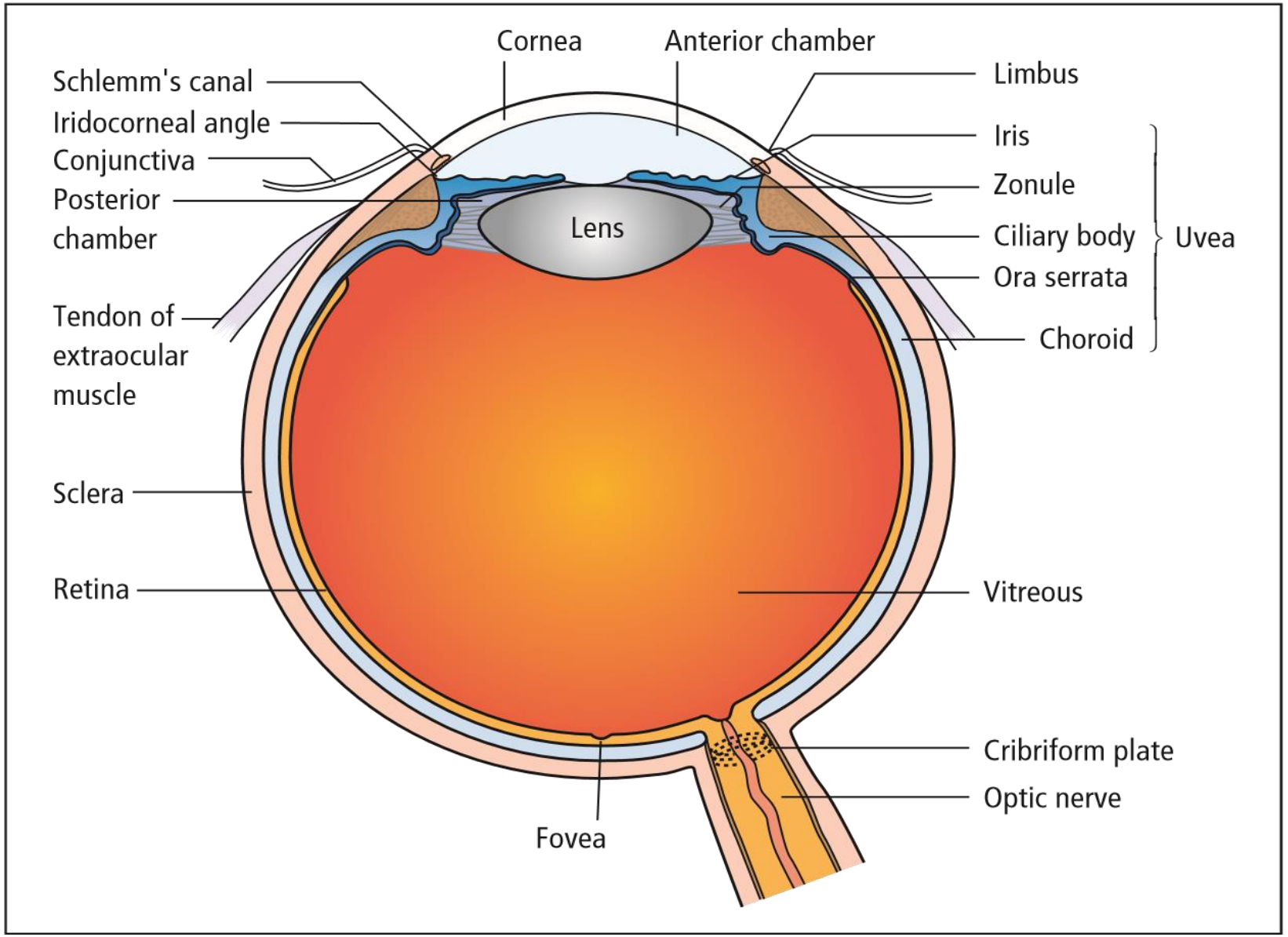
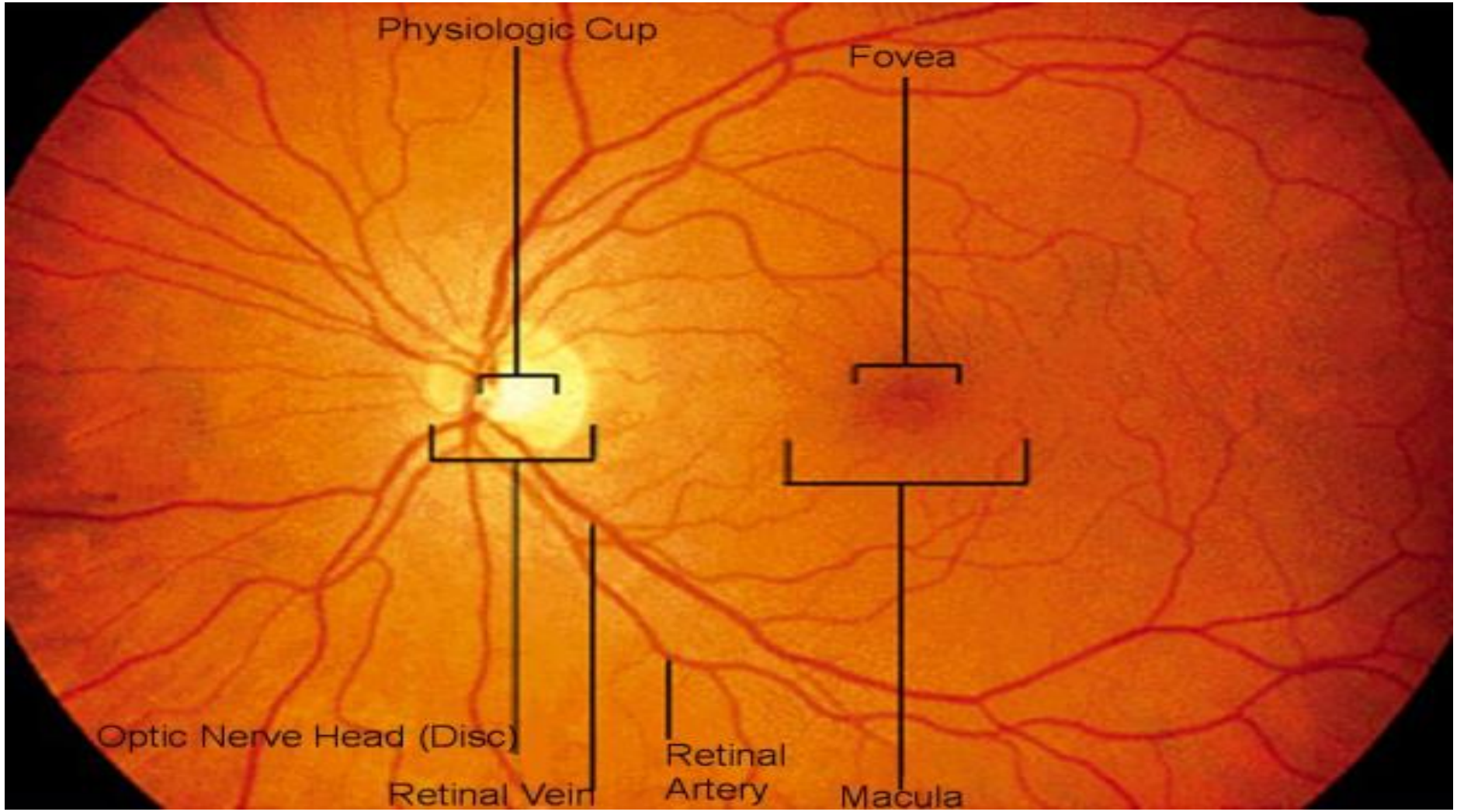
RETINAL VASCULAR DISEASES

ANATOMY


Cornea
Anterior chamber
Schlemm's canal
Limbus
Iridocorneal angle
Iris
Conjunctiva
Zonule
