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VISUALISING the diseased macula

This is here you group them into

**EXUDATIVE or NON-EXUDATIVE ARMD.**

(wetness and dryness; basically the dry-type is going to be 80-90% of your patients)

**SLIT LAMP EXAMINATION:**

You're mainly looking for corneal issues;

Eg.: Is there anything cataractiform? Is the anterior chamber healthy? Is there a corneal ulcer present, which would nicely explain a history of acute unilateral blurring?

**ARCUS SENILIS:** peripheral corneal opacity, caused by lipid deposition; mainly in the elderly – NORMAL UNLESS UNILATERAL…! they won't go away, EVER – not even after cholesterol falls again

**FUNDOSCOPY + FUNDUS PHOTOGRAPHY**

Reproduced without permission from Stone, Sheffield and Hageman's "Molecular Genetics of Age-related Macular Degeneration" in Human Molecular Genetics, 2001 Vol. 10 No. 20 2285-2292

![Images of fundus photographs](image)

**Figure 1.** Range of ophthalmoscopic phenotypes consistent with the diagnosis of AMD. (A) Normal fundus (for comparison); (B) classic geographic atrophy; (C) drusen intermixed with small pigment epithelial detachments; (D) large and small drusen confined to the macula; (E) flat, calcified drusen surrounding patches of geographic atrophy; (F) geographic atrophy; (G) large and small drusen throughout the posterior pole; (H) a wreath of large and small drusen surrounding a circular area of geographic atrophy; (I) retinal hemorrhage secondary to a choroidal neovascular membrane; (J) numerous tiny drusen that spare the macula; (K) drusen limited to the temporal aspect of the macula; (L) RPE hyperpigmentation and subretinal fibrosis secondary to a choroidal neovascular membrane.

**Bottom Line:** DRUSEN. ATROPHY. HAEMORRHAGE. Rule out the DIFFERENTIALS.

**OPTIC NEURITIS**

Bulgy swollen disk with indistinct margins

**OPTIC NERVE ATROPHY**

Flat pale disk with sharp margins

**MACULA LOOKS NORMAL?**

...But... there's still a visual defect! Suspect something left-field, like...

**Diffuse Oedema** - a definitive diagnosis requires stereoscopic examination by an ophthalmologist, to look for subtle papilloedema

**Retinal Ischaemia** - diagnosed by fluorescein angiographic demonstration of capillary non-perfusion.

**Retinal ischaemia:**

Cannot be picked up on plain funduscopy - will need to do specialised tests. ALSO, non-dramatic changes which may cause blurriness but which are NOT MACULAR DEGENERATION include:

- Diabetic retinopathy
- Hypertensive Retinopathy
- Retinal vein/artery occlusion
- Internal carotid stenosis
- Sickle-cell retinopathy
HUMPHREY FIELD TEST

Automated visual fields test: maps the field using

**THIS IS USEFUL to monitor progression, but it is by no means diagnostic.** Still, better than the manual Amsler Grid. (the Humphrey visual field tester is an expensive ophthalmologist’s toy)

Is it Wet or Dry? Exudative or Non-Exudative? In summary….

**Classification of Macular Degeneration:**

**EARLY:** Non-exudative, just drusen and small areas of atrophy- largely asymptomatic
May complain of worsening night vision, difficulty reading, recognising faces

**LATE:** Geographic Atrophy (big confluent islands of atrophy)... AND / OR:
Neovascularisation (exudative form of ARMD) and diskiform scarring
Retinal detachment, etc –THUS:
Symptomatic, acute visual loss maybe with chronic blurring and metamorphopsia.

**IS NEOVASCULARISATION taking place ??**

- Metamorphopsia
- RPE elevation on fundoscopy
- Subretinal haemorrhage
- Exudate in the vitreous
- Disk-shaped scars: These imply that neovascularisation has occurred and left an atrophic area

You cant actually see the choroidal neovascular vessels, but you can infer their presence from the bulges they create by protruding through Bruch’s membrane- this being RPE elevation, which causes metamorphopsia (as the warped retina now receives light at a different angle- and also because the lifted RPE becomes atrophic and eventually graduates to scotoma)

**Any suspicion of neovascularisation is an indication for angiography!**

**FLUORESCEIN ANGIOGRAPHY**

Fluorescein sodium, 500mg injection and subsequent retinoscopy under violet light
- synthesized from the petroleum derivatives resorcinol and phthalic anhydride
- usually well tolerated, bar the occasional catastrophic anaphylaxis

The injection is given and a rapid sequence of fluorescence photographs is taken, to view the patterns of blood flow across the retina.

F. Angiography is the investigation of choice for most conditions related to the vascular supply of the retina. Diabetic retinopathy, hypertensive retinopathy, and any weird vascular events involving the retina.

Yes, it’s the same sort of fluorescein you drip into somebody’s eye to look for corneal ulcers with a slit lamp. Except the IV contrast fluorescein is a sodium salt.


**BIOCHEMICAL TESTING:** purely for completeness

**BSL? Hba1c?** Are they diabetic? A bsl of 40 or so may nicely explain an episode of visual blurring
Consider the Zebras, do an ESR to convince yourself that it cant be Giant Cell Arteritis. Do an ECG to clear your conscience of atrial fibrillation.

