put together by Alex Yartsev: Sorry if i used your images or data and forgot to reference you. Tell me who you are.
aleksei.igorevich@gmail.com

Macular Degeneration

- Gradual - USUALLY Bilateral
- Painless - Central
visual loss in the elderly

FIRST SYMPTOM IS USUALLY A
DELAYED ADAPTATION TO DARKNESS
(when going from well-lit environment to dark)

History of Presenting Illness

AVAILABLE IN WET AND DRY FLAVOURS
(Dry is most common)

Centrally Blurred Vision:
which may be ACUTE
or INSIDIOUS in onset

ACUTE BLURRYNESS:
Be slightly worried; ? stroke, retinal haemorrhage, optic neuritis, corneal ulcer, amaurosis fugax etc?

INSIDIOUS ONSET OF BLURRYNESS:
Could it be glaucoma, cataract, a tumour, diabetic or hypertensive retinopathy, retinal detachment, or even a pituitary tumour? Must exclude the zebras.

- Difficulty READING, plus COLOUR and CONTRAST DISTURBANCES

DRUSEN are responsible

CENTRAL SCOTOMA
METAMORPHOPSIA:

SCOTOMAE:
Poorer prognosis; - Late Presentation;
an area of foveal atrophy has appeared somewhere

USUALLY BILATERAL:
- UNILATERAL loss
prompts closer investigation,
BUT eventually both eyes will succumb to the same fate.

WEIRDNESS OF DEALING WITH SCOTOMA:
Your brain will FILL ANY VISUAL DEFECT with its own idea of what should be going on there. The scotoma is an area filled with such an elaborate illusion. Straight lines such as pillars or fence posts become distorted, appearing wavy or bent. This plays havoc with face recognition and reading small text. **IT MAY CAUSE THE NICE OLD LADY TO APPEAR MORE DEMENTED THAN SHE IS**, when she mistakes you for her son / grocer / former lover, and completely misinterprets your carefully written medication instructions.

Make sure its not a manifestation of:

DIABETES VASCULITIS
HYPERTENSION MULTIPLE SCLEROSIS

Also Ask About RISK FACTORS:

AGE-RELATED macular degeneration cannot be diagnosed in individuals younger than age 50, according to the international classification system.

SMOKING also for stroke + carotid stenosis
HIGH CHOLESTEROL
FAMILY HISTORY of ARMD
MULTIPARITY
(?… connection with estrogen levels)

Controversial risk factors:
not supported by evidence:
- Iris colour
- Sunlight exposure
- Low Serum Zink levels

UNILATERAL CHANGE? Probably not behind the chiasm, but better be sure…

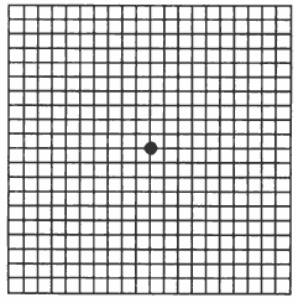
PHYSICAL EXAMINATION: need to rule out the zebras.

- **Start with everything behind the chiasm, and work forward:**
  - Is there a **systemic vasculitis** active? Does the patient have obvious lupus?
  - Is there **atrial fibrillation?** i.e could this sudden-onset blindness be the result of a tiny thromboembolism?
  - Is there a **carotid artery bruitt?** Could they be suffering a retinal TIA?
  - Is there a **PALPABLE TEMPORAL ARTERY?**

It should be hard to confuse temporal arteritis and ARMD;
BUT rarely temp. arteritis is PAINLESS.
USUALLY PRESENTS WITH THIS PICTURE:
- in the ELDERLY (~ 70 y.o)
- PAIN: localised temporal headache
- JAW CLAUDICATION
- PALPABLE T. ARTERY
- - MASSIVE ESR (over 50)
- SHOULDER STIFFNESS
- ANOREXIA, MALAISE

  - ARE THERE ANY **FOCAL NEURO SIGNS?**
    - Do the cranial nerve exam. ESPECIALLY –
      - Swinging lamp sign (optic neuritis);
      - Nerve palsies: are 3rd nerve muscles affected?
      - LOOK FOR XANTHOMAE of high cholesterol
      - Look for SCOTOMA
      - Look for CATARACT
      - Look for HORNERS
      - MEASURE THE INTRA-OCULAR PRESSURE
      - Do a SNELLEN CHART VISUAL ACUITY TEST for both eyes
      - Examine COLOUR DISCRIMINATION
      - Use the AMSLER GRID to test for metamorphopsia (some of the lines will become wavy or invisible)- indeed it has been shown that this sort of test is THE BEST THING for monitoring for progression of DRY into WET ARMD