Posterior chamber
Lens
Ciliary body
Uvea
Ora serrata
Tendon of extraocular muscle
Choroid
Sclera
Retina
Vitreous
Cribriform plate
Optic nerve
Fovea

GROSS ANATOMY



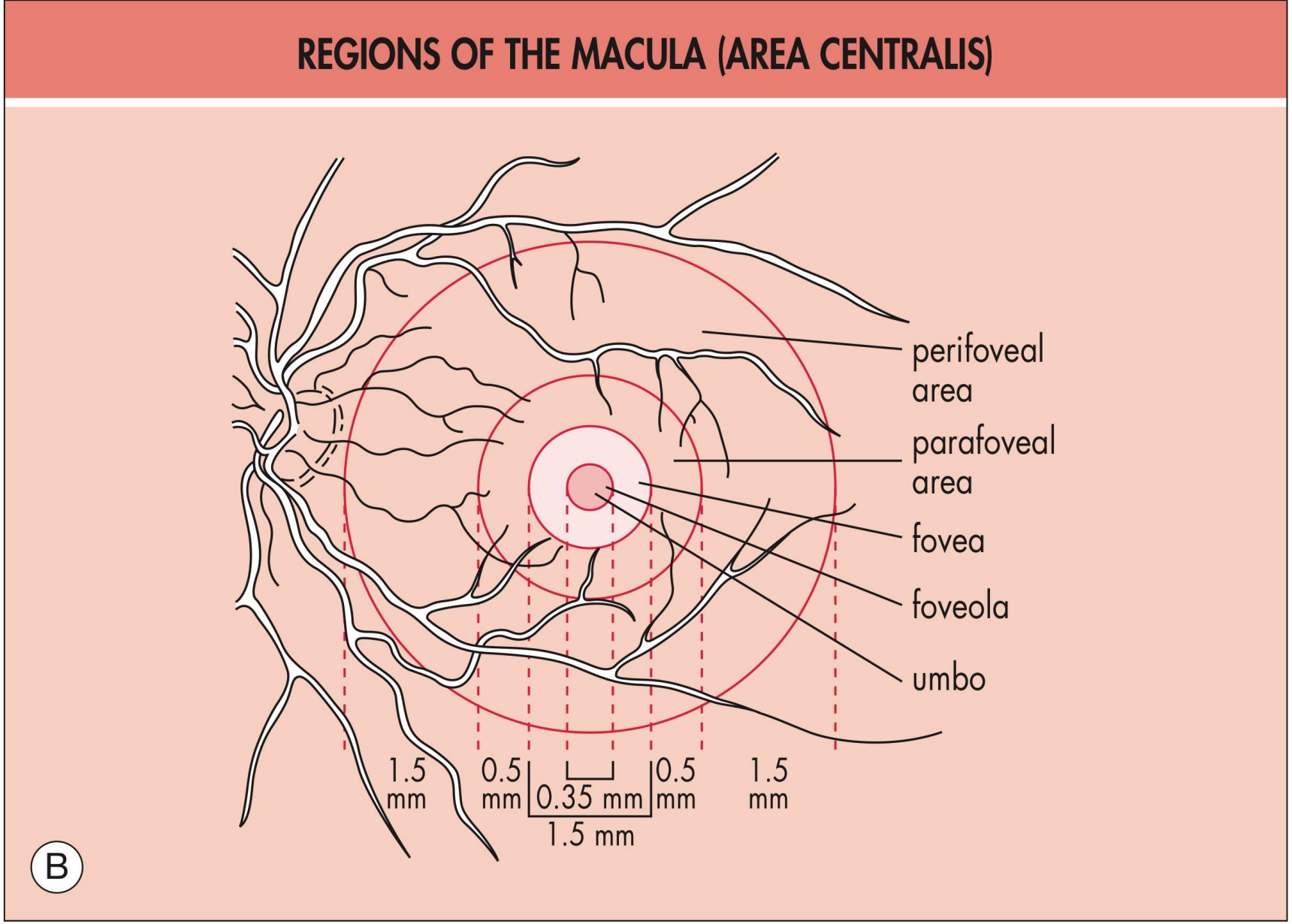


Fig. 6-1-7 Normal fundus with macula encompassed by major vascular arcades.
The macula, or central area, has the following components from center to periphery: umbo, foveola, fovea, parafovea, and perifovea.

