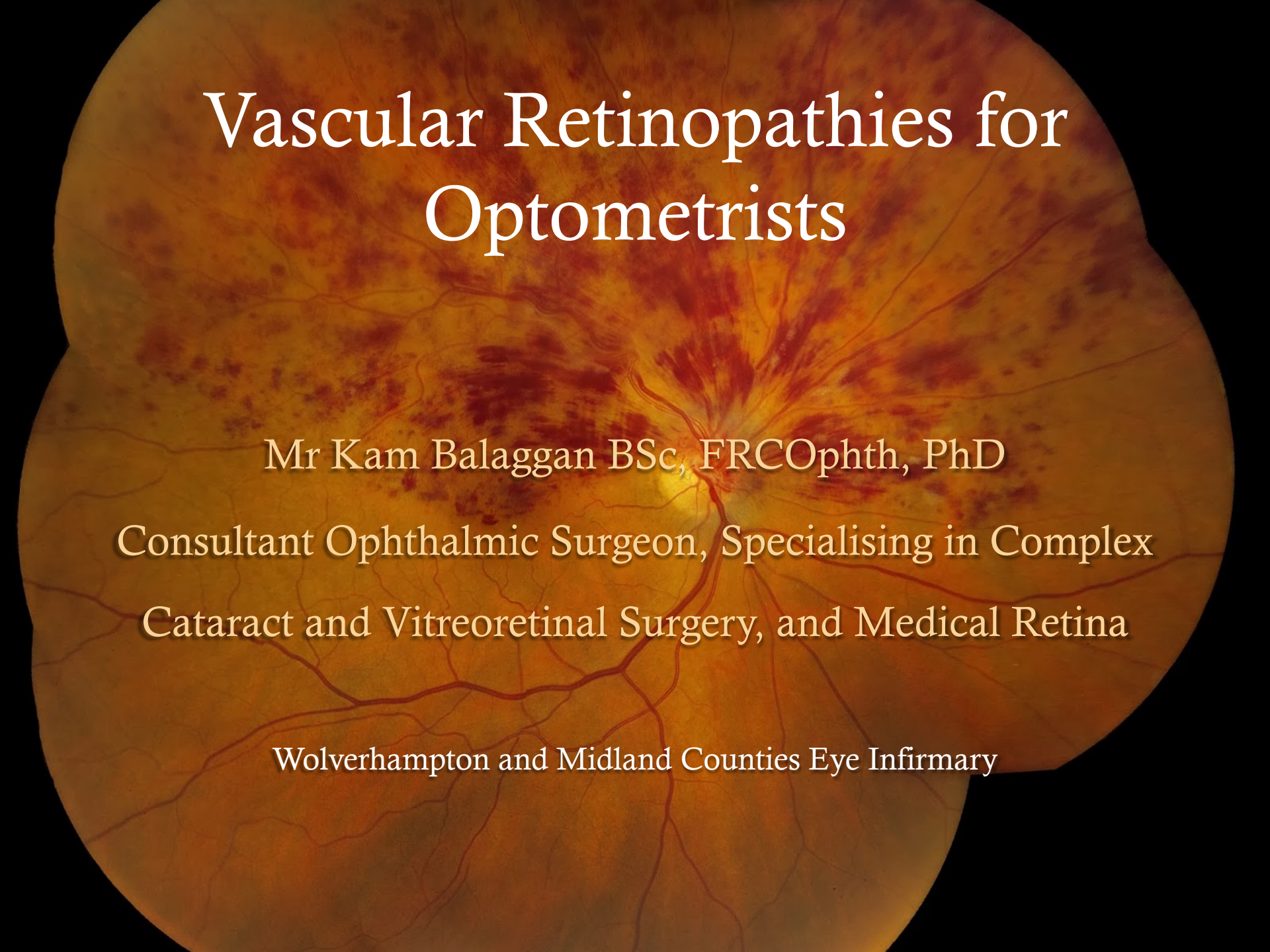
Vascular Retinopathies for Optometrists



Mr Kam Balaggan BSc, FRCOphth, PhD

Consultant Ophthalmic Surgeon, Specialising in Complex Cataract and Vitreoretinal Surgery, and Medical Retina

Wolverhampton and Midland Counties Eye Infirmary

Disclosures

- Non-relevant

Aims:

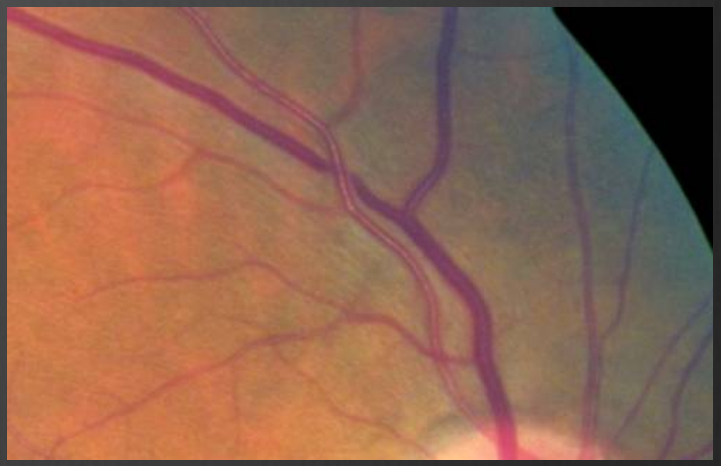
- Consolidate knowledge, and provide update on the diagnosis, and referral and medical management of:
  - Hypertensive retinopathy
  - Diabetic retinopathy
  - Diabetic macular oedema
  - Retinal vein occlusion
  - Retinal arterial occlusion
- Test session!

Hypertensive Retinopathy

- STATE OF PERSISTENT ELEVATED BLOOD PRESSURE ABOVE 140/90 mmHg.
- 5TH JOINT NATIONAL COMMITTEE CLASSIFICATION OF BLOOD PRESSURE
- NORMAL: <130<85 mmHg
- HIGH NORMAL: 130-139/85-89
- STAGE 1: (MILD) 140-159/90-99
- STAGE 2: (MOD.) 160-179/100-109
- STAGE 3: (SEVERE) 180-209/110-119
- STAGE 4: (V. SEVERE) >210/ >120

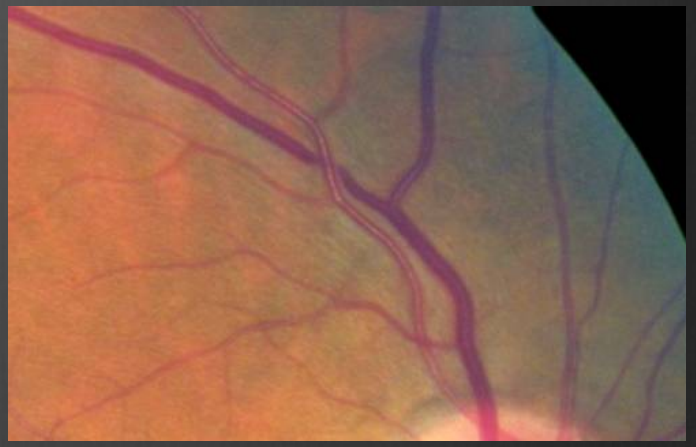
Hypertensive Retinopathy

- PATHOPHYSIOLOGICAL CHANGES IN HYPERTENSIVE OCULAR DISEASE
- HYPERTENSIVE CHOROIDOPATHY
- HYPERTENSIVE RETINOPATHY
- -- VASOCONSTRICTIVE PHASE
- -- SCLEROTIC PHASE
- -- EXUDATIVE PHASE
- -- COMPLICATIONS OF THE SCLEROTIC PHASE
- HYPERTENSIVE OPTIC NEUROPATHY
- -- OPTIC DISC EDEMA
- -- OPTIC ATROPHY
- -- ISCHEMIC OPTIC NEUROPATHY

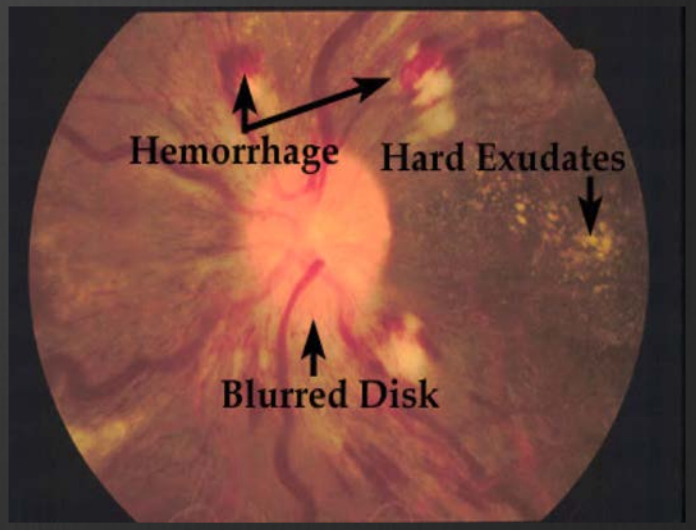


Hypertensive Retinopathy

- Chronic "essential" hypertention (most)
  - Sclerosis +narrowing of retinal and choroidal vessels
  - Usually asymptomatic



- Accelerated "malignant" hypertension (1%)
  - >220 systolic or > 120 diastolic
  - Headache, dizziness, visual disturbance, diplopia
  - Fibrinoid necrosis of arterioles and end organ damage



Hypertensive Retinopathy - Prevalence

- The second most common retinal vascular disease
- Systemic hypertension (>160/90mmHg)
  10-15% in the UK >40 age group
- Malignant hypertension (240/140mmhg)
  0.5-0.75%
- Hypertensive retinopathy 4-10%

Hypertensive Retinopathy – Diagnostic Techniques & Signs

- Arteriolar Narrowing
  - Young patients, autoregulation causes uniform narrowing of retinal arterioles
  - Older patients, arteriosclerosis and autoregulation cause focal arteriolar narrowing
  - Can assess the arterio-venous calibre ratio as a percentage
    - adjacent arteries and veins
    - equivalent numbers of bifurcations
    - between 1 and 3 DD from optic disc

Hypertensive Retinopathy - Classification

Grade	Description	Alternative description	A:V ratio
I	minimal narrowing of the retinal arteries	Non-malignant	50%
II	narrowing of the retinal arteries in conjunction with regions of focal narrowing and arterio-venous nipping	Non-malignant	33%
III	abnormalities seen in Grades I and II, as well as retinal haemorrhages, hard exudation, and cotton-wool spots	Malignant	25%
IV	abnormalities encountered in Grades I through III, as well as swelling of the optic nerve head and macular star	Malignant	<20%

Hypertensive Retinopathy – Classification

- HR grades I and II are typically chronic
- HR grades III and IV are typically acute
  - diastolic blood pressure >= 110 correlates with grade III
  - diastolic blood pressure >= 130 correlates with grade IV

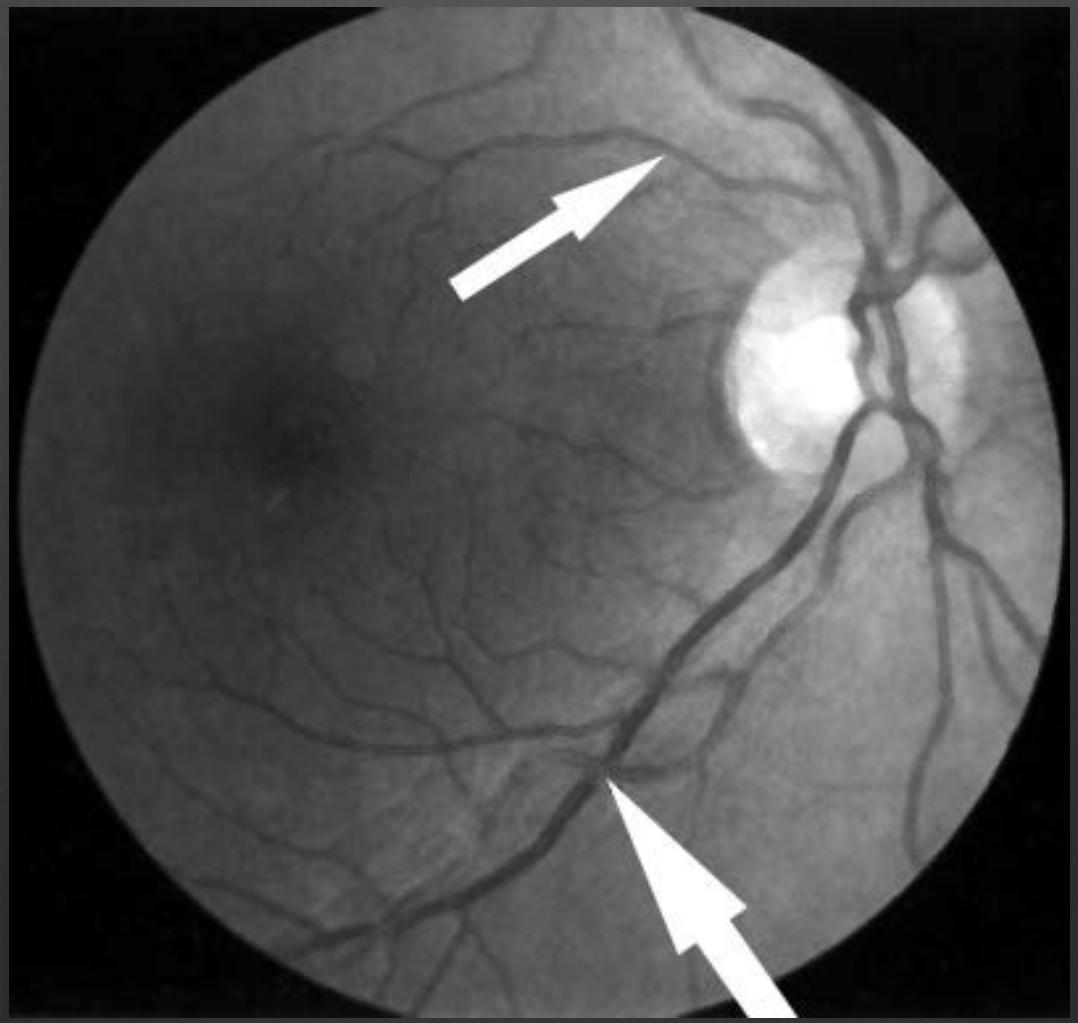
GRADE 1 HTR

- GENERALIZED ARTERIOLAR ATTENUATION
- BROADENING OF ARTERIOLAR LIGHT REFLEX
- CONCEALMENT OF VEIN AT A-V CROSSINGS

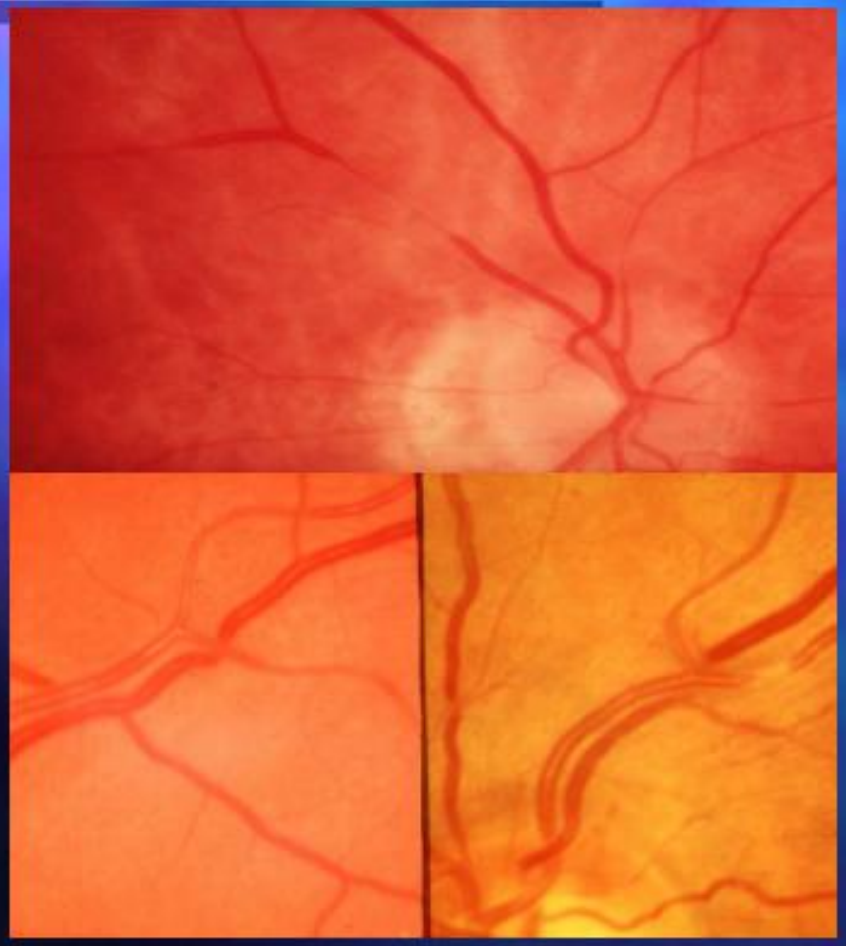
Hypertensive Retinopathy - Classification