? Marcus Gunn Pupil?? This demonstrates an afferent pupillary defect, but what does it actually teach you? Not much. In ARMD there will always be a slowly worsening mild afferent pupillary defect. A sudden onset Severe Afferent Pupillary Defect is probably NOT due to ARMD. Suddenness suggests retinal artery or vein thrombi, optic neuritis, or anything else that's not ARMD.



- This is all just a prelude to fundoscopy and slit-lamp examination - but you need to know where to look.

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)

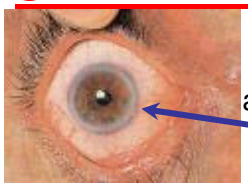
MACULA LOOKS NORMAL?

…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.

SLIT LAMP EXAMINATION:



Youre 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 wont 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***

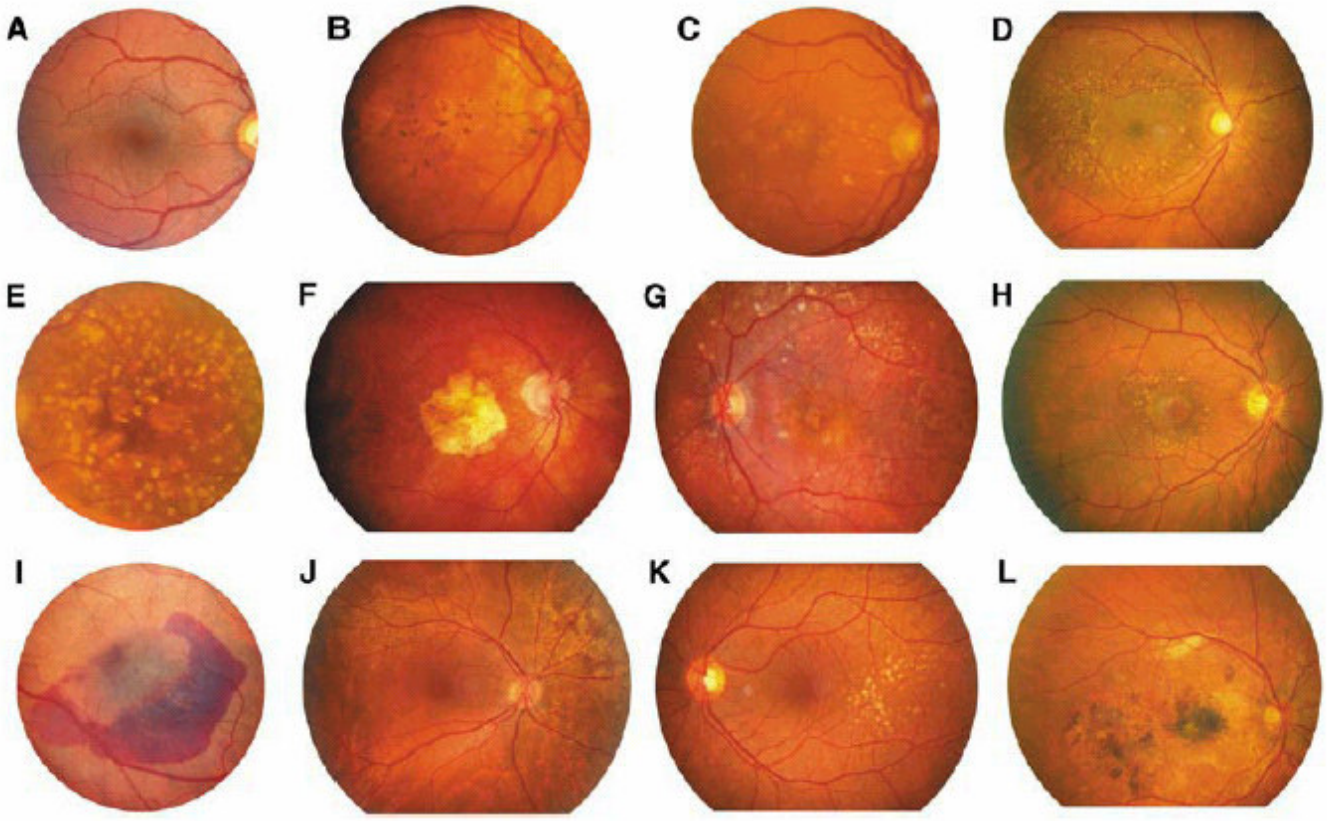
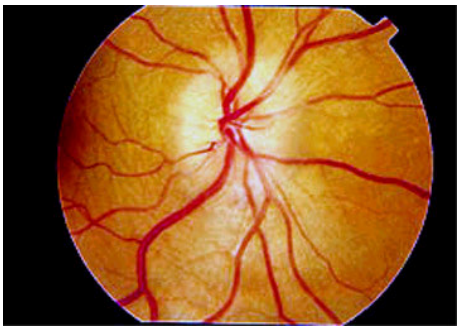