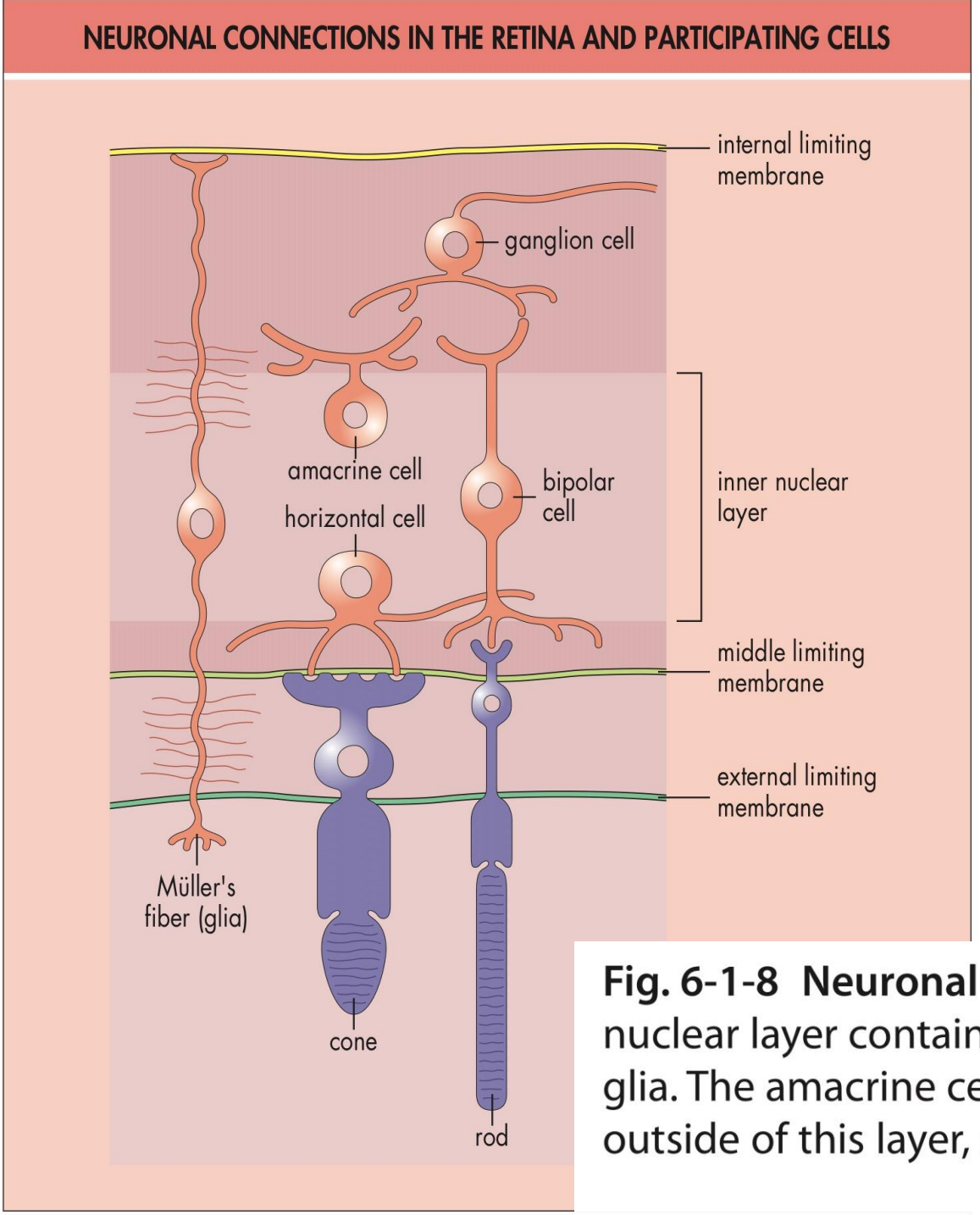
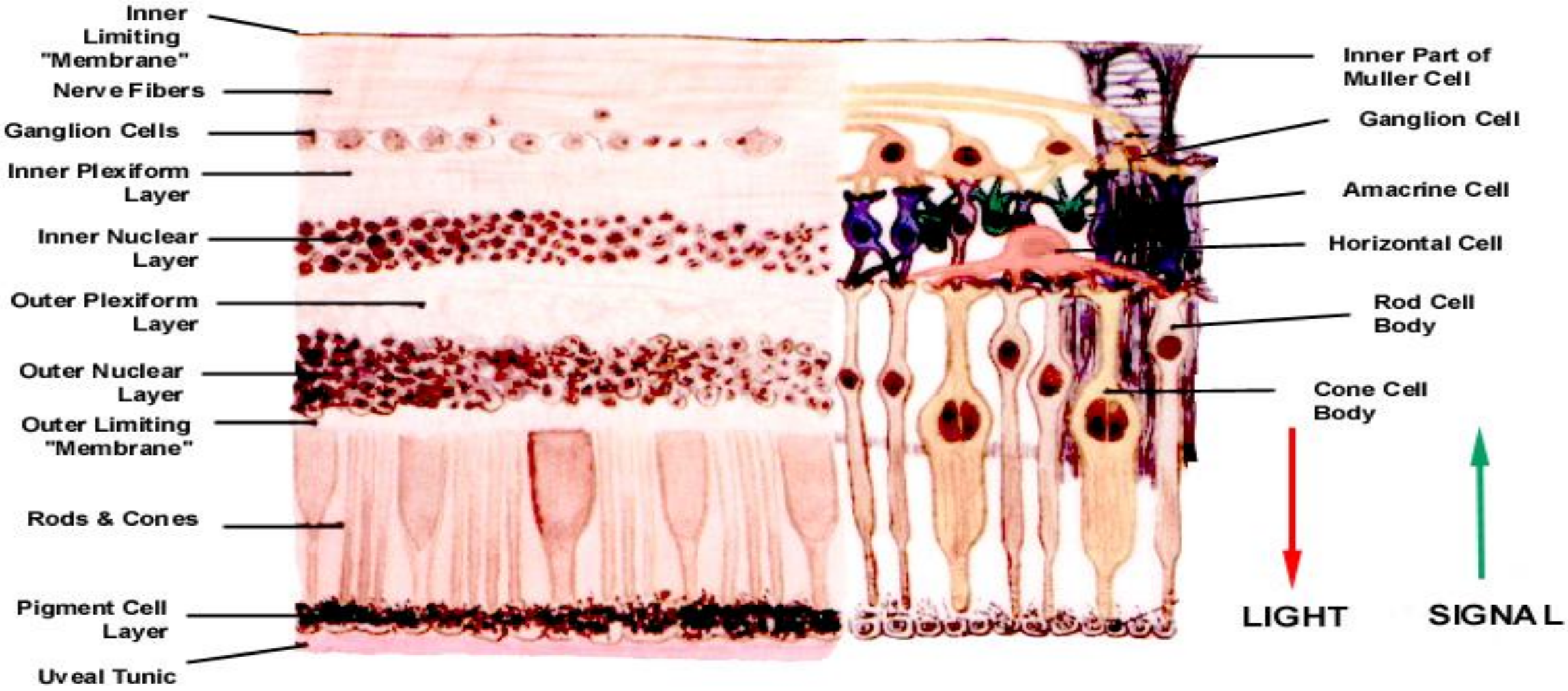
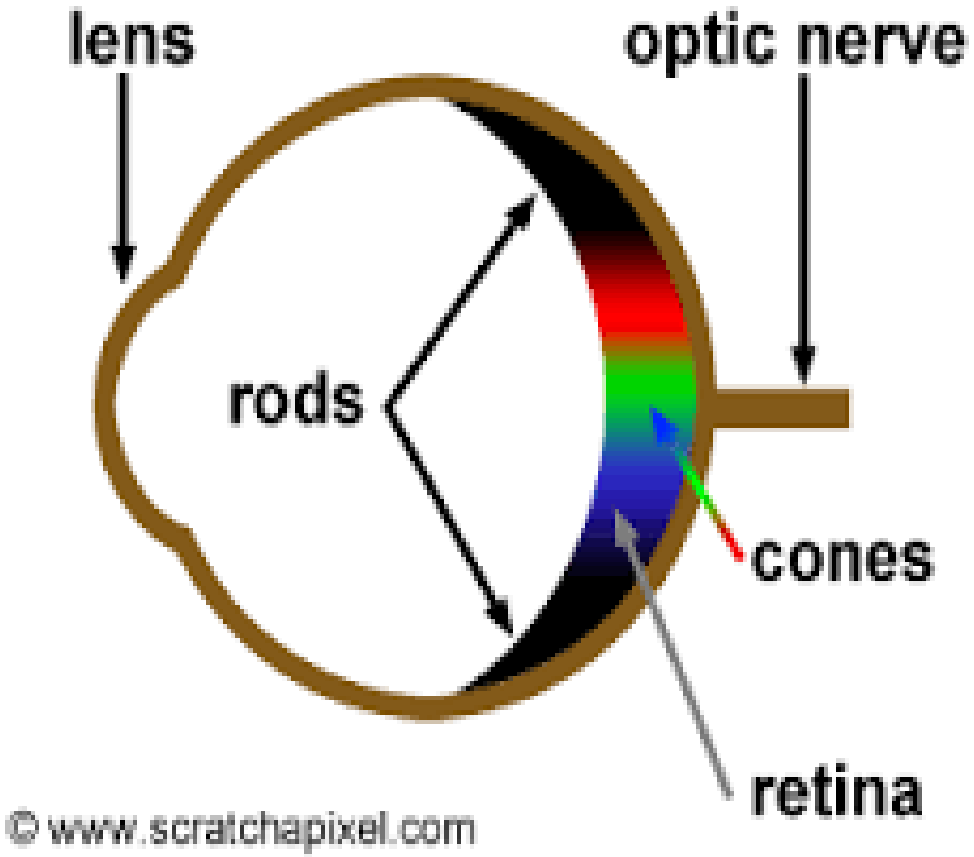


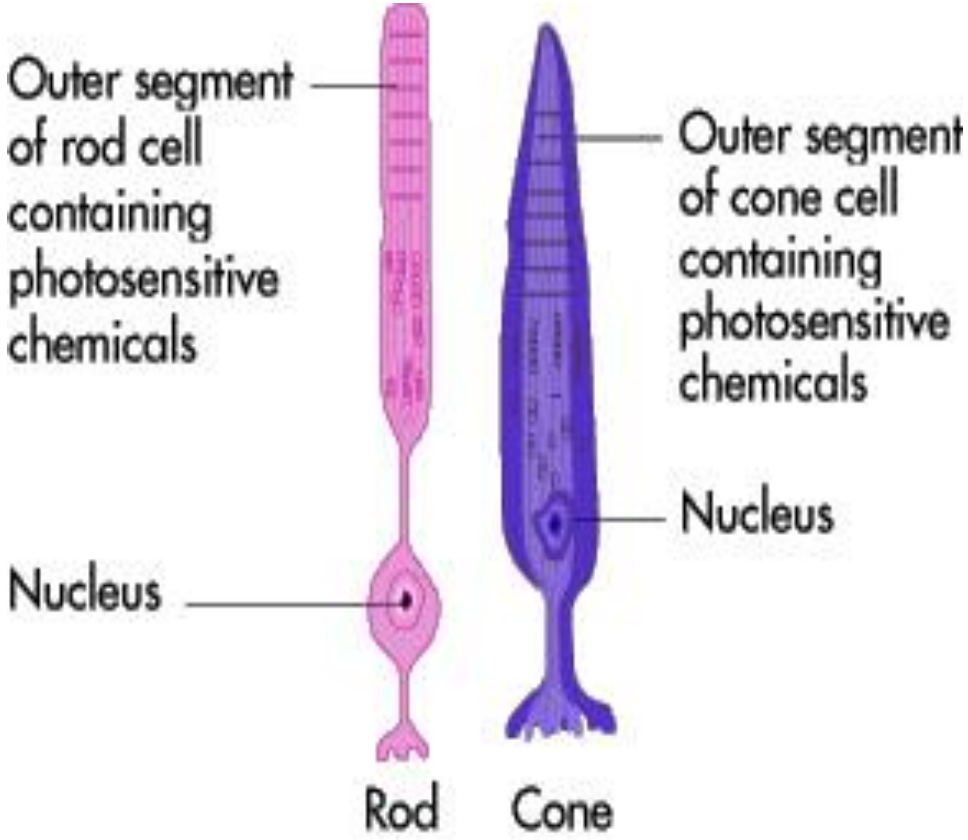
Fig. 6-1-8 Neuronal connections in the retina and participating cells. The inner nuclear layer contains the nuclei of the bipolar cells (second neuron) and Müllerian glia. The amacrine cells are found on the inside and the horizontal cells on the outside of this layer, next to their respective plexiform connections.