Grade	Description	Alternative description	A:V ratio
I	minimal narrowing of the retinal arteries	Non-malignant	50%
II	narrowing of the retinal arteries in conjunction with regions of focal narrowing and arterio-venous nipping	Non-malignant	33%
III	abnormalities seen in Grades I and II, as well as retinal haemorrhages, hard exudation, and cotton-wool spots	Malignant	25%
IV	abnormalities encountered in Grades I through III, as well as swelling of the optic nerve head and macular star	Malignant	<20%

Hypertensive Retinopathy – Classification Grade 2



GRADE 2 HTR

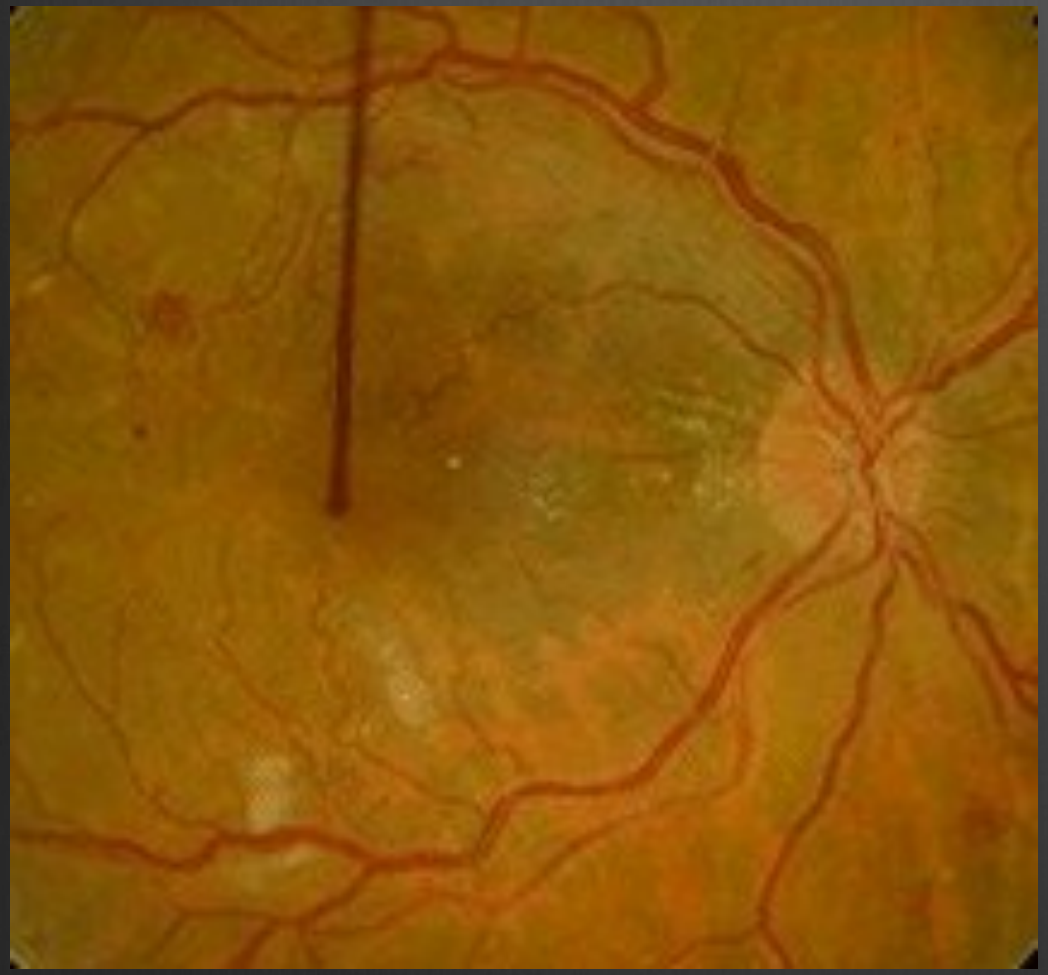


- SEVERE GENERALIZED AND FOCAL ARTERIOLAR CONSTRICTION
- A-V CROSSING CHANGES (SALUS SIGN)

Hypertensive Retinopathy - Classification

Grade	Description	Alternative description	A:V ratio
I	minimal narrowing of the retinal arteries	Non-malignant	50%
II	narrowing of the retinal arteries in conjunction with regions of focal narrowing and arterio-venous nipping	Non-malignant	33%
III	abnormalities seen in Grades I and II, as well as retinal haemorrhages, hard exudation, and cotton-wool spots	Malignant	25%
IV	abnormalities encountered in Grades I through III, as well as swelling of the optic nerve head and macular star	Malignant	<20%

Hypertensive Retinopathy – Diagnostic Techniques & Signs



Early malignant
Dot and blot haemorrhages
Hard and soft exudates
Diffuse arteriolar narrowing
Arterio-venous crossing defects

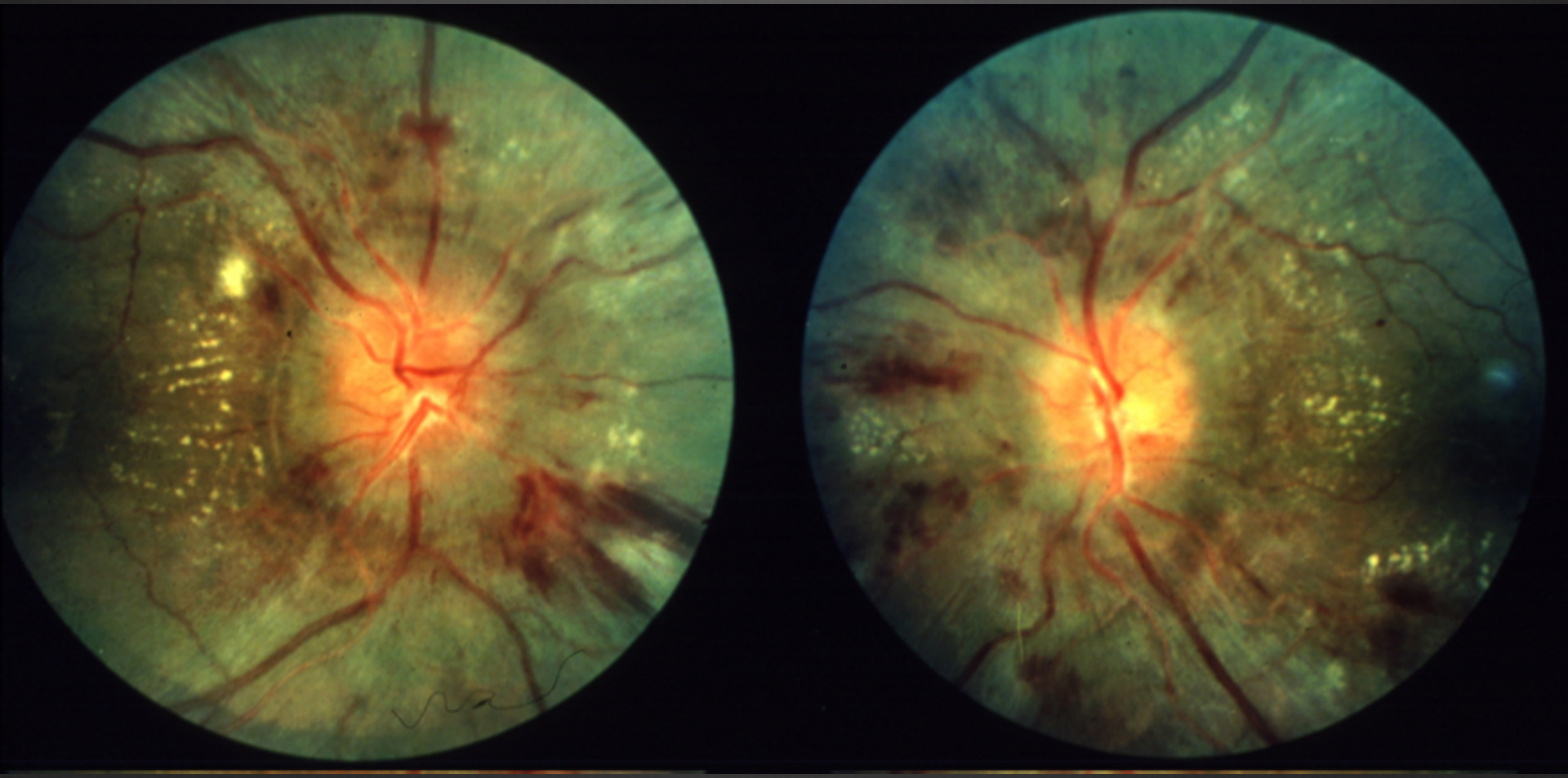
GRADE 3 HTR

- Copper wiring of arterioles
- Venous banking distal to A-V crossing (bonnet's sn)
- Venous tapering on either side of crossing (gunn's sn)
- Right angle deflection of veins.
- Flame shaped hemorrhages cotton wool spots, hard exudates.

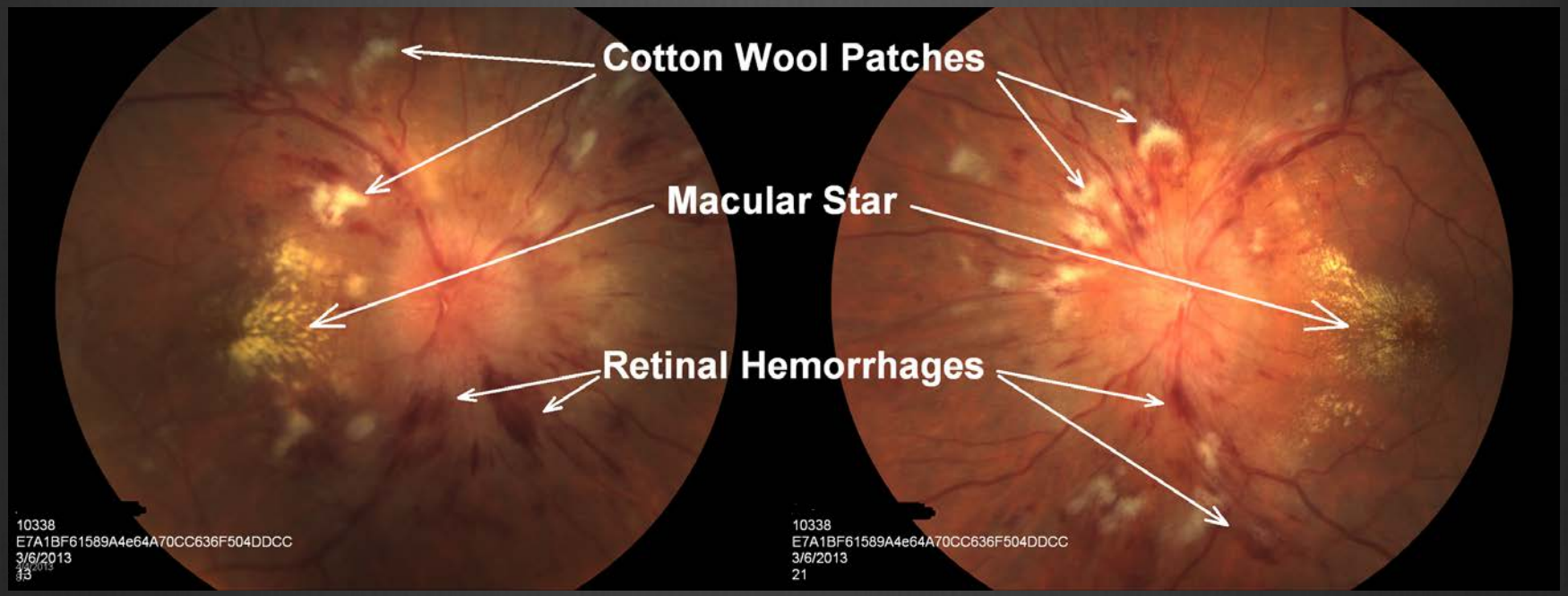
Hypertensive Retinopathy - Classification

Grade	Description	Alternative description	A:V ratio
I	minimal narrowing of the retinal arteries	Non-malignant	50%
II	narrowing of the retinal arteries in conjunction with regions of focal narrowing and arterio-venous nipping	Non-malignant	33%
III	abnormalities seen in Grades I and II, as well as retinal haemorrhages, hard exudation, and cotton-wool spots	Malignant	25%
IV	abnormalities encountered in Grades I through III, as well as swelling of the optic nerve head and macular star	Malignant	<20%

Hypertensive Retinopathy – Classification Grade 4



Hypertensive Retinopathy – Grade 4



Advanced malignant
Macular star
Papilloedema

Hypertensive Retinopathy – Optometric management

- HR grades I and II are typically chronic
  - Refer to GP?
  - Refer to Hospital Eye services?
  - Complications (RVO etc) refer to HES?

Hypertensive Retinopathy – Classification

- HR grades III and IV are typically acute
  - diastolic blood pressure >= 110 correlates with grade III
  - diastolic blood pressure >= 130 correlates with grade IV

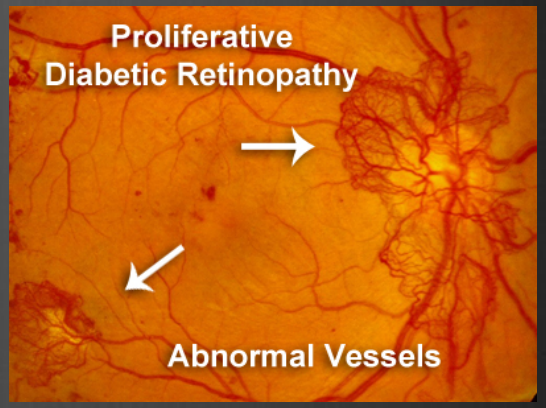
- Refer to GP?
- Refer to HES?
- Refer to A/E?

- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?

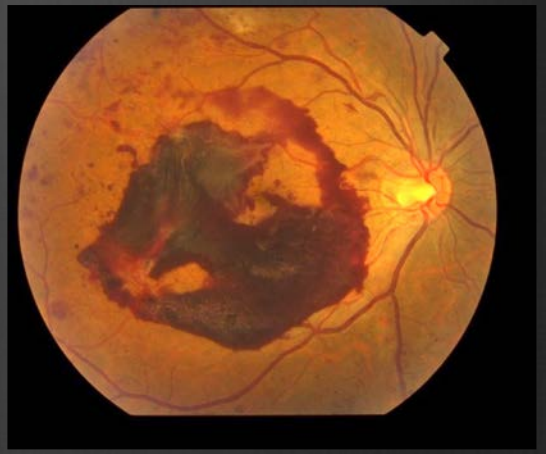
Hypertensive Retinopathy – Medical management

- Do we ”treat” grades I, II, III, IV retinopathy?
- What do we treat in HES?
- How does this influence your referral practices?

Diabetic retinopathy



- Leading cause of blindness in 25-74 years in USA
- Non-proliferative DR
  - Mild
  - Moderate
  - Severe
  - Very severe
- Proliferative diabetic retinopathy
  - NVD/ NVE
- Vitreous haemorrhage
- Tractional retinal detachment
- Neovascular glaucoma



Grading retinopathy

	Normal eye	Mildly ischaemic eye	Moderately ischaemic eye	Severely ischaemic eye
Grading	Mild NPDR	Moderate NPDR	Severe NPDR	Proliferative DR
Clinical signs	No retinopathy Occasional microaneurysms Dot haemorrhages Scattered hard exudates	Microaneurysms Dot haemorrhages Hard exudates Cotton wool spots PLUS Larger (blot) haemorrhages Venous beading /irregularity		Larger (blot) haemorrhages Venous beading PLUS New vessels at the disc (NVD) New vessels elsewhere (NVE)
Examples				
	Fig. 4 Mild NPDR.	*Fig. 5. Moderate NPDR. Blot haemorrhages and maculopathy.*	*Fig. 6. Severe NPDR. Blot haemorrhages and maculopathy.*	*Fig. 7. Proliferative DR. New vessels (NVD and NVE).*
Action	Review in 1 year	Refer		

NPDR = non-proliferative diabetic retinopathy; DR = diabetic retinopathy.

