Age-related Macular Degeneration

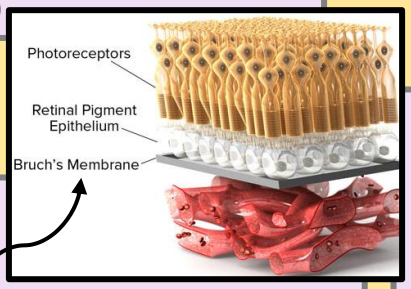
Epidemiology

Main cause of irreversible blindness in developed countries

Multi-hit threshold model- genetics + environment

- Amyloid-β, high cholesterol & complement proteins involved

Risk factors: age (>55), family history, smoking, previous cataracts surgery, western diet(?)



Pathophysiology

Inflammation + oxidative stress

Deposits on Bruch's membrane→ altered permeability→ reduced nutrients to the retinal pigment epithelium (RPE) → ***metabolic stress***

Vascular endothelial growth factor- pro-angiogenic

Ischaemia of RPE→***VEGF*** production→ neovascularisation

Mitochondria produce reactive oxygen species (ROS), healthy RPE can deal with these efficiently

In damaged RPE:

- Impaired phagocytosis
- Inhibited waste clearance
- Lipofuscin and ROS accumulation damages cells
- ***Chronic inflammation*** and ***pro angiogenic*** state

Distinct clinical stages

Early AMD: deposits under the retina and RPE (***drusen***) and macular ***pigmentary changes***

Late AMD: either ***dry***/ geographic (80%) or ***wet***/ neovascular

- Part of the same continuum or distinct pathways?

Wet AMD: severe haemorrhage, Choroidal Neovascularisation ***(CNV)***

- New leaky capillaries in choroid plexus. Fluid accumulates under/ within the retina causing damage

Dry AMD: RPE/ photoreceptor atrophy

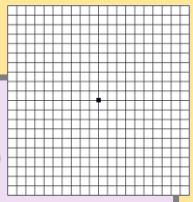
Symptoms

Early stages: no or only mild visual complaints

Late stage: gradual progressive loss of vision in one or both eyes

Wet AMD: Sudden blurring/ distortion of vision

Investigations



Amsler grid (also used to monitor)

Dilated fundus examination

If CNV suspected: Optical Coherence Tomography (***OCT***)/ Fluorescein Angiography

Management

Reduce progression rate + treat CNV if present

Refer to ***consultant ophthalmologist***

Early/ intermediate: risk factor modification

Advanced dry AMD: no effective treatment

Advanced wet AMD: treat CNV with monthly ***anti-VEGF injections***

- Ranibizumab, Bevacizumab, Aflibercept
- Maturation of leaky capillaries and reduction of fluid accumulation. Can get photoreceptor reattachment
- Expensive, doesn't work for everyone

Amyloid-beta (Ab) in AMD

Possible trigger, associated with progression

Retina/RPE is a major site of Ab deposition

Retinal ganglion cells and RPE express APP and have the cellular machinery to generate Ab

Ab exposure increases with age- induces structural abnormalities