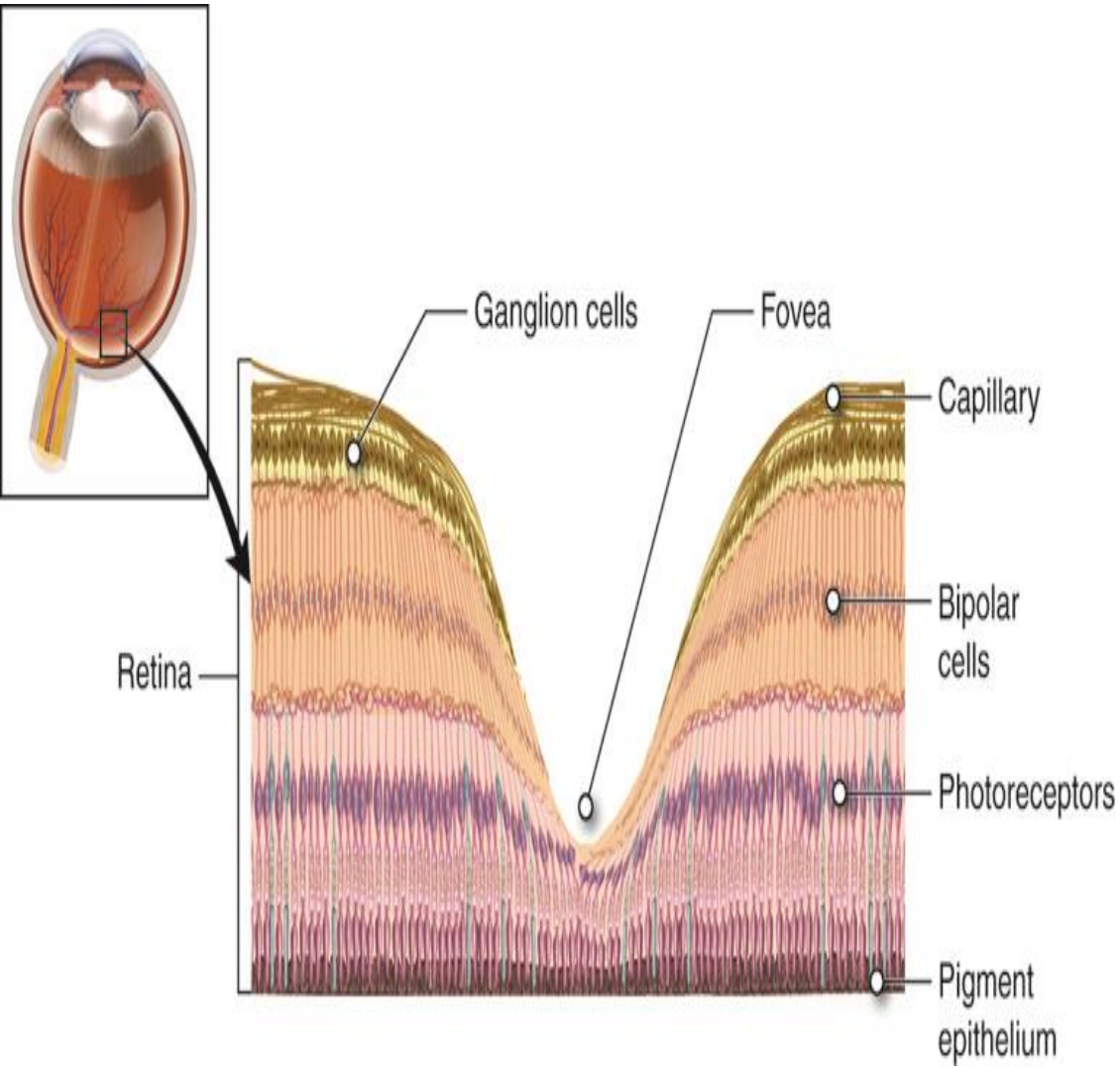
LAYERS OF THE RETINA