Diabetic retinopathy in the UK

NSC	International Term	Symptoms	Features (new)	Action
R0	No DR	None	Normal retina. Grade 0 (US)	annual rescreen
RI	Mild non-proliferative (mild pre-proliferative)	None	Haemorrhages & microaneurysms, only see photo Grade 1 (US). Very minor IRMAs	Inform diabetes team see M1
R2	Moderate non-proliferative, moderate pre-proliferative	None	Previously termed mild pre-proliferative. Extensive Microaneurysm, intraretinal haemorrhage, and hard exudates. See photo and photo Grade 2 (US)	refer HES see R2
R2	Severe non-proliferative severe pre-proliferative	None	Previously termed severe pre-proliferative. Venous abnormalities, large blot haemorrhages, cotton wool spots (small infarcts), venous beading, venous loop, venous reduplication, IRMA, See photo and photo . Grade 3 (US)	urgent refer HES see R2
R3	Proliferative retinopathy	Floaters, sudden visual loss	New vessel formation either at the disc (NVD) or elsewhere (NVE). Photos: flat new vessels, raised, florid Grade 4a (US)	urgent refer HES see R3
R3	Pre-retinal fibrosis+/- tractional retinal detachment	Floaters, central loss of vision	Extensive fibrovascular proliferation, retinal detachment, pre-retinal or vitreous haemorrhage, glaucoma. Grade 4b (US). Traction photo and photo. Subhyaloid haemorrhage photo	urgent refer HES
R3s	treated proliferative retinopathy (s = stable)		no haemorrhages or exudates or new vessels, laser ('P' added)	annual rescreen

- http://www.diabeticretinopathy.org.uk/gradingretinopathy.htm

Diabetic retinopathy in the UK

M 0			no maculopathy	annual rescreen
M 1	Diabetic maculopathy	Blurred central vision	The macula is defined as a circle centred on the fovea, with a radius of the distance to the disc margin. If the leakage involves or is near the fovea the condition is termed clinically significant macular oedema (CSME). Exudative maculopathy presents with leakage , retinal thickening, microaneurysms, hard exudates at the macula. Ischaemic form can have a featureless macular with NVE and poor vision. Photos: moderate, severe Milder forms: • exudate < or = 1DD of centre of fovea • circinate or group of exudates within macula • any microaneurysm or haemorrhage < or = 1DD of centre of fovea only is associated with a best VA of < or = 6/12 retinal thickening < or = 1DD of centre of fovea (if stereos available)	refer HES see M1
P	Photocoagulation	Reduced night vision, glare	Small retinal scars through out the peripheral retina. Grade 4b (US)	
OL/ UG	Other lesion / Un-gradable		Un-gradable is usually due to cataract, other lesions usually referred for assessment	

http://www.diabeticretinopathy.org.uk/gradingretinopathy.htm

FIGURE 1: STANDARD PHOTO 2A FROM THE WISCONSIN GRADING SYSTEM[2,4]

FIGURE 2: STANDARD PHOTO 8A FROM THE WISCONSIN GRADING SYSTEM[2,4]

FIGURE 3: STANDARD PHOTO 10A FROM THE WISCONSIN GRADING SYSTEM[2,4]

Table 1 : Classification of diabetic retinopathy into retinopathy stages (Wisconsin level) and predictive value of retinal lesions (adapted from Focal Points)

Retinopathy Stage	Definition	Rate of progression (%)			
		to PDR		to high-risk stage	
		1 year	3 years	1 year	5 years
Minimal NPDR (level 20)	Ma only	not documented			
Mild NPDR (level 35)	Ma and one or more of: retinal haem, HEx, CWS, but not meeting Moderate NPDR definition	5	14	1	15
Moderate NPDR (levels 43,47)	H/Ma≥ std photo 2A (Figure 1) in at least one quadrant and one or more of: CWS, VB, IRMA, but not meeting Severe NPDR definition	12-26	30-48	8-18	25-39
Severe NPDR *preproliferative* (level 50+)	Any of: H/Ma>std photo 2A in all four quadrants, IRMA >std photo 8A (Figure 2) in one or more quadrants, VB in two or more quadrants	52	71	15	56
PDR (level 60+)	Any of: NVE or NVD <std photo 10A (Figure 3)w, vitreous/preretinal haem and NVE<1/2 disc area (DA) without NVD			46	75
High-risk PDR (level 70+)	Any of: NVD>1/4 to 1/3 disc area, or with vitreous/preretinal haem, or NVE>1/2 DA with vitreous/preretinal haem	Severe visual loss (VA≤6/240) develops in 25-40% within two years			
Advanced PDR	High-risk PDR with tractional detachment involving macula or vitreous haem obscuring ability to grade NVD and NVE				
Macular Oedema	Retinal thickening wtihin two disc diameters of macula centre	Can occur at any stage of DR			
Clinically significant Macular Oedema (CSME)	Retinal thickening within 500µ of macular centre with adjacent thickening	Can occur at any stage of DR			

Classification of severity of diabetic retinopathy

Early Treatment Diabetic Retinopathy Study Research Group. Early photocoagulation for diabetic retinopathy. ETDRS Report 9. *Ophthalmology*. 1991;98:766–785.

- *Nonproliferative DRP :*

Mild NPDR	Microaneurysms, retinal hemorrhage and hard exudate
Moderate NPDR	Mild NPDR plus cotton wool spots .
Severe NPDR 4 : 2 : 1 Rule	Moderate NPDR plus one of : 2. Intraretinal Hges in four quadrants . 3. marked venous beading in two or more quadrants 4. IRMA one or more quadrants.
Very severe NPDR	Two or more of the above features described in severe NPDR

*You may wish to view these images in a larger size by downloading the PDF version at www.cfeh.com.au/clinical-guidelines

FIGURE 4: MINIMAL NPDR (RED FREE)

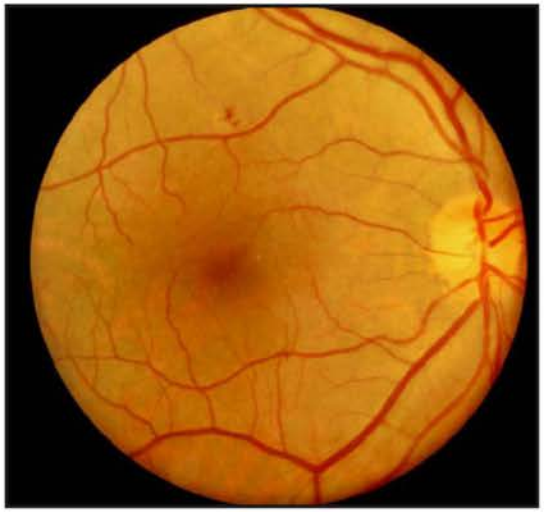


FIGURE 5: MILD NPDR

FIGURE 6: MODERATE NPDR

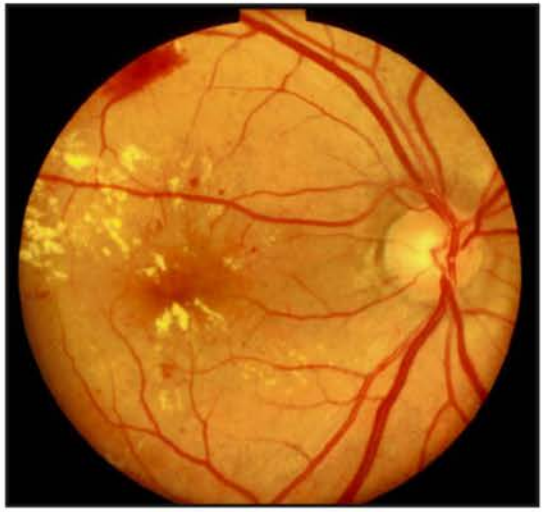


FIGURE 7: SEVERE NPDR WITH CSME

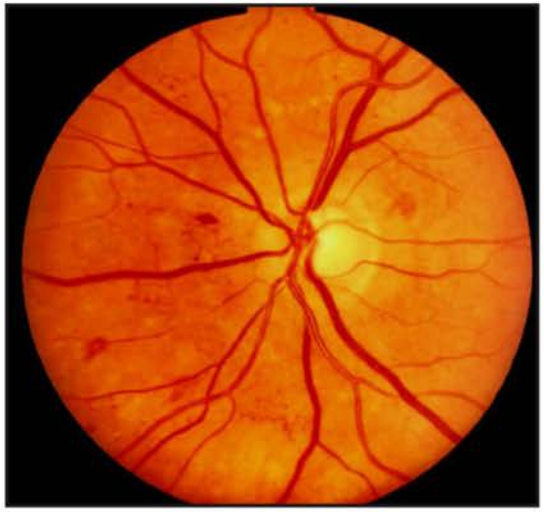


FIGURE 8: SEVERE NPDR WITH IRMA

FIGURE 9: PROLIFERATIVE DIABETIC RETINOPATHY

Diabetic Retinopathy – Optometric management

NSC	International Term	Symptoms	Features	Action
R0	No DR	None	Normal retina. Grade 0 (US)	annual rescreen
RI	Mild non-proliferative (mild pre-proliferative)	None	Haemorrhages & microaneurysms, only see photo Grade 1 (US). Very minor IRMAs	Inform diabetes team see M1
R2	Moderate non-proliferative, moderate pre-proliferative	None	Previously termed mild pre-proliferative. Extensive Microaneurysm, intraretinal haemorrhage, and hard exudates. See photo and photo Grade 2 (US)	refer HES see R2
R2	Severe non-proliferative severe pre-proliferative	None	Previously termed severe pre-proliferative. Venous abnormalities, large blot haemorrhages, cotton wool spots (small infarcts), venous beading, venous loop, venous reduplication, IRMA, See photo and photo . Grade 3 (US)	urgent refer HES see R2
R3	Proliferative retinopathy	Floaters, sudden visual loss	New vessel formation either at the disc (NVD) or elsewhere (NVE). Photos: flat new vessels, raised, florid Grade 4a (US)	urgent refer HES see R3
R3	Pre-retinal fibrosis+/- tractional retinal detachment	Floaters, central loss of vision	Extensive fibrovascular proliferation, retinal detachment, pre-retinal or vitreous haemorrhage, glaucoma. Grade 4b (US). Traction photo and photo. Subhyaloid haemorrhage photo	urgent refer HES
R3s	treated proliferative retinopathy (s = stable)		no haemorrhages or exudates or new vessels, laser ('P' added)	annual rescreen
M 0			no maculopathy	annual rescreen
M 1	Diabetic maculopathy	Blurred central vision	The macula is defined as a circle centred on the fovea, with a radius of the distance to the disc margin. If the leakage involves or is near the fovea the condition is termed clinically significant macular oedema (CSME). Exudative maculopathy presents with leakage , retinal thickening, microaneurysms, hard exudates at the macula. Ischaemic form can have a featureless macular with NVE and poor vision. Photos: moderate, severe Milder forms: • exudate < or = 1DD of centre of fovea • circinate or group of exudates within macula • any microaneurysm or haemorrhage < or = 1DD of centre of fovea only is associated with a best VA of < or = 6/12 retinal thickening < or = 1DD of centre of fovea (if stereos available)	refer HES see M1
P	Photocoagulation	Reduced night vision, glare	Small retinal scars through out the peripheral retina. Grade 4b (US)	
OL/ UG	Other lesion / Un-gradable		Un-gradable is usually due to cataract, other lesions usually referred for assessment	

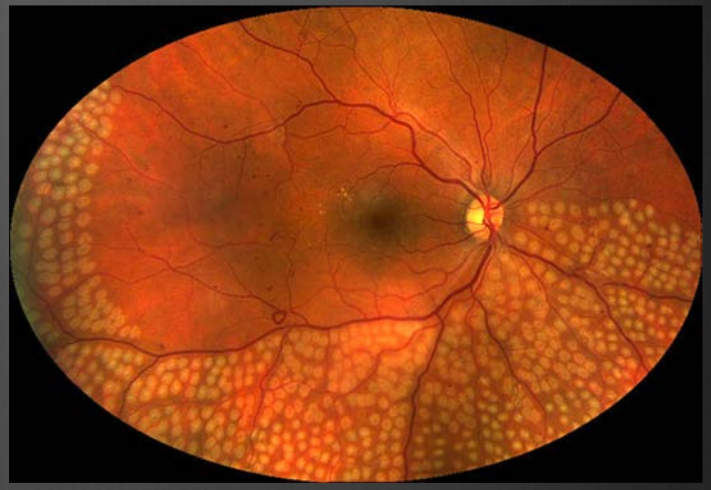
Diabetic Retinopathy – Optometric management

NSC	International Term	Symptoms	Features	Action
R0	No DR	None	Normal retina. Grade 0 (US)	annual rescreen
RI	Mild non-proliferative (mild pre-proliferative)	None	Haemorrhages & microaneurysms, only see photo Grade 1 (US). Very minor IRMAs	Inform diabetes team see M1
R2	Moderate non-proliferative, moderate pre-proliferative	None	Previously termed mild pre-proliferative. Extensive Microaneurysm, intraretinal haemorrhage, and hard exudates. See photo and photo Grade 2 (US)	refer HES see R2
R2	Severe non-proliferative severe pre-proliferative	None	Previously termed severe pre-proliferative. Venous abnormalities, large blot haemorrhages, cotton wool spots (small infarcts), venous beading, venous loop, venous reduplication, IRMA, See photo and photo . Grade 3 (US)	urgent refer HES see R2
R3	Proliferative retinopathy	Floaters, sudden visual loss	New vessel formation either at the disc (NVD) or elsewhere (NVE). Photos: flat new vessels, raised, florid Grade 4a (US)	urgent refer HES see R3
R3	Pre-retinal fibrosis+/- tractional retinal detachment	Floaters, central loss of vision	Extensive fibrovascular proliferation, retinal detachment, pre-retinal or vitreous haemorrhage, glaucoma. Grade 4b (US). Traction photo and photo. Subhyaloid haemorrhage photo	urgent refer HES
R3s	treated proliferative retinopathy (s = stable)		no haemorrhages or exudates or new vessels, laser ('P' added)	annual rescreen

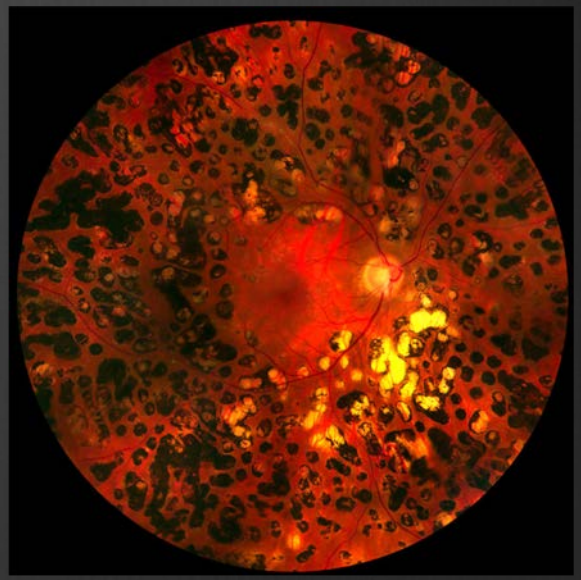
- What do we mean by "Urgent"?

- neovascularisation without vitreous haemorrhage
- Vitreous haemorrhage
- Tractional retinal detachment of the macula
- Traction RD not involving macula
- Combined tractional rhegmatogenous detachment

Diabetic retinopathy- current treatments



- Pan retinal photocoagulation when neovascularisation occurs or in some high risk individuals
- Advantages:
  - Reduces severe visual loss by 50%
  - Endpoint
  - Does not involve surgery/ injection
  - Can be repeated as required by slit lamp/ indirect laser/ intra-operatively
  - Well tolerated in early phases
- Disadvantages
  - Progressive loss of visual field and impeded night vision, driving vision
  - Repeated treatments can become painful
  - Can worsen diabetic macular oedema



LUCENTIS/ AVASTIN

VEGF-A

EYLEA

IGF-1

bFGF

PlGF

*PDGF

Ang 1,2

*Tie 2

MMP 1, 2, 9

*Angiostatin

*Endostatin

*PEDF

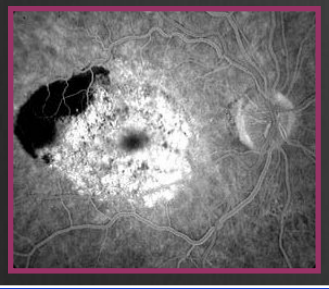
*sFLT-1

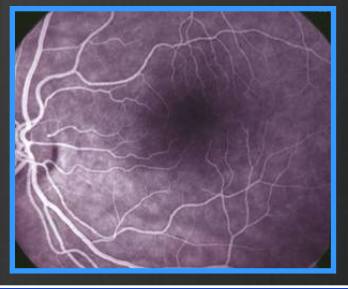
siRNAs

shRNAs

vasostatin

IL 10, 12



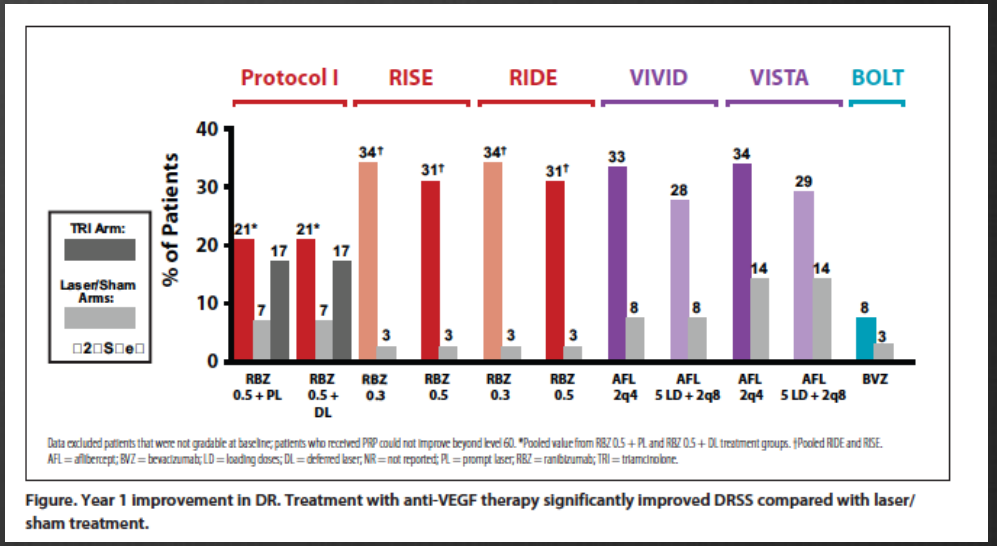


Angiogenesis

Angiostasis

Proliferative diabetic retinopathy- future treatments

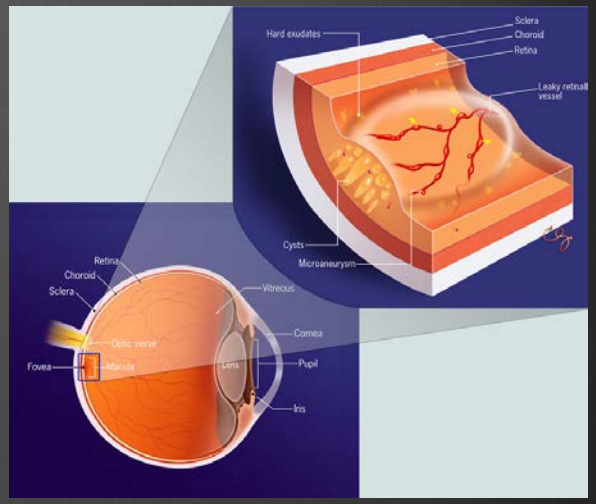
- Anti-VEGF - Protocol S non-inferiority trial 2 years
  - ranibizumab (191) vs PRP laser (203)
  - Non-inferior VA (+2.8 letters vs +0.2)
  - Less peripheral visual field loss
  - Less new DMO (9% vs 23%)
  - Less requirement for vitrectomy (4% vs 15%)
  - No significant safety concerns
  - Need longer review
- Other anti-VEGFs
- Gene therapy



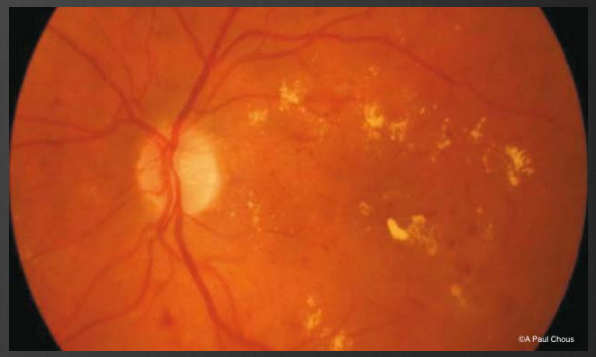
Data excluded patients that were not gradable at baseline; patients who received PRP could not improve beyond level 60. *Pooled value from RBZ 0.5 + PL and RBZ 0.5 + DL treatment groups. †Pooled RIDE and RISE. AFL = aflibercept; BVZ = bevacizumab; LD = loading doses; DL = deferred laser; NR = not reported; PL = prompt laser; RBZ = ranibizumab; TRI = triamcinolone.

