalise with punctate spots of normal, hyper- or hypo-fluorescence</td>
</tr>
<tr>
<td>• Should not show any characteristics of early, intermediate or late AMD</td>
<td>• Some drupelets may be too small for OCT to resolve</td>
<td>• FAF may also appear normal with the central macula showing diffuse, homogeneous autofluorescence and a gradual reduction in signal approaching the fovea</td>
</tr>
</tbody>
</table>

### Early AMD

| Medium drusen only (63 to 125µm diameter) | Medium drusen typically appear as discrete elevations of the RPE with variable internal reflectivity (similar to drupelets) | Similar to drupelets, medium drusen may display a variable normal, hyper- or hypo-fluorescence pattern |
| Should not have any of the characteristics of intermediate or late AMD | | • A range of patterns may be observed in early and intermediate AMD including: normal, minimal change, focal increased, patchy, linear, lacelike, reticular, speckled, focal confluent, focal plaque-like or scattered |
| May present with a different stage of AMD in the fellow eye | | |

### Intermediate AMD

| Large drusen (>125µm in diameter) and/or pigmentary abnormalities (hyper- or hypo-pigmentary changes associated with at least medium sized drusen) | Large drusen may appear as dome shaped, occasionally confluent, elevations of the RPE, with visible underlying BM | • May reveal any of the patterns described under early AMD |
| No characteristics of late AMD | • May be associated with: overlying disruption of the EZ and ELM, subsidence of INL or OPL, and/or inhomogeneous choroidal hypertransmission due to focal interruptions of RPE (incomplete RPE and outer retinal atrophy) | • Predominantly reveals spots or punctate hyper-fluorescence |
| | • Hyper-pigmentary abnormalities may be seen as discrete hyper-reflective foci (in the ONL or attached to drusen) with posterior shadowing | • Less commonly, spots of hypo-fluorescence and lines of hyper-fluorescence may also be observed |
| | | • Patchy, linear and reticular FAF patterns have been associated with a higher risk of conversion to neovascular AMD |

### Late AMD (Geographic atrophy or Complete RPE and Outer retinal atrophy)

| Any sharply delineated round or oval hypopigmented areas at least 250µm in diameter that feature apparent absence of the RPE and increased visibility of choroidal vessels | Absence of RPE causes sharply demarcated areas of homogenous choroidal hypertransmission >250µm | Single or multiple areas of well-demarcated marked hypo-fluorescence |
| Areas may coalesce to form a ring type configuration, eventually involving the fovea centralis | Associated outer retinal atrophy is seen as thinning or loss of the ONL, ELM and EZ which may extend or taper beyond the margins of the GA | • Foveal sparing is characterised by irregular hypo-fluorescence at the residual foveal island (such as in this example) or a symmetrical and gradual reduction in FAF approaching the fovea |
| May be preceded by calcification of large drusen and/or drusen regression | Also displays signs of other AMD stages | • The “diffuse trickling” pattern in this image is associated with a significantly higher rate of progression |
| Also displays signs of other AMD stages | | • FAF may enable better detection of discrete/small areas of GA |

**Abbreviations:** Bruch’s membrane (BM), Ellipsoid zone (EZ), External limiting membrane (ELM), Inner nuclear layer (INL), Outer plexiform layer (OPL), Outer nuclear layer (ONL)
### AMD phenotype and distinguishing clinical features

#### Late AMD (Neovascular AMD)
- May be characterised by any of: RPE detachment(s), neurosensoryst retinal detachment, intraretinal, subretinal or sub-RPE scar/ glial tissue or fibrin like deposits, subretinal haemorrhages and/or hard exudates
- Neovascular lesions may appear subtle, green-grey or pink-yellow often complicated by the secondary signs above
- End-stage: Regression of the vascular component and an increase in the fibrous component, and may appear as a disciform scar

#### Reticular macular disease
- Indistinct, typically interlacing, yellow-white, round or oval lesions ranging from 125 - 250µm in diameter
- Visibility enhanced with blue or infrared light
- Can present in conjunction with other AMD features

#### Cuticular drusen
- Numerous, densely packed, relatively uniform, small drusen, better seen using FA, described as a “starry-sky” pattern
- 50 to 75µm in diameter

#### Familial dominant drusen/Doyne’s honeycomb dystrophy/Malattia leventinese
- Numerous drusen that extend beyond the vascular arcades and often nasal to the optic disc
- Age of presentation is typically between 20-30 years (younger than of typical AMD)
- Bilateral, radially distributed and relatively symmetrical

### Optical coherence tomography (OCT)

- PEDs present as broad elevations of the RPE band anterior to BM
- Fibrovascular PEDs show irregular internal reflectivity with/without serous exudation
- Serous PEDs are well demarcated, dome shaped and smooth with internal homogeneous hyporeflectivity
- Haemorrhagic PEDs appear as elevations of the RPE with no reflectivity within or under the PED
- Sub-RPE, subretinal or intra-retinal fluid may be present and indicative of AMD related choroidal neovascularisation
- End stage: Well-demarcated, highly hyper-reflective lesions associated with loss and dysplasia of the overlying retinal layers

### Fundus autofluorescence (FAF)

- FAF changes corresponding with areas of choroidal neovascularisation may be characterised by its inherent features as follows:
  - Subretinal fluid corresponds with increased FAF in approximately 56.5% of cases
  - Haemorrhages, exudate and fibrovascular membranes are likely to cause hypo-autofluorescence patterns
  - Can also present with normal or near normal FAF imaging results
  - End stage: Disciform scarring consistently demonstrates uneven hypo-autofluorescence of the lesion, surrounded by marked hyper-autofluorescence

- Reticular pseudodrusen may colocalise with subretinal drusenoid deposits which appear as deposits above the RPE

- Appearance as low contrast hypo-fluorescent, circular, networked deposits
- Individual lesions may also have a “target-like” appearance (iso-fluorescent core and surrounding hypo-fluorescent halo)

- Blunted triangular appearance with a saw tooth pattern

- May reveal numerous hypo-fluorescent “dots”

- Drusen characteristics are similar to those seen in AMD
- Larger, round drusen are typified by confluence and more diffuse deposition between the RPE and BM

- Reveals marked hyper-fluorescence of large drusen
- Smaller radially distributed drusen appear more faint