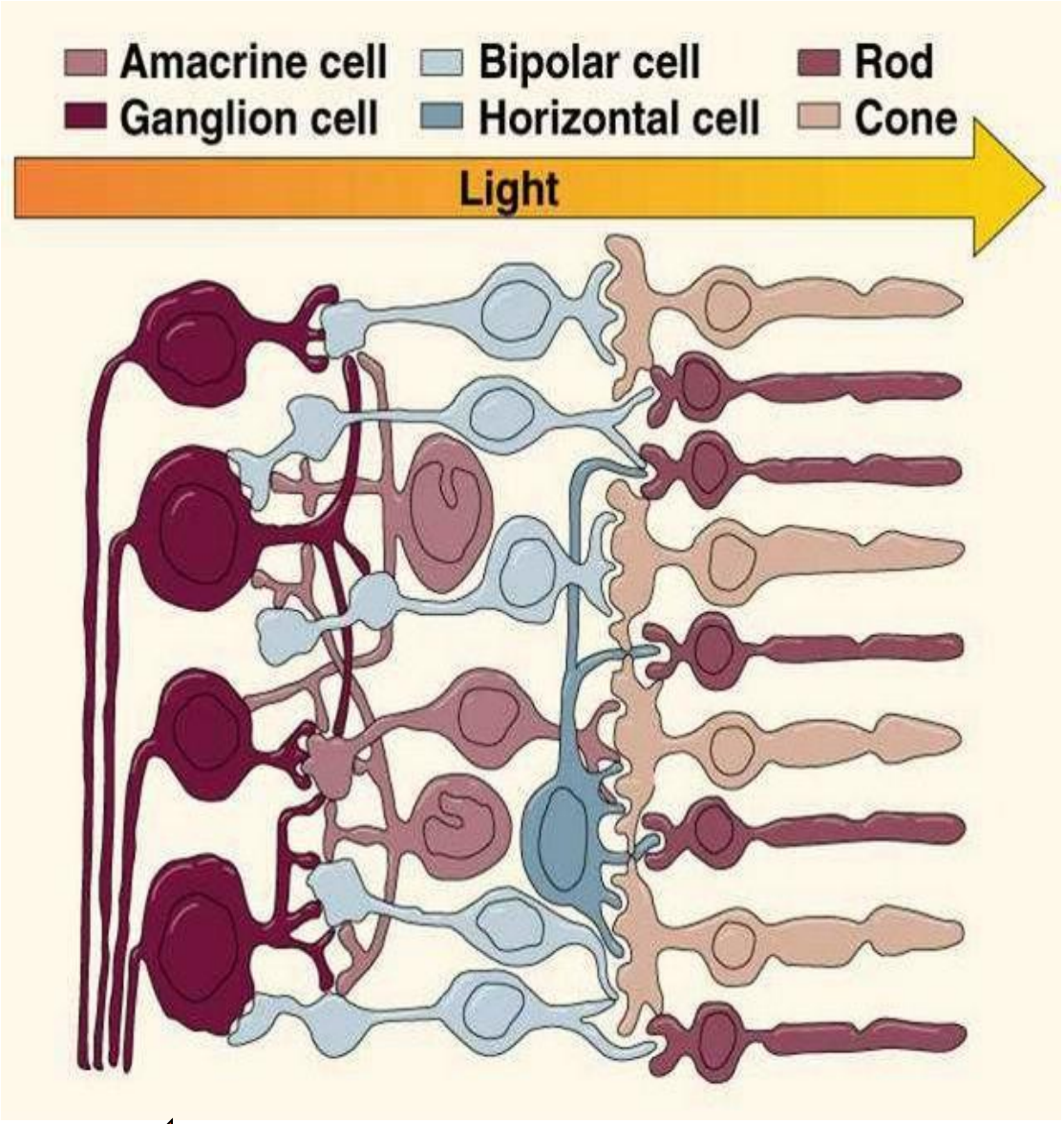


PHYSIOLOGY OF THE RETINA









Visual processing