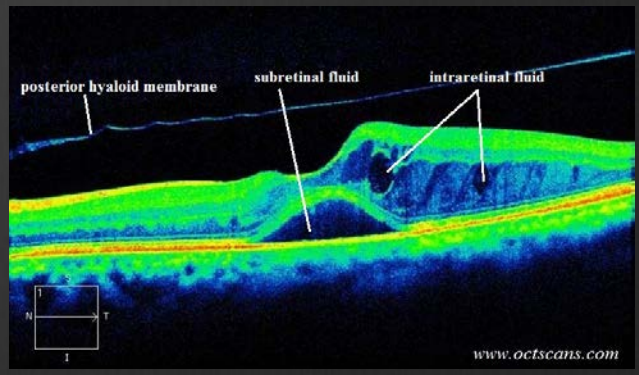
Figure. Year 1 improvement in DR. Treatment with anti-VEGF therapy significantly improved DRSS compared with laser/sham treatment.

Diabetic macular oedema

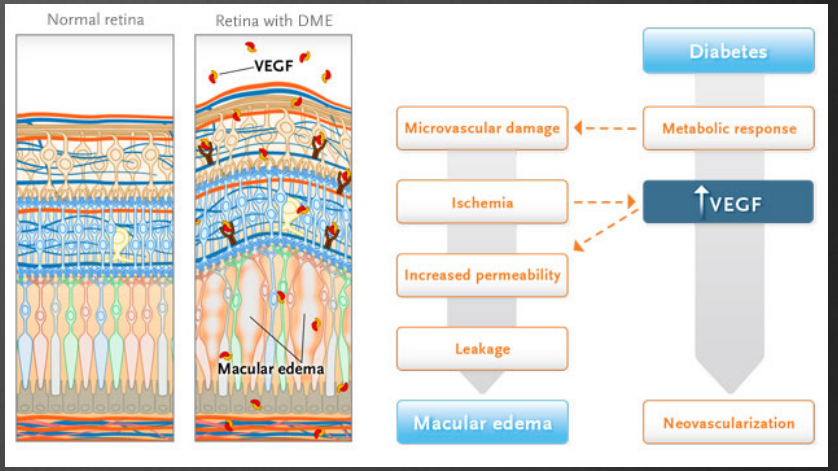


- 5.6 million diabetics in USA in 1980 vs 20.9 million in 2011 (7% of population)
- 3.8% have DMO (798,000)
- Retinal thickening within 2 DD of macular
- Microvascular changes causing intra/subretinal exudation and moderate visual loss

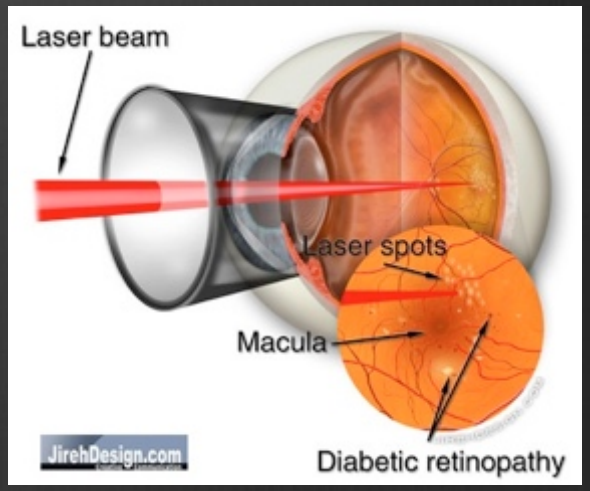




Diabetic macular oedema- current treatments



- Macular laser– grid/focal, single or multispot
  - Reduces moderate visual loss by 50% (ETDRS) vs observation
- Anti-VEGF injections (centre-involving)
  - Bevacizumab - BOLT
  - Ranibizumab
    - RISE, RISE, RESTORE, Protocol I
    - monthly or PRN + prompt/ deferred laser superior to laser alone
    - NICE approved if >400um CSFT
  - Aflibercept
    - VIVID, VISTA
    - NICE approved if >400um CSFT



Diabetic macular oedema- current treatments

- Intravitreal Steroids
  - (Triamcinolone) - off licence
  - Dexamenthasone (Ozurdex) MEAD
    - 3-4 months
    - NICE approved if pseudophakic and insufficient ANTI-VEGF response
  - Flucinolone – (Illuvien implant) FAME
    - 36 months
    - NICE approved if chronic DMO, pseudophakic and insufficient anti-VEGF response
  - Risks of raised IOP (38-42%) + cataract
  - Cost of flucinolone implant (£5500 + VAT = discounted price)

Iluvien, a cylindrical fluocinolone acetonide implant, can be injected in the office.

Diabetic macular oedema- future treatments

- Luminate (Allegro Ophthlamics)
  - Blocks integrin receptors on vascular endothelial cells
  - Phase 1
    - 3 injections then 3 months F/U
    - ? Sustained effects
  - Phase II – recruiting for DMO and PVD induction in NPDR
- Angiopoietin/ Tie 2 pathway
  - Activate Tie2 (Aerpio Therapeutics)
  - Inhibit angiopoeitin (Regeneron)
- Micropulse (subthreshold) lasers

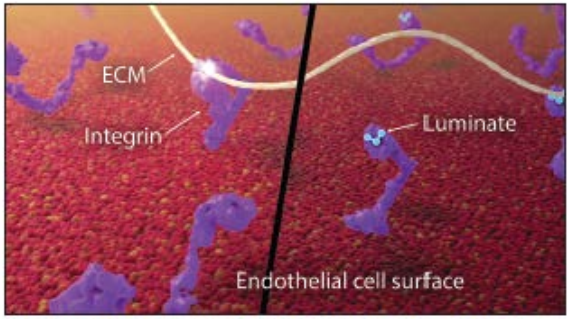


Figure 2. Integrins regulate cell functions and interactions among cells and between cells and the extracellular matrix (ECM). As they bind or attach to the ECM, integrins activate intracellular signaling pathways and proteolytic changes that promote angiogenesis. Luminate inhibits the connection between the integrins (shown here in purple) and the ECM, preventing the downstream angiogenic effects.

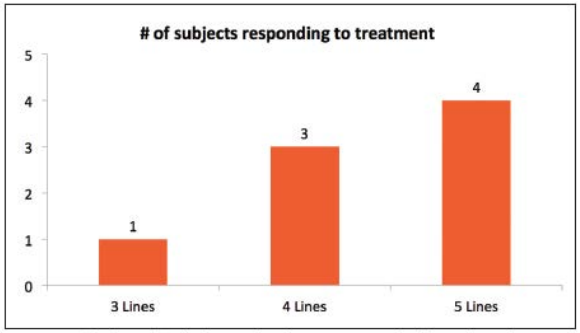


Figure 3. Eight of 15 individuals treated with Luminate gained at least 3 lines of BCVA at 90 days, and those gains were maintained through 3 months off treatment. No subjects lost BCVA or had an increase in macular thickness while off treatment.

Retinal Vein Occlusion

- 2nd most common cause of reduced VA due to retinal vascular disease after diabetic retinopathy
- Worldwide – 16.4 million individuals affected in at least one eye
- Prevalence increases with advancing age

RVO: epidemiology

- Incidence
  - 49 - 60 yrs - 0.7%
  - 80 yrs + - 4.6%

  - Middle-aged
  - Elderly

  - M=F

Types of RVO

- Central Retinal Vein Occlusion (CVRO)
  - Non-ischaemic
  - Ischaemic
- HRVO
  - Non-ischaemic
  - Ischaemic
- BRVO
  - Major branch
  - Macular branch

Major Associations

Patient Group	HT %	Hyper-lipidaemia %	DM%	No clear cause
<50yrs	25	35	3	40
>50yrs	64	34	4-15	21
Asian	64	50	29	10
W Indian	83	33	38	8
Recurrent cases	88	47	3	6

RVO: aetiology and systemic risk factors

- Hypertension
  - >140/85
  - 64% of pts over 50
  - BRVO > CRVO
  - New or uncontrolled > treated
  - Poor control – recurrence
- Hyperlipidaemia
  - > 4.8mmol/l
  - Major risk for < 50
  - Up to 50% of > 50
- DM
  - Fasting glucose > 7mmol/l
  - HBA1C > 7%

RVO: aetiology and ocular risk factors

- Glaucoma
  - POAG assoc with CRVO – up to 20-40%
  - unilateral CRVO/HRVO
    - Prevalence glaucoma 9.9%, OHT 16.2%
  - Increased IOP should be treated in fellow eye if IOP raised
  - IOP lowering drugs not necessary if IOP already normal

- Retrobulbar external compression
  - TED, Haemorrhage, Orbital tumour

CRVO - Clinical features

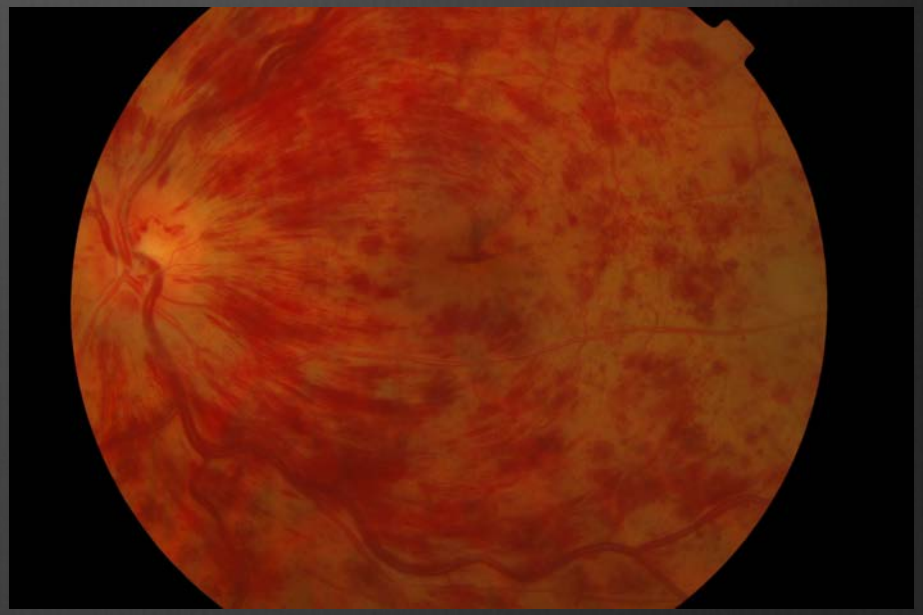
- Diffuse retinal haemorrhages in all 4 quads
- Dilated tortuous vessels
- Disc oedema
- Retinal oedema
- NVI/A, NVD, NVE

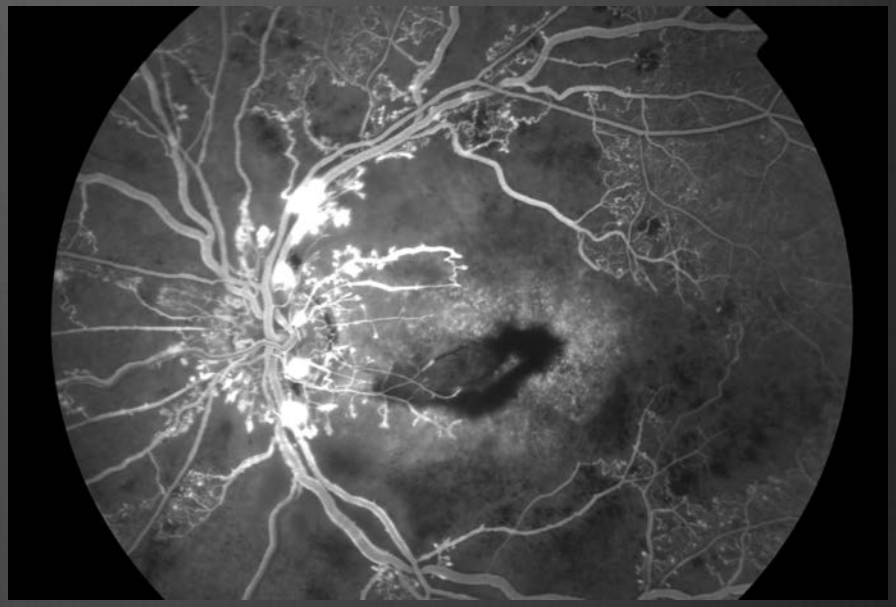
Non-Ischaemic

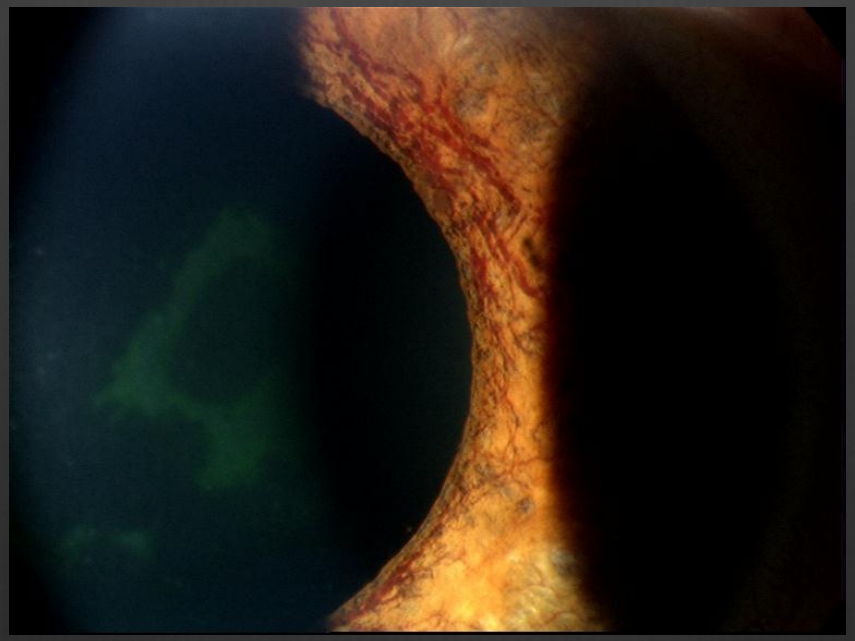
- More common form – 75% of cases
- < 10DD of non-perfusion on fundus fluorescein angiography (FFA)
- Better prognosis
  - Reduced VA often secondary to macular oedema
  - Neovascular glaucoma (NVG) rare

Ischaemic CRVO

- RAPD
- VA <6/60
- Multiple, deep, dark, intra-retinal haemorrhages
- Multiple CWS
- FFA >10DD capillary non-perfusion
- Neovascular glaucoma more likely







CRVO: Pathogenesis

- Thrombus formation in the retinal venous system
  - Atherosclerosis of adjacent CRA compresses CRV at lamina cribrosa
  - Increased blood viscosity
  - Vascular endothelial damage
  - Abnormal platelet function

Branch Retinal Vein Occlusion

- Pathogenesis
  - Compression of vein by artery at a/v crossing
  - Decreased lumen of the vein
  - Upstream venous dilatation
  - Thrombus formation
- Effect on visual function depends on:
  - Extent/location of involved vein
  - Relative location to fovea
  - Extent of collateral formation

RVO: complications

- Neovascularisation of retina/ iris / angle / neovascular glaucoma
  - CRVO > HRVO > BRVO
  - Urgent pan-retinal photocoagulation
  - IOP lowering if NVG : drops/ tube shunts/ cyclodiode laser

- Macular oedema – limits vision
  - In CRVO only < 20% will improve spontaneously
  - In BRVO – milder and can observe selected cases with good VA for signs of resolution

RVO macular oedema

CRVO

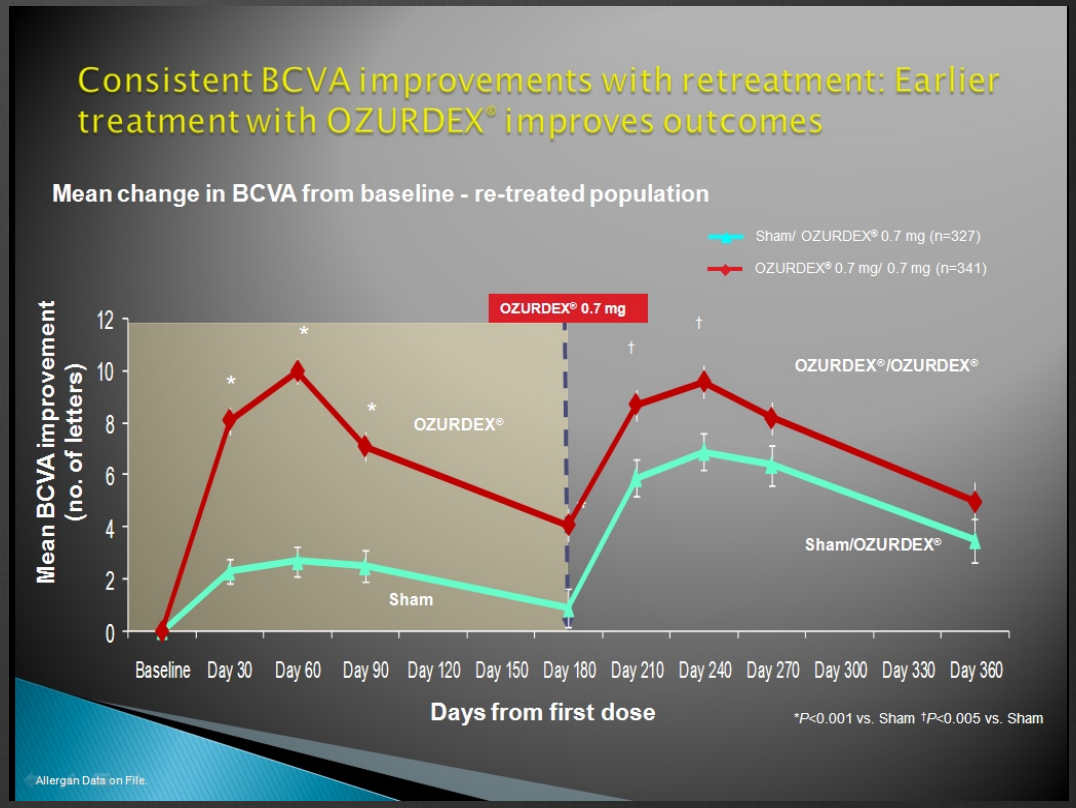
- Intravitreal steroids
- Intravitreal Anti-VEGF
- Laser-induced chorio-retinal anastamosis
- Radial Optic neurotomy
- Intravenous tPA

BRVO

- Intravitreal steroids
- Intravitreal Anti-VEGF
- Macular grid laser
- Laser-induced chorio-retinal anastamosis
- Adventitial sheathotomy
- Surgical PVD

RVO macular oedema- current treatments

- Intravitreal steroids (NICE approved)
  - Triamcinolone (Kenalog/ Triescence/ Trivaris)
  - Ozurdex (GENEVA)

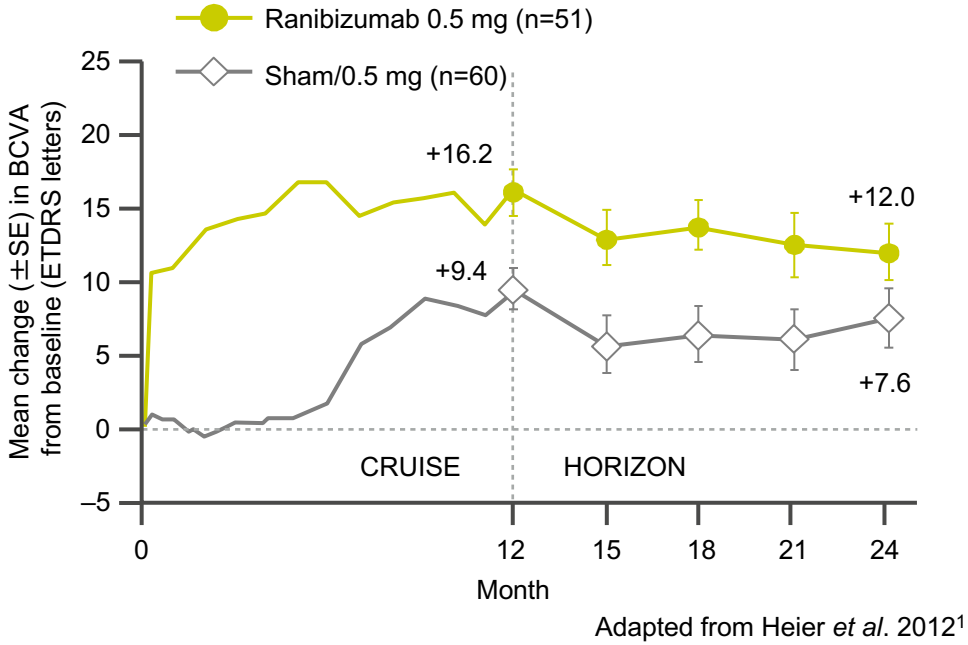


RVO macular oedema- current treatments

- Anti-VEGF (NICE approved)
  - Ranibizumab (CRUISE, BRAVO, HORIZON, RETAIN)
  - Aflibercept (GALILEO, COPERNICUS)

Efficacy for visual impairment following RVO is sustained with long-term treatment

- Long-term safety and efficacy of Lucentis treatment for visual impairment following RVO was assessed in the HORIZON follow-on study[1]
  - Patients with CRVO from CRUISE, n=304
  - Patients in the sham treatment group received 0.5 mg Lucentis PRN treatment after Month 6[1,2]



Adapted from Heier *et al*. 2012[1]

Study arm	Mean number of injections	
	Year 1 (CRUISE[2])	Year 2 (HORIZON[1])
Ranibizumab 0.5 mg	5.5	3.5
Sham/ ranibizumab 0.5 mg	5.4	2.9

The HORIZON study included quarterly visits. The Lucentis SPC recommends that patients are monitored monthly.
RVO, retinal vein occlusion; CRVO, central RVO; VA, visual acuity

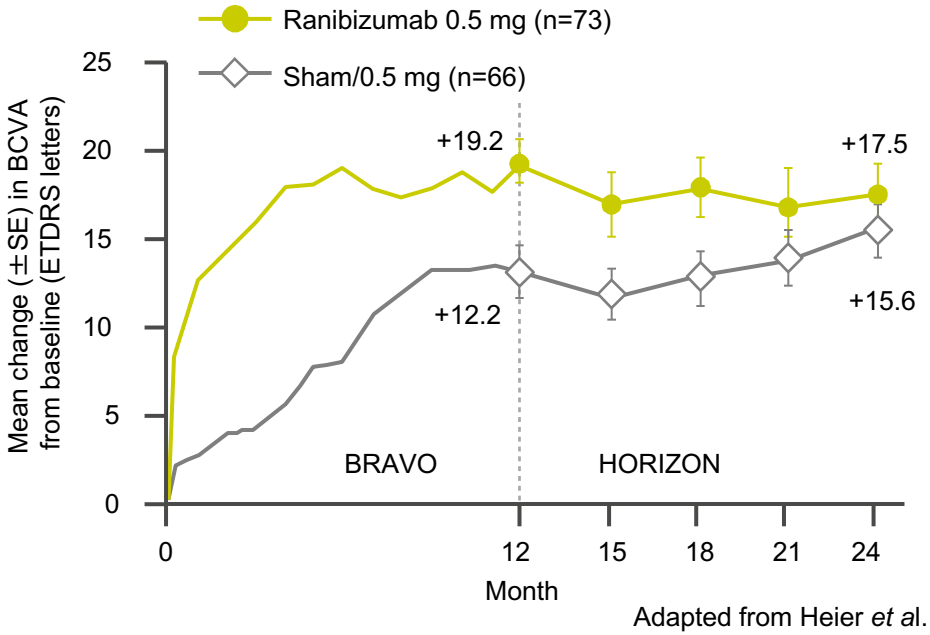
1. Heier *et al. Ophthalmology* 2012;119:802–9
2. Campochiaro *et al. Ophthalmology* 2011;118:2041–9

This meeting is funded and organised by Novartis Pharmaceuticals UK Ltd.

NOVARTIS PHARMACEUTICALS

Efficacy for visual impairment following RVO is sustained with long-term treatment

- Long-term safety and efficacy of Lucentis treatment for visual impairment following RVO was assessed in the HORIZON follow-on study[1]
  - Patients with BRVO from BRAVO, n=304
  - Patients in the sham treatment group received 0.5 mg Lucentis PRN treatment after Month 6[1,2]
- Efficacy in patients with BRVO was sustained up to 2 years (end of study) with fewer injections in the second year[1,2]



Adapted from Heier *et al.* 2012[1]

Study arm	Mean number of injections	
	Year 1 (BRAVO[2])	Year 2 (HORIZON[1])
Ranibizumab 0.5 mg	5.5	2.1
Sham/ ranibizumab 0.5 mg	5.7	2.0

The HORIZON study included quarterly visits. The Lucentis SPC recommends that patients are monitored monthly.
RVO, retinal vein occlusion; BRVO, branch retinal vein occlusion; BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error

1. Heier *et al. Ophthalmology* 2012;119:802–9
2. Brown *et al. Ophthalmology* 2011;118:1594–602

This meeting is funded and organised by Novartis Pharmaceuticals UK Ltd.

NOVARTIS PHARMACEUTICALS

RVO macular oedema- current treatments

- Anti-VEGF (NICE approved)
  - Ranibizumab (CRUISE, BRAVO, HORIZON, RETAIN)
  - Aflibercept (GALILEO, COPERNICUS)
    - Similar results

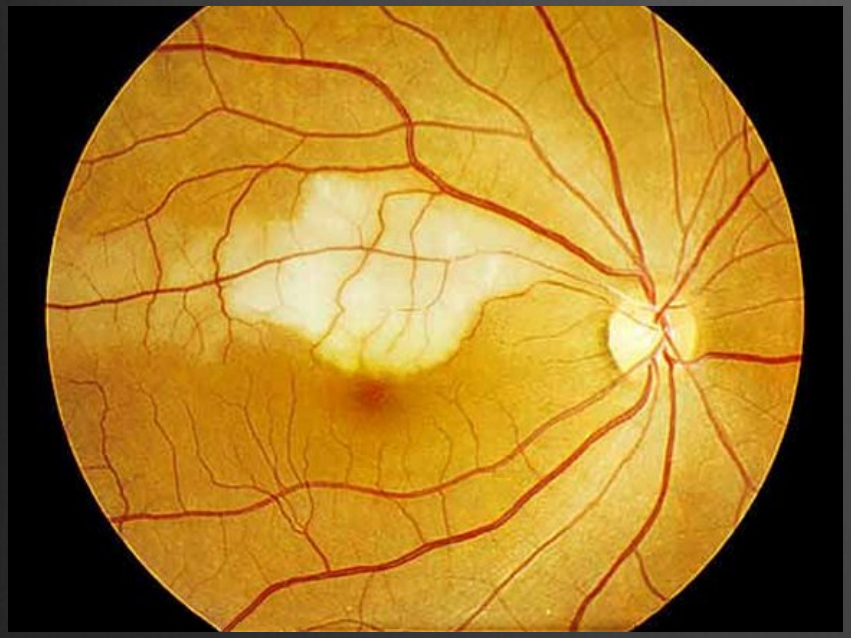
  - Messages:
    - Start treatment early – especially for CRVO
    - Fewer treatments required after first year
    - Previously utilised PRN schedule although "treat and extend" now more common
    - No direct comparison of anti-VEGFs yet
    - Consider anti-VEGF or steroid switch if poor responders – switch earlier
    - Consider combination therapy

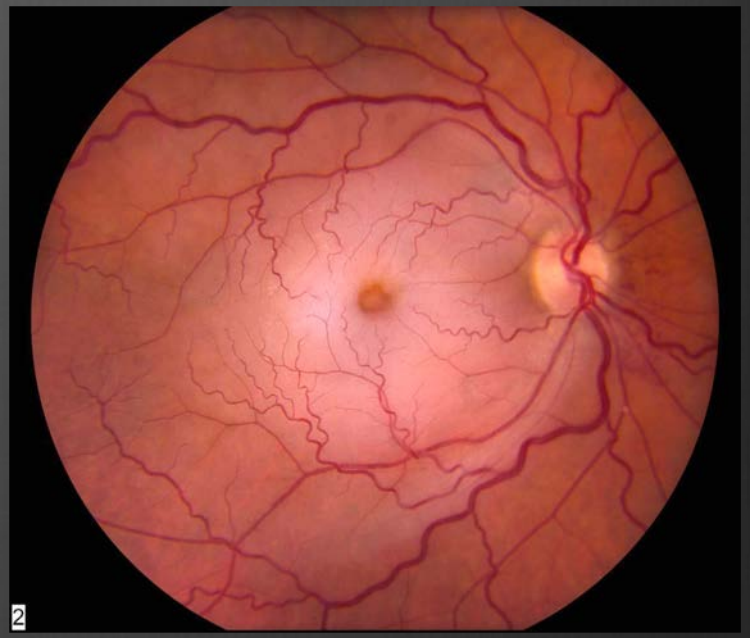
Retinal vein occlusion – Optometric management

- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?

- BRVO with no neovascularisation, not involving temporal veins?
- BRVO with no neovascularisation, involving the temporal veins but no macular oedema
- BRVO with no neovascularisation, involving the temporal veins with macular oedema
- BRVO with neovascularisation with/without macular oedema
- CRVO with no neovascularisation with/without macular oedema
- CRVO with retinal neovascularisation
- CRVO with rubeosis and normal/high IOP

Retinal arterial occlusion

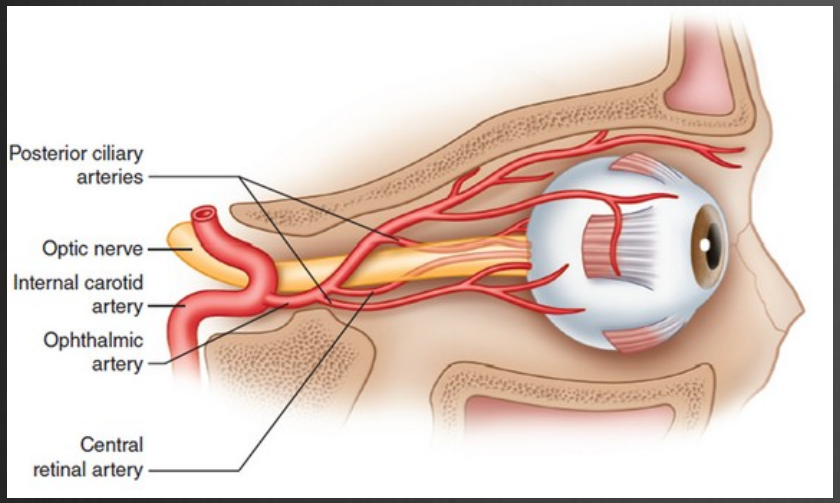




- Branch retinal artery
- Central retinal artery

- Acute obstruction to retinal blood flow in central or branch retinal artery sufficient to result in severe inner retinal ischemia

Central retinal arterial occlusion



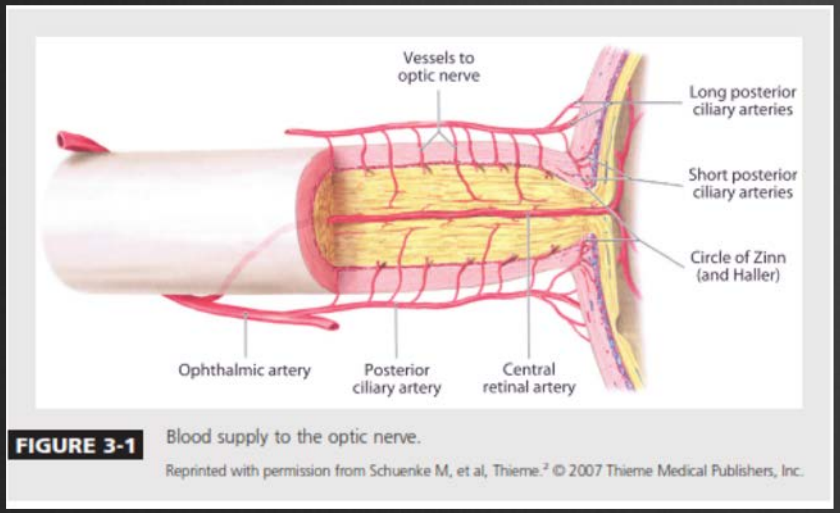
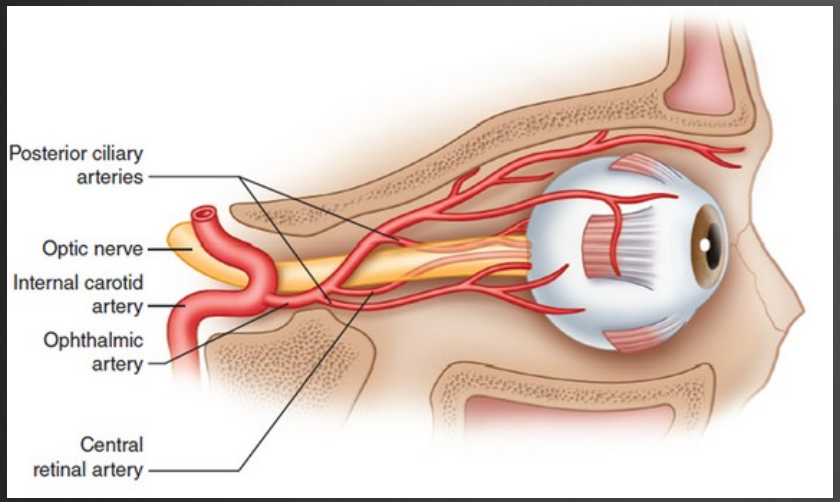


FIGURE 3-1 Blood supply to the optic nerve.

- Obstruction usually just posterior to lamina cribosa
- Mean age 60 years
- Bilateral in 1-2 %
- Causes
  - Thrombosis (atherosclerosis) –most
  - Embolic (carotid artery disease/ cardiac emboli) 1/3
  - Younger patients: migraine, trauma, coagulation disorders
- Irreversible damage after 90 minutes

Central retinal arterial occlusion



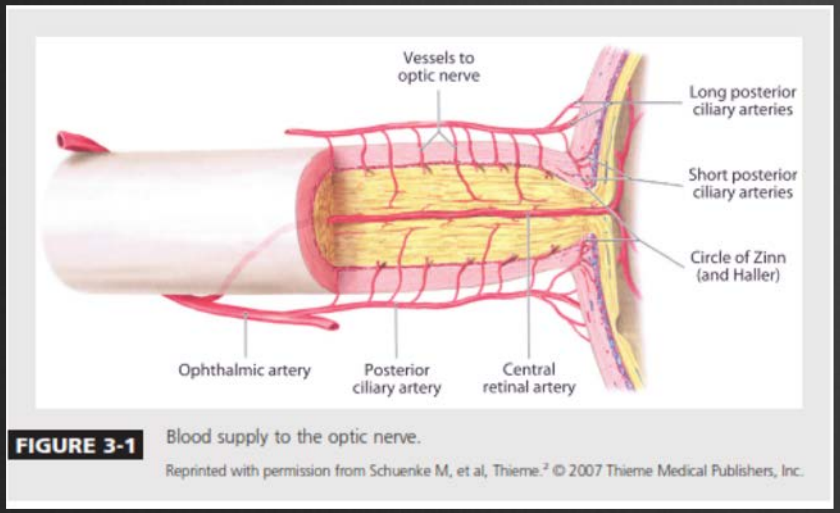
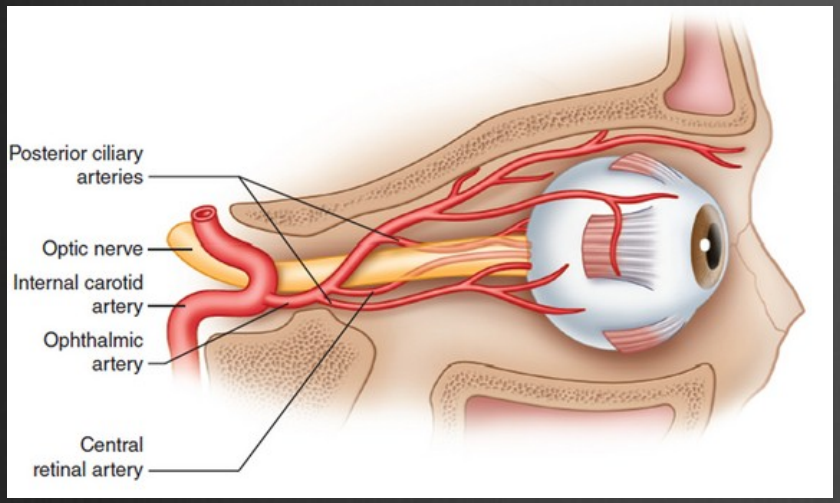


FIGURE 3-1 Blood supply to the optic nerve.

- Thrombosis (atherosclerosis)
  - Hypertension, diabetes, smoking, raised lipids
- Embolic
  - Carotid arteries, aortic artery, cardiac valve vegetations, cardiac tumours
- Haematological
  - Protein S and C deficiencies
  - Antiphospholipid syndrome
  - Lymphoma, leukaemia

Central retinal arterial occlusion



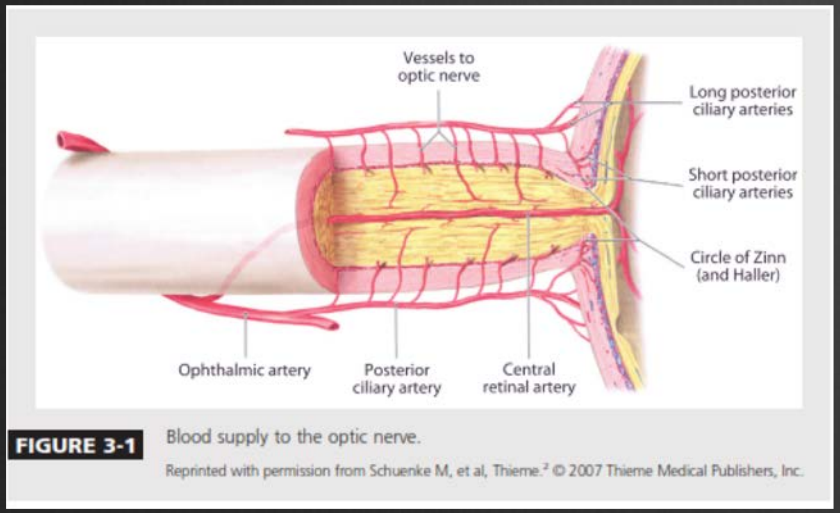


FIGURE 3-1 Blood supply to the optic nerve.

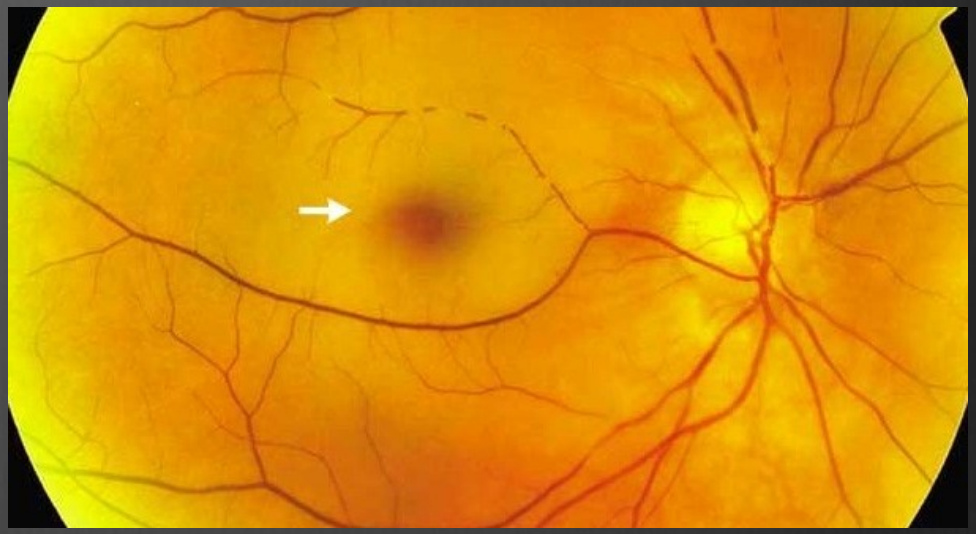
- Inflammatory
  - Giant cell arteritis, Polyarteritis nodosa, SLE, Wegener's granulomatosis
- Infective
  - Syphillis, toxoplasmosis
- Medications
  - Oral contraceptive pill
- Other
  - Trauma, migraine, optic disc drusen

Central retinal arterial occlusion

- Abrupt, painless significant visual loss
- 10% have preceding symptoms of amaurosis fugax
- Symptoms of underlying causes, especially giant cell arteritis (GCA)
  - Jaw claudication, temporal tenderness, headache, myalgia
  - MUST EXCLUDE GCA

Central retinal arterial occlusion

- VA typically < 6/240 or worse
- VA PL/NPL suggests ophthalmic artery occlusion
- RAPD
- ACUTE PHASE:
  - Pale swollen retina
  - "Cherry red spot at macula"
  - Severe arteriolar attenuation
  - "cattle-trucking" blood flow in retinal vessels
  - May have patent cilioretinal artery and better VA than expected (25% of cases)



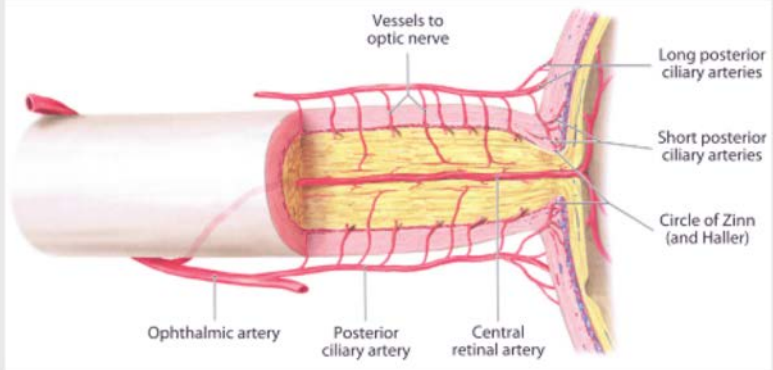
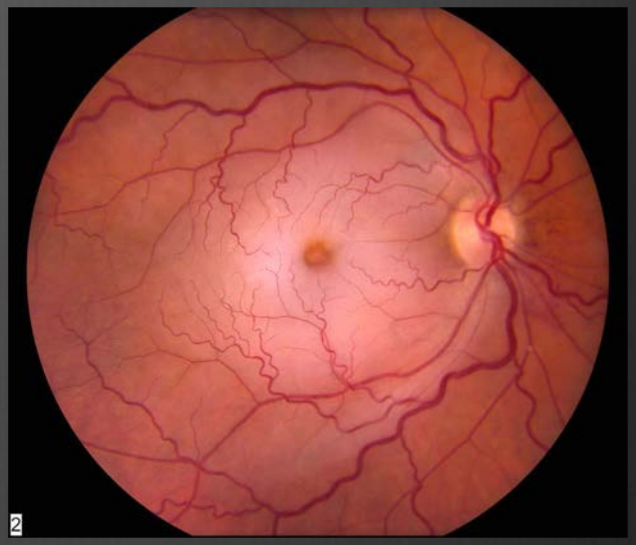
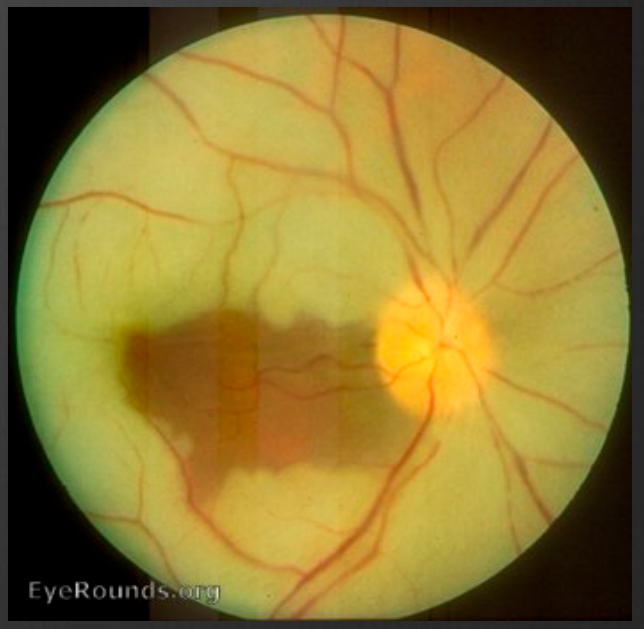


FIGURE 3-1 Blood supply to the optic nerve.

Central retinal arterial occlusion

- POST-ACUTE PHASE:
  - Resolution of whitening in 4-6 weeks
  - Retina may look remarkably normal on fundoscopy
  - Optic atrophy
  - Absence of inner retinal layers on OCT
  - Neovascularisation / rubeosis uncommon unlike CRVO
  - Most have poor VA (CF or less)
  - If patent ClRA then usually 20/50 or better



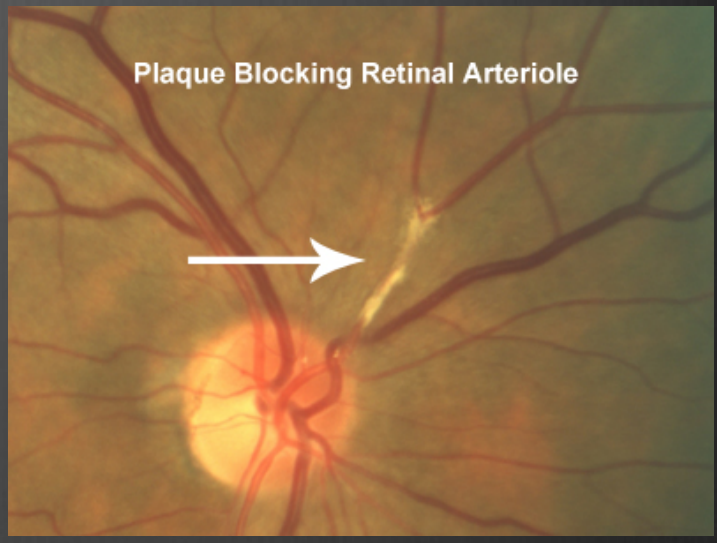


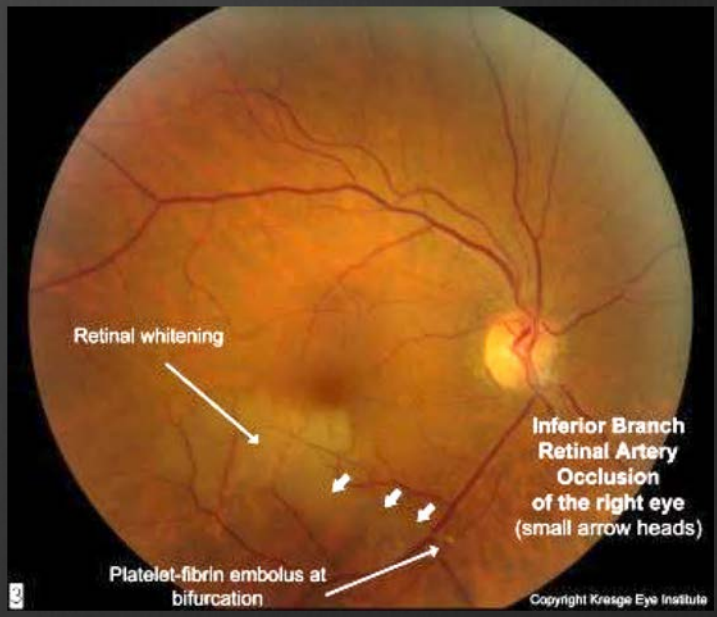
Branch retinal arterial occlusion

- Branch occlusion rather than central
- Men more than women
- Right more then left
- Temporal more than nasal
- Sudden, painless altitudinal field loss
- White swollen retina along territory of occluded arterial branch, emboli visible in 60% of cases

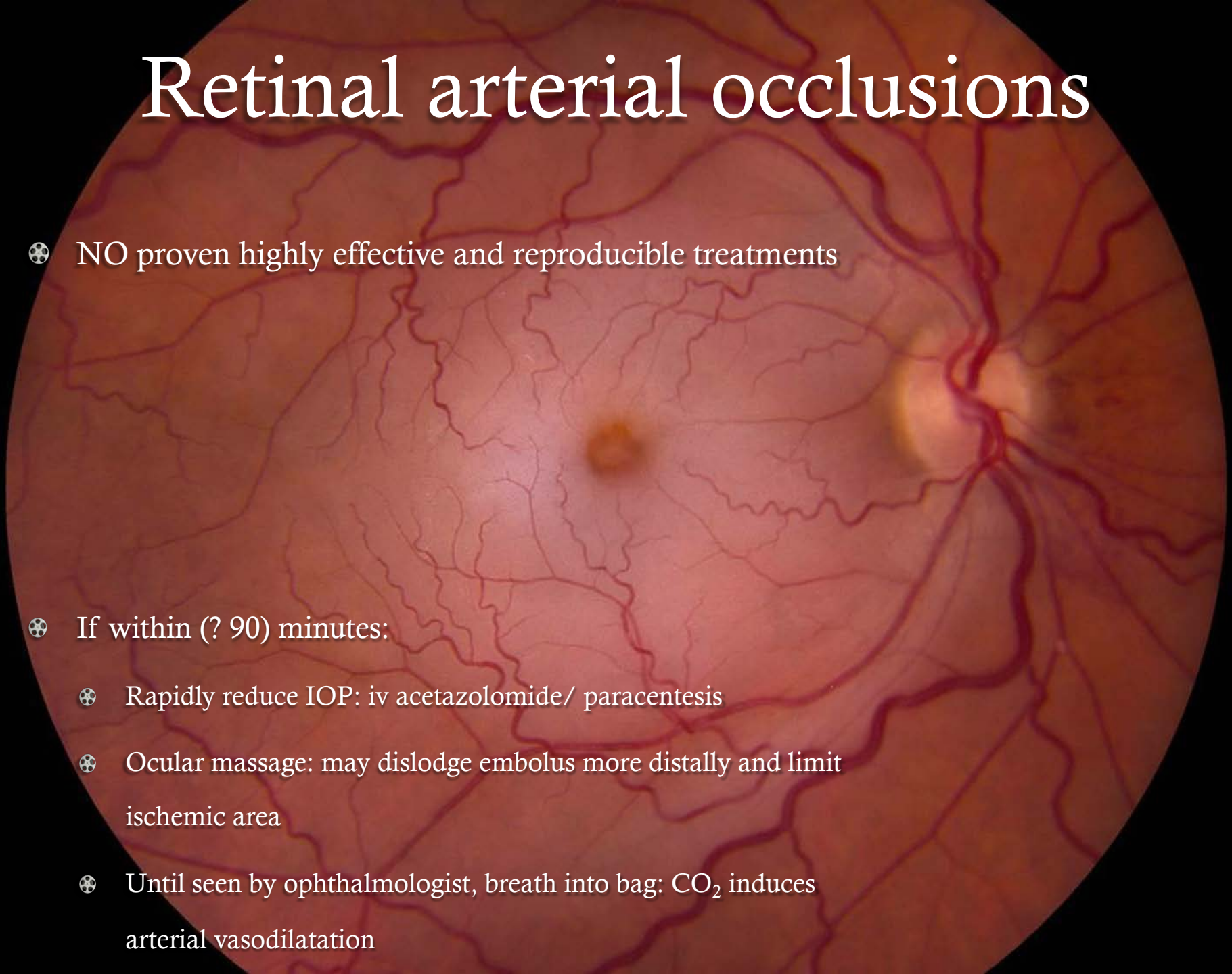
Branch retinal arterial occlusion

- EMBOLIC > THROMBOTIC (unlike CRAO)
  - Cholesterol (Hollenhorst plaque)
    - yellow/orange, not always result in complete occlusion, cardiac/ carotid stenosis
  - Calcific
    - Solid white, non-refractile, calcification of heart valves or aorta
  - Fibrinoplatelet
    - Long, smooth white intraretinal plugs, may be mobile and break up over time, carotid or cardiac thrombosis
- 80% recover to 6/12 or better
- Visual field loss permanent
- Neovascularisation very rare





Retinal arterial occlusions



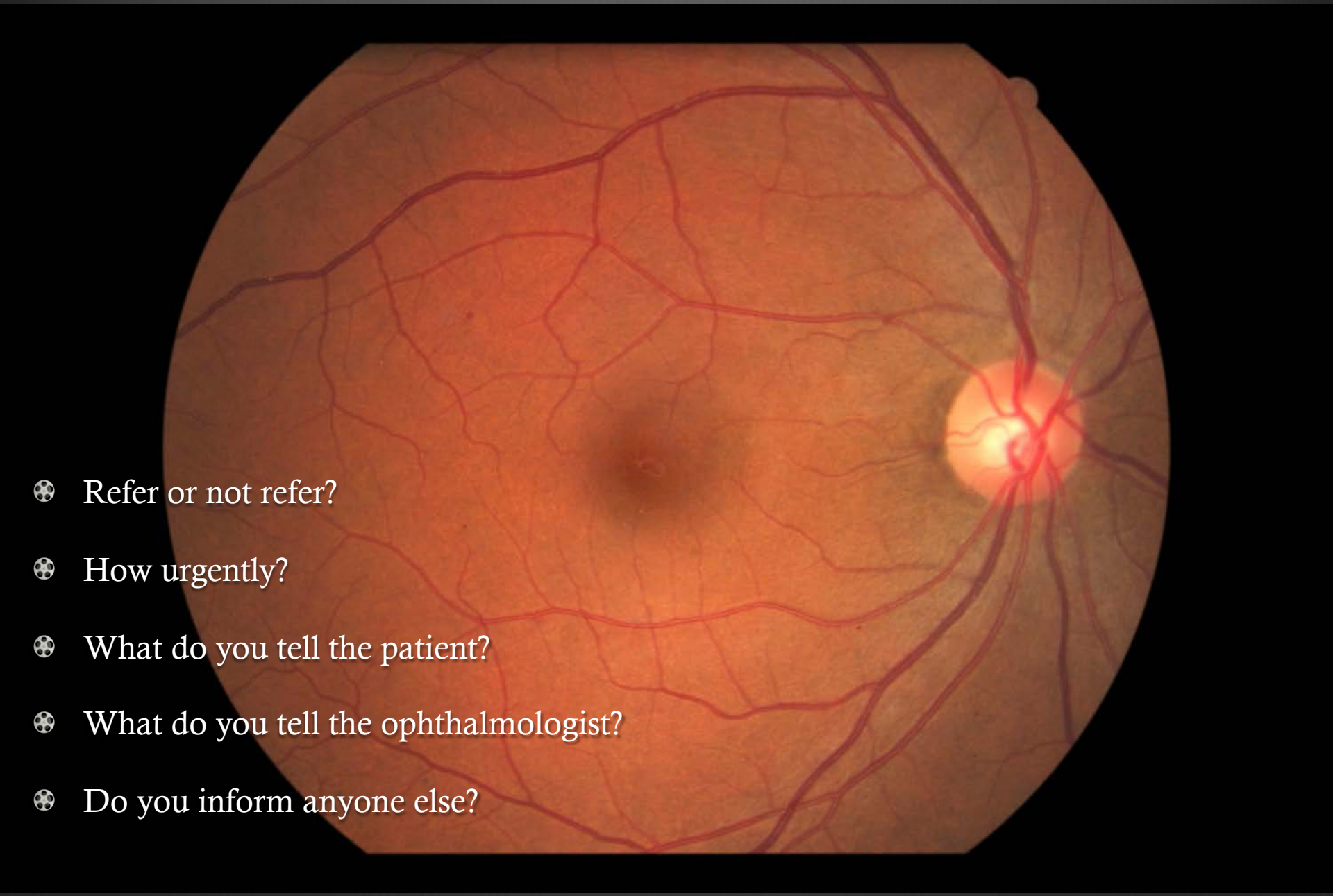
- NO proven highly effective and reproducible treatments

- If within (? 90) minutes:
  - Rapidly reduce IOP: iv acetazolomide/ paracentesis
  - Ocular massage: may dislodge embolus more distally and limit ischemic area
  - Until seen by ophthalmologist, breath into bag: CO_2 induces arterial vasodilatation

Retinal arterial occlusion occlusion – Optometric management

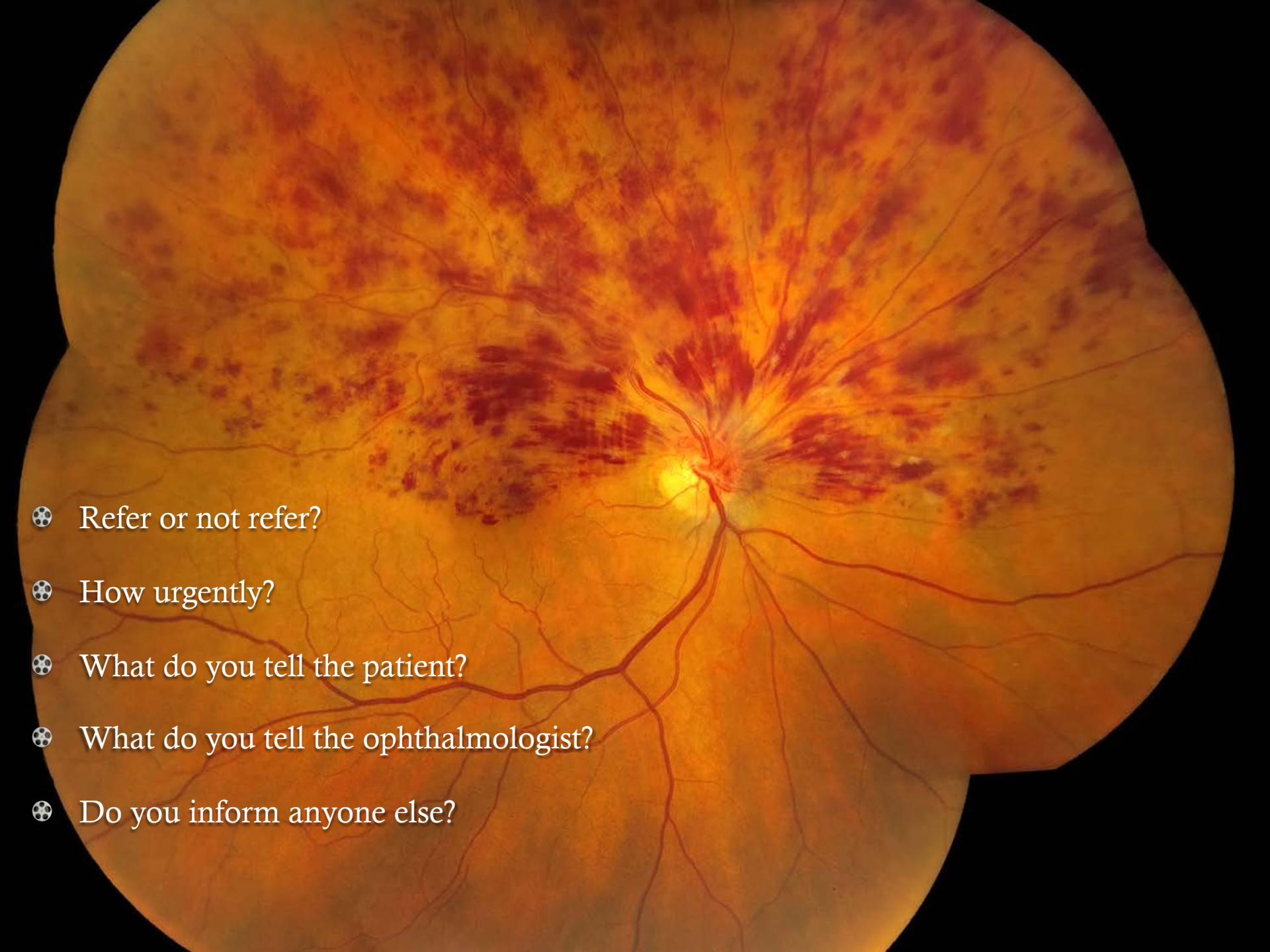
- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?
- BRAO not involving temporal artery?
- BRAO involving the temporal artery?
- CRAO
- RAO with symptoms within a few hours?
- RAO with symptoms over 12 hours?

QUIZ!



- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?

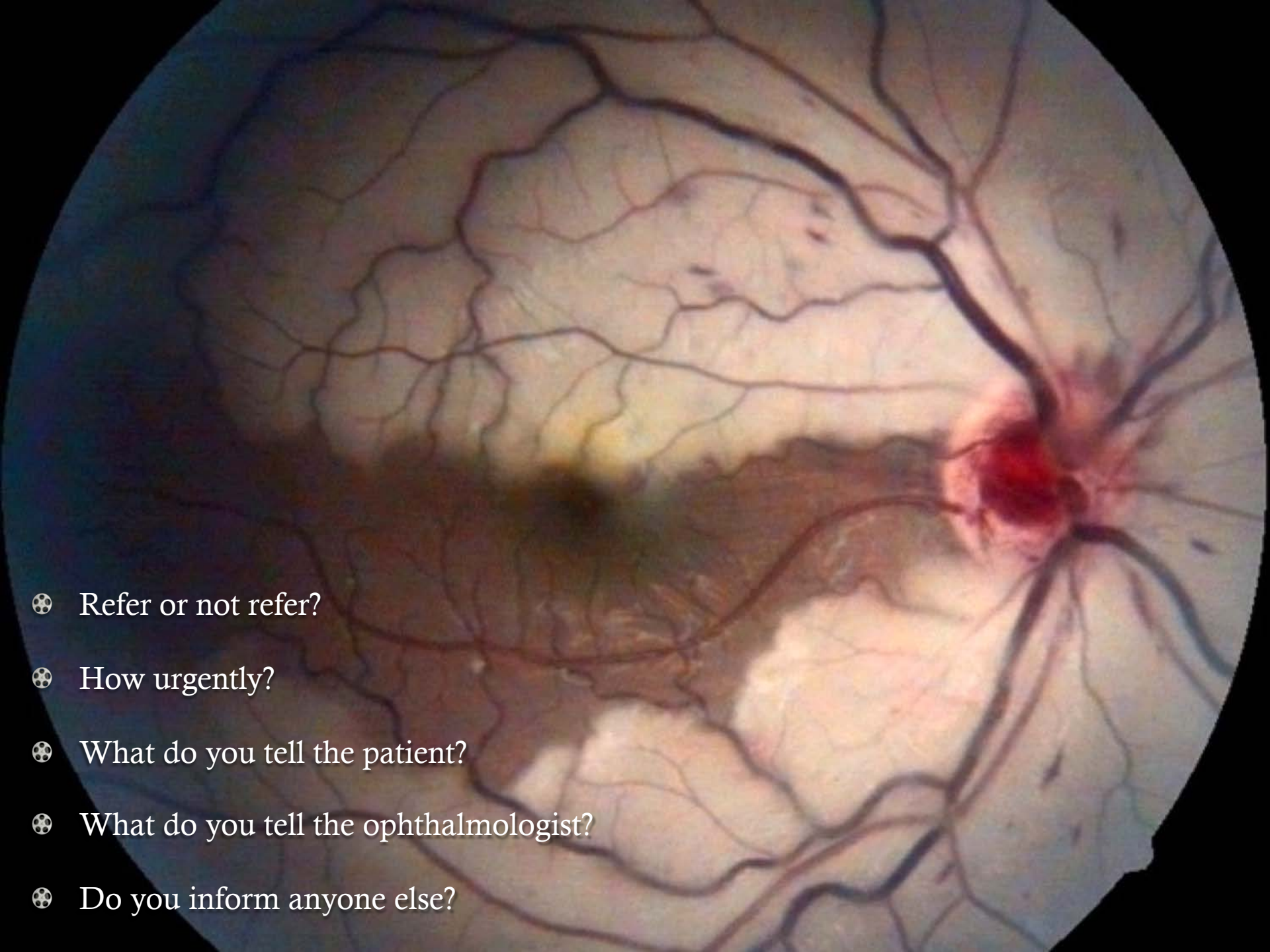
- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?