Figure 1. Range of ophthalmoscopic phenotypes consistent with the diagnosis of AMD. (**A**) Normal fundus (for comparison); (**B**) RPE hyperpigmentation; (**C**) drusen intermixed with small pigment epithelial detachments; (**D**) large and small drusen confined to the macula; (**E**) flat, calcified 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**) subretinal 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.

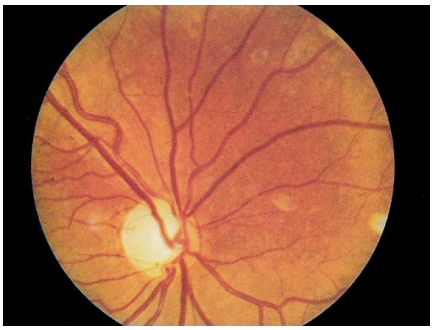
Bottom Line: DRUSEN. ATROPHY. HAEMORRHAGE. Rule out the DIFFERENTIALS.

OPTIC NEURITIS



Bulgy swollen disk with indistinct margins

OPTIC NERVE ATROPHY



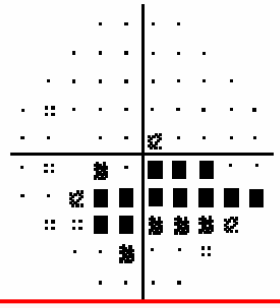
flat pale disk with sharp margins

Retinal ischaemia:

Cannot be picked up on plain fundoscopy- will need to do specialised tests.
ALSO, non-dramatic changes which may cause blurryness 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 ??

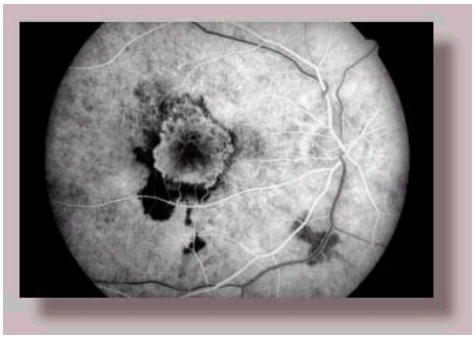
- Metamorphopsia
- RPE elevation on fundoscopy
- Subretinal haemorrhage
- Exudate in the vitreous
- **Disk-shaped scars:** These imply that neovascularisation has occurred and left an atrophic area

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.

More at http://www.opsweb.org/Op-Photo/Angio/FA/FA1.htm

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

GOALS OF MANAGEMENT are to minimise visual loss and disability in order to maintain independence.

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 youre 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)
  - **May need to contact the Roads and Traffic Authority** regarding your failing vision
- **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 youre 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 cant 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)

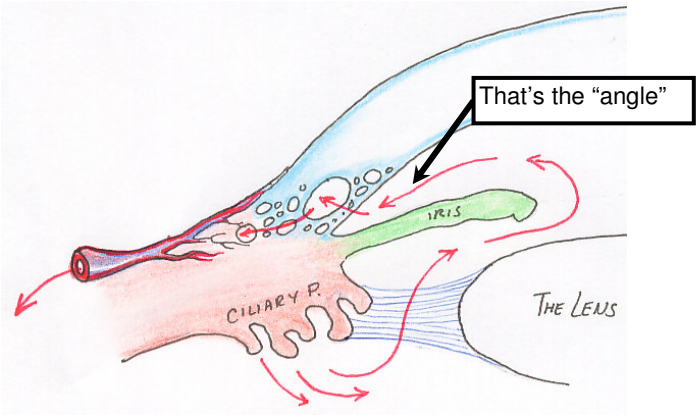
- **Antiangiogenic agents** to halt or prevent the formation of new blood vessels in the retina
- **Radiation Therapy:** Cumulative doses (multiple fractions) of up to 25 Gy cause no damage to the retina or optic nerve, and the susceptibility of retinal vasculature endothelial cells has been confirmed.
- **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 !!