**BOTTOM LINE:** this is how we investigate age-related macular degeneration

- Rule out the cranial nerve causes with history + exam
- Rule out corneal causes with fundoscopy
- Gather suspicion of Choroidal Neovascularisation with fundoscopy
- Perform fluorescein angiography to determine location / extent of neovascular change
- Perform automated visual field test for purposes of monitoring progression
- Fundoscopic photography for the same reason.
MANAGEMENT OPTIONS

EARLY and LATE DRY ARMD:
- **PREVENTATIVE MEASURES**: seeing as there is no real serious treatment option...
  - Definitely stop smoking
  - Maybe start eating vitamin E and Zinc
  - Especially if you have a family history
- **Educate the patient**: makes you feel like you're doing something
- **COPING STRATEGIES**
  - **Delayed darkness Adaptation?** Not to worry; just wear dark sunglasses - thereby reducing the necessary range of the adjustment which must be made
  - **Scotoma preventing you from reading?** Low vision specialists often prescribe magnifiers with a line marker so that patients do not lose their place while reading.
  - **Tripped over the cat and fractured your NOF?** Consider altering the level of lighting, pet access and the pattern of floor-situated ornaments (OT's job)
- **FOLLOW-UP**: you want to know when the dry ARMD turns wet. **THUS:**
  - Regular Fundus Photography and Humphrey Visual field Testing

LATE EXUDATIVE ARMD:
- **Laser Photocoagulation**: trial-proven to help - even if you're hypertensive (and thus at risk of bleeding into your vitreous humor out of the charred stump of a retinal arteriole.)
  But it requires a well-defined lesion to target, and it can't be obscured by haemorrhage or anything. Need a clear shot.
  - **Angiography** customarily is performed within 72 hours of laser photocoagulation, since CNVM morphology and resulting treatment parameters can evolve rapidly
  - **Retrobulbar anesthesia** is used to immobilize the eye during treatment
  Then, create a uniform white treatment lesion (a burnt patch)
  - Compare before and after angiograms and fundus photographs.
  - Ask the patient to return in 2-3wks for followup (vis. acuity etc)
  - Assess several times within the first 3 months after treatment and then at 3-4 month intervals

  Laser treatment itself irreversibly damages the RPE and retina, causing an absolute scotoma, which correlates with the site of the laser coagulation scar.

- **Things Not Yet Blessed by Cochrane**:
  - **STATINS** are rumoured to prevent and delay the progression of ARMD - no trials so far
  - **All manner of laser therapies** which aim at the destruction of feeding vessels to the CNVM
    - **Photodynamic Therapy** which involves giving the patient a sensitising agent to enhance the damage done to the CNVM, or to make that damage more selective (eg. a photosensitising agent which selectively binds to new blood vessels)
    - **Antiangiogenic agents** to halt or prevent the formation of new blood vessels in the retina
    - **Radiation Therapy**: Cumulative doses (multiple fractions) of up to 25 Gy cause no damage to the retina or optic nerve, and the susceptibility of retinal vasculature endothelial cells has been confirmed.
    - **Surgical Macular Translocation**: A peripheral retinotomy/retinal detachment/retinal rotation around the optic nerve, and retinal reattachment in order to rotate the foveal region away from the diseased underlying choroid and RPE is carried out. !! GREAT RISK !!

GOALS OF MANAGEMENT are to minimise visual loss and disability in order to maintain independence.
GLAUCOMA: elevation of intraocular pressure, → damage to the optic nerve
Closed angle vs. open angle: anatomical classification.
OPEN ANGLE GLAUCOMA is a chronic progressive thing without acute symptoms.

CLOSED ANGLE GLAUCOMA is an acute emergency: the outflow of aqueous humor is blocked!
PATHOPHYSIOLOGICAL MECHANISM OF AGE-RELATED MACULAR DEGENERATION
A glib synthesis of seven or so actual scholarly mechanisms, found in Human Molecular Genetics, 2001 pp.2285

MODIFIABLE
Smoking ~29%
Diet, cholesterol, hypertension,
Lack of vitamins... 21%

NON-MODIFIABLE
GENETICS ~50%

To rant a little about the retina...
The RPE = - ingests used-up outer tips of the rod and cone cells
and provides them with essential nutrients
Bruch’s membrane = a noncellular structure (made mostly of
collagen) that separates the RPE from the choroidal circulation
below.
The chorio capillaris provides the blood supply to the rods,
cones, and RPE cells.

THE EFFECT OF THESE RISK FACTORS
Genetics: may have something to do with superoxide
dismutase, apolipoprotein genes, a receptor for something
that processes outer rod segments in the retina, etc etc.
Oxidative damage: retina is highly oxygenated and
occupationally exposed to radiation. Thus, exposed to high levels
of free radicals. This produces the fatty autodioxidative product
lipofuscin which collects in the RPE, impairing its phagocytic
function. This causes a buildup of filth, like drusen for one. Bruch’s
membrane permeability to these by-products decreases with age,
which may be why age is a risk factor for ARMD. Among other
things, free radicals induce an increased sensitivity to VEGF in the
retina (that’s the vascular endothelial growth factor implicated in
CNV formation).

THE EARLIEST PATHOLOGICAL CHANGES
Basal Linear Deposits
Vesicular material;
Basal Laminar Deposits
membrano-granular material and
foi of wide spaced collagen,
sitting in the basal lamina above the
choroid vessels.
DRUSEN ALONE do not contribute much to visual loss;
…but CONFLUENT LARGE DRUSEN can cause a
deforimty of Bruch’s membrane, and
detachment of the pigment epithelium
Any RPE damage, such as arising from RPE
detachment or from degeneration of a CNV, will lead to
GEOGRAPHIC ATROPHY i.e areas
of retina which are useless and barren

VISUAL LOSS
- Delayed darkness adaption,
- scotoma,
- metamorphopsia
- colour and contrast disturbances

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