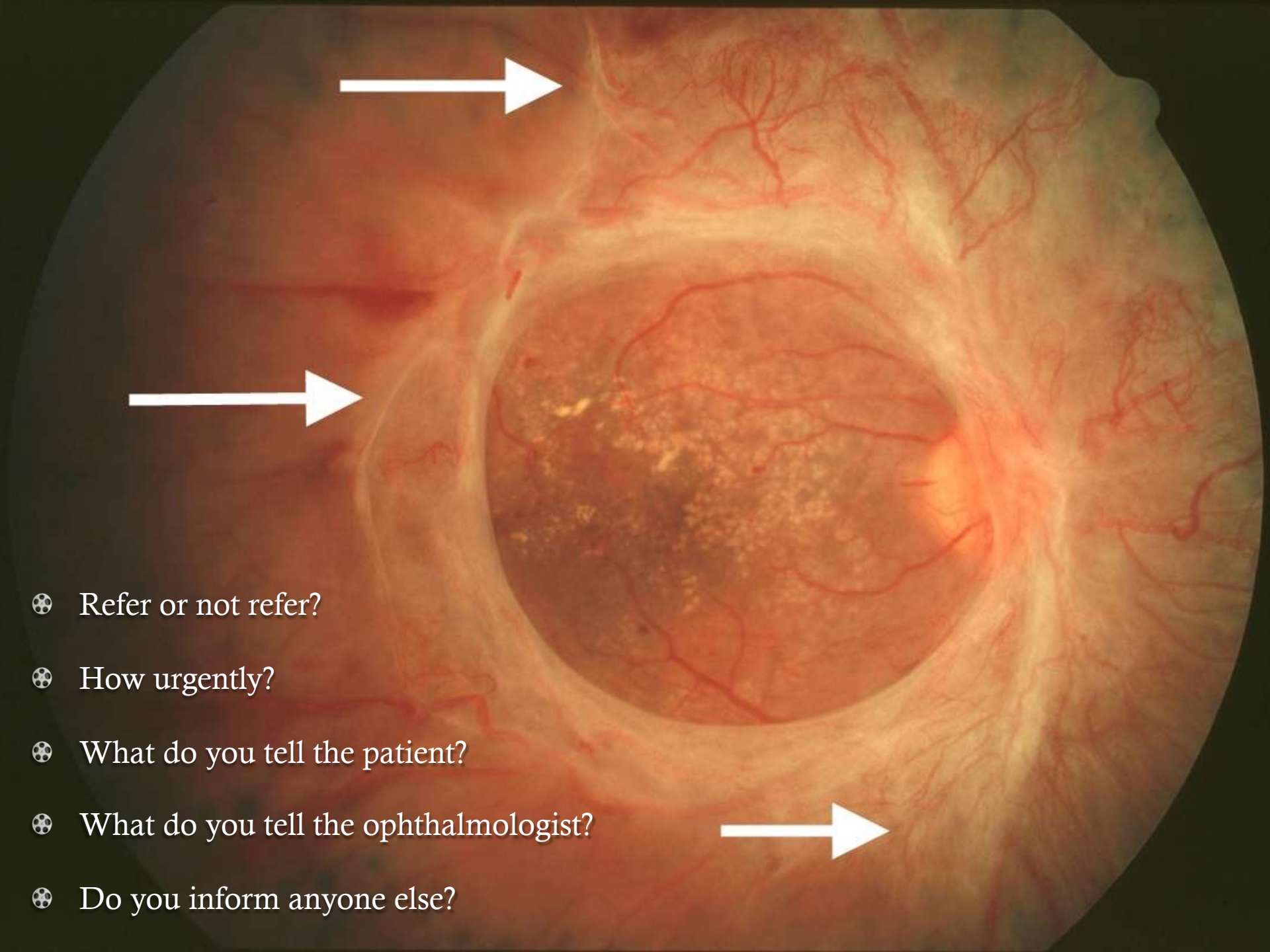
- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?

- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?

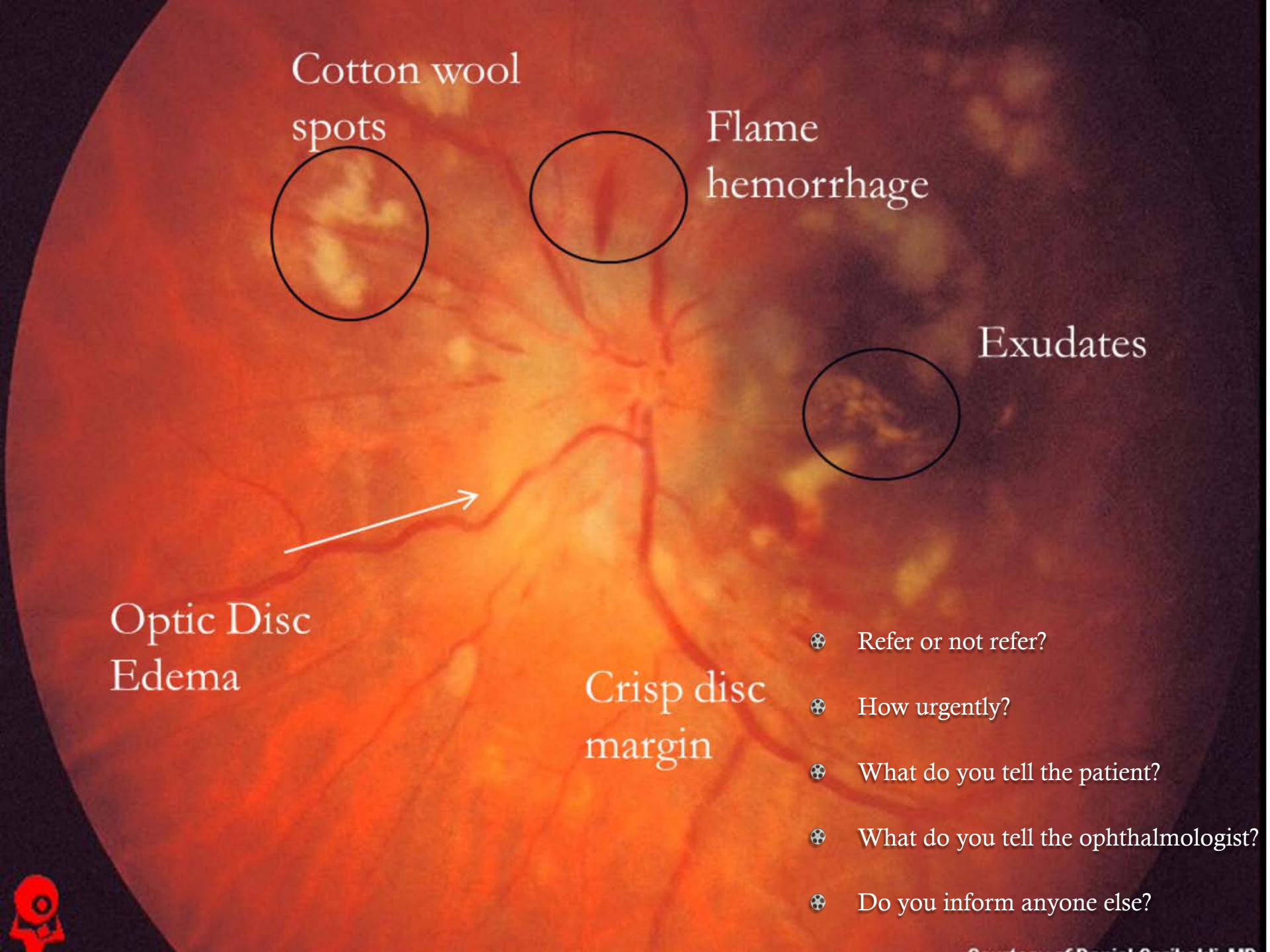
- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?



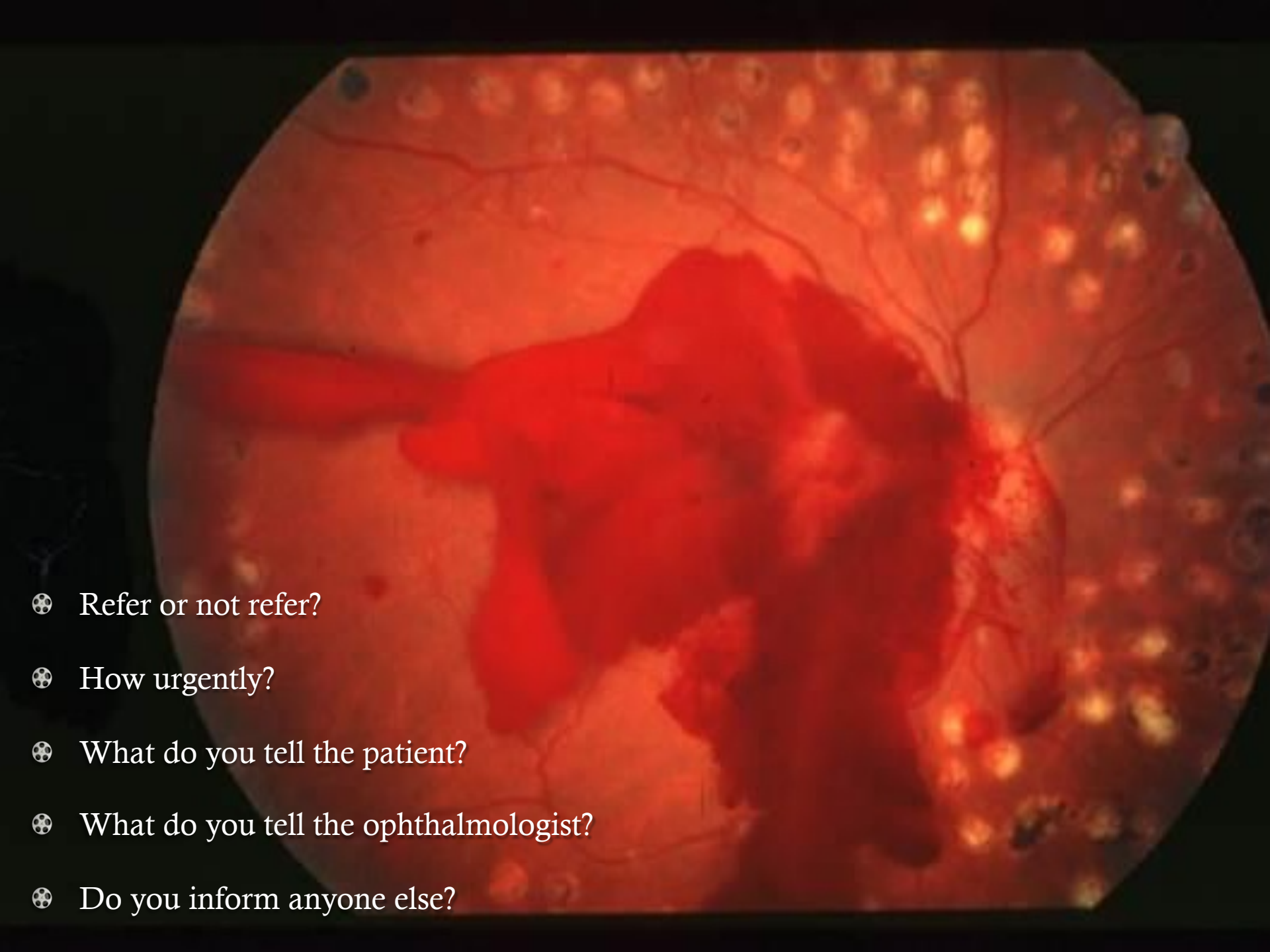
- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?



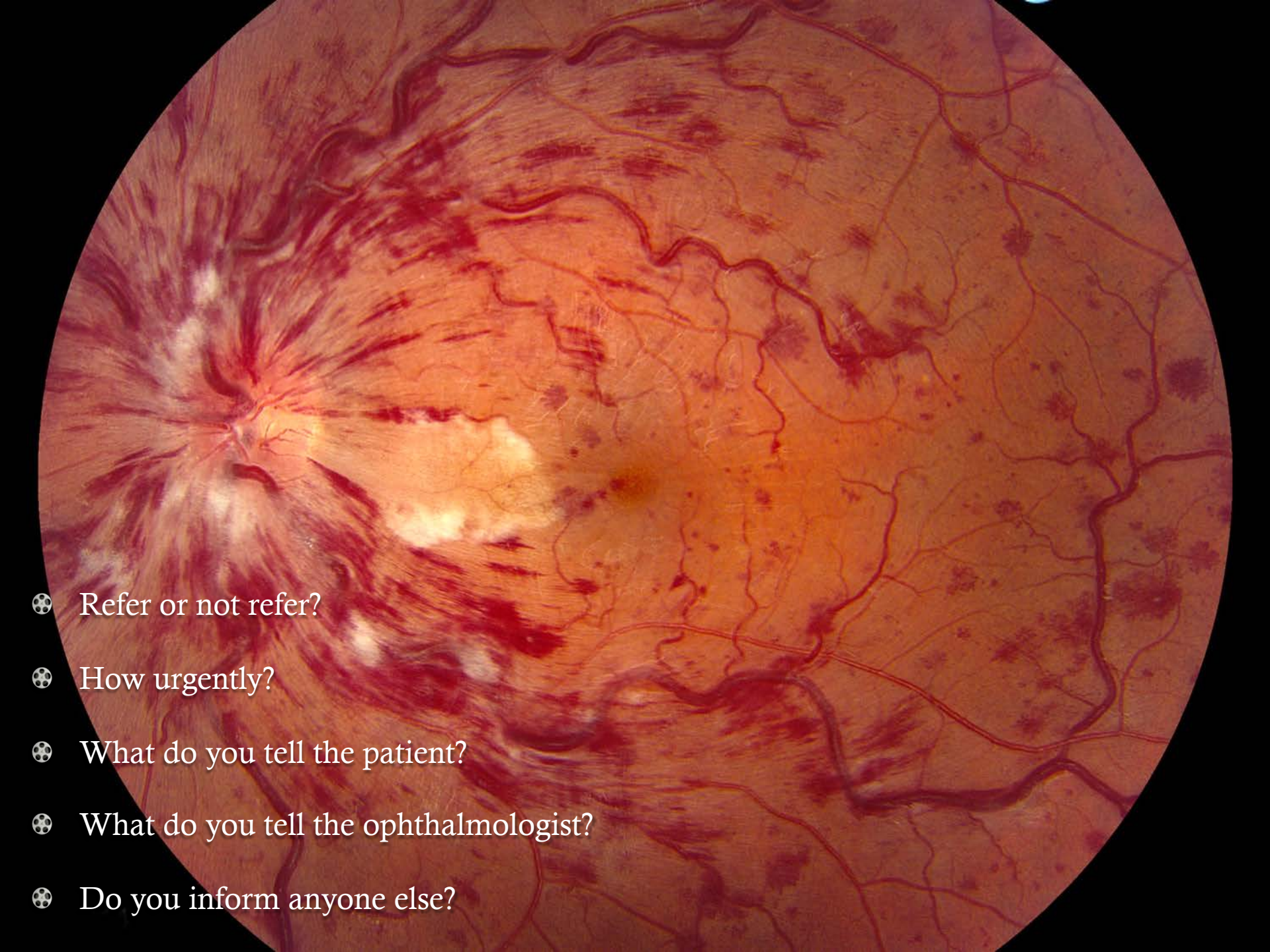
- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?



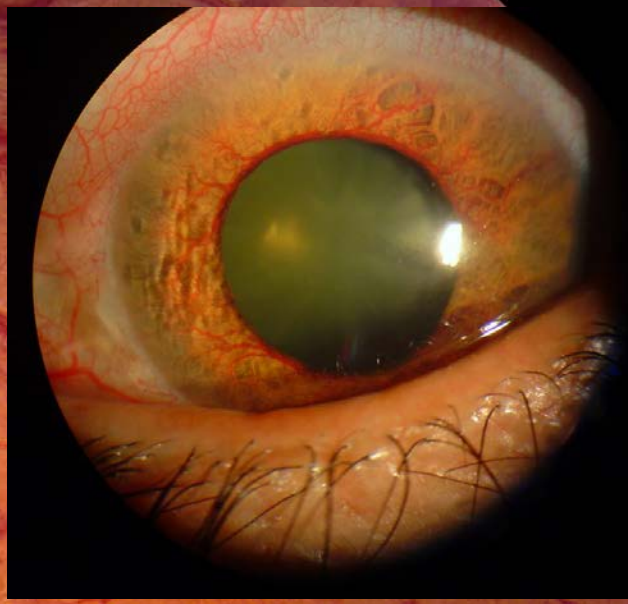
- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?



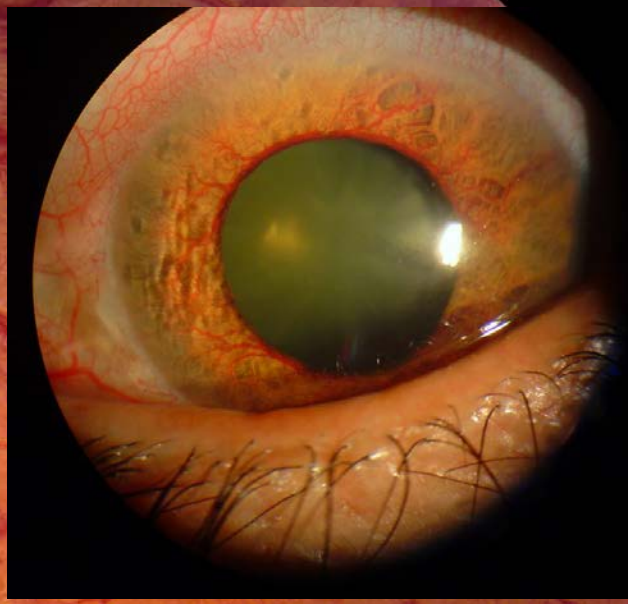
- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?



- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?



- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?



IOP 60mmHg

- Refer or not refer?
- How urgently?
- What do you tell the patient?
- What do you tell the ophthalmologist?
- Do you inform anyone else?

Conclusion

- Dramatic change in management and prognosis of patients with common medical retina conditions
- Intravitreal steroids and anti-VEGF agents transformed MR landscape (and created many medical retina consultant posts!)
- Newer therapies in pipeline to address limitations of current therapies
- Important to recognise key retinal vascular conditions in your practices and exercise appropriately timed referrals
- Exciting times!

Consultations for cataract surgery and all medical and surgical retinal conditions

New Dedicated Floaters Assessment and Treatment Clinics at

Spire Hospital Little Aston
Nuffield Hospital, Wolverhampton
Rowley Hall Hospital, Stafford

by Mr Kam Balaggan

Nuffield Health
For the love of life®

Spire Little Aston Hospital

Optegra
EYE HEALTH CARE

Optometry 2018
Tomorrow

MR KAM BALAGGAN

Consultant Eye Surgeon

Medical and Surgical Retina

kambalaggan@yahoo.co.uk

Mr Kam Balaggan – Consultant Ophthalmic Surgeon

@MrKamBalaggan

For requests to attend VR clinic/theatre, advice and referrals: surgeon@kambalaggan.com