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 H*uman Molecular Genetics, 2001 pp.2285

← RISK FACTORS →

MODIFIABLE

Smoking ~29%

Diet, cholesterol, hypertension, Lack of vitamins… 21%

NON-MODIFIABLE

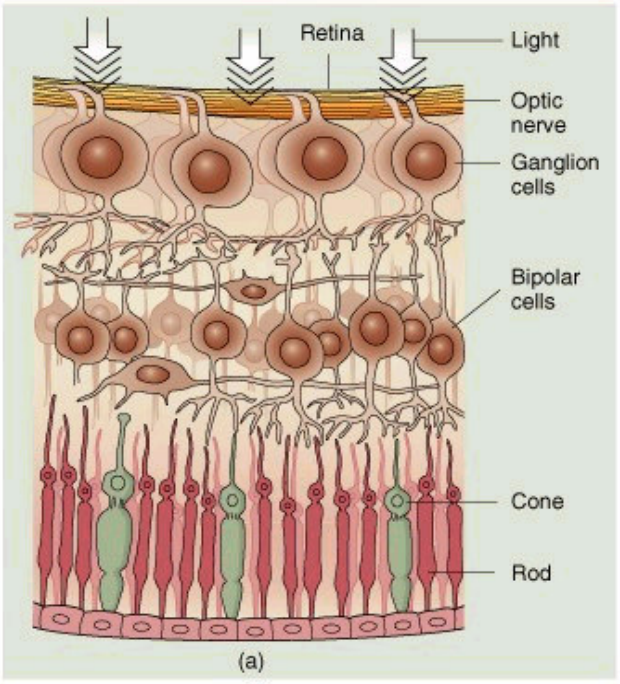
GENETICS ~50%

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.

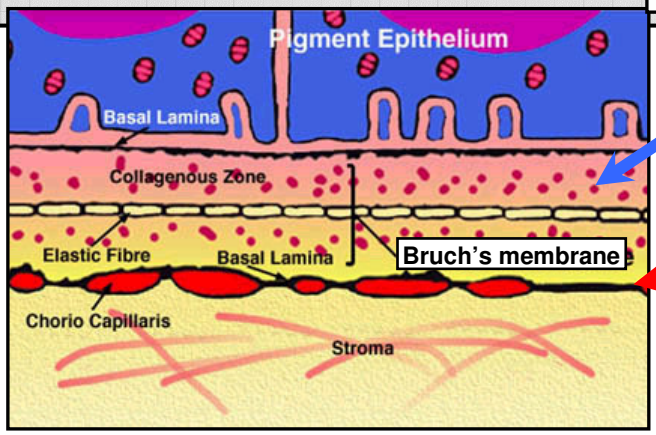
The chorio capillaris provides the blood supply to the rods, cones, and RPE cells.



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 autooxidative 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 agea, 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 foci of wide spaced collagen, sitting in the basal lamina above the choroid vessels.

Apolipoproteins B + E, immunoglobulins, amyloid P component, complement C5 and C5b-9 terminal complexes, fibrinogen, vitronectin.
These things have been found in drusen.

DRUSEN ALONE do not contribute much to visual loss; …but CONFLUENT LARGE DRUSEN can cause a deformity 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

CHOROIDAL NEOVASCULARISATION (CNV)

Arises as a capillary-like structures from many points of origin; penetrates through a defect in Bruch's membrane. These new vessels cause **HAEMORRHAGE, and leakage of drusen content.**

Recurrent leakage of blood, lipid and protein from the CNV will induce a "fibro-glial organisation reaction" via which a scar forms over the leaky inflamed CNV.

This is a **DISKIFORM SCAR** , naturally all the retina around and over the scar will degenerate and become useless

VISUAL LOSS

- Delayed darkness adapation,
- scotomae,
- metamorphopsia
- colour and contrast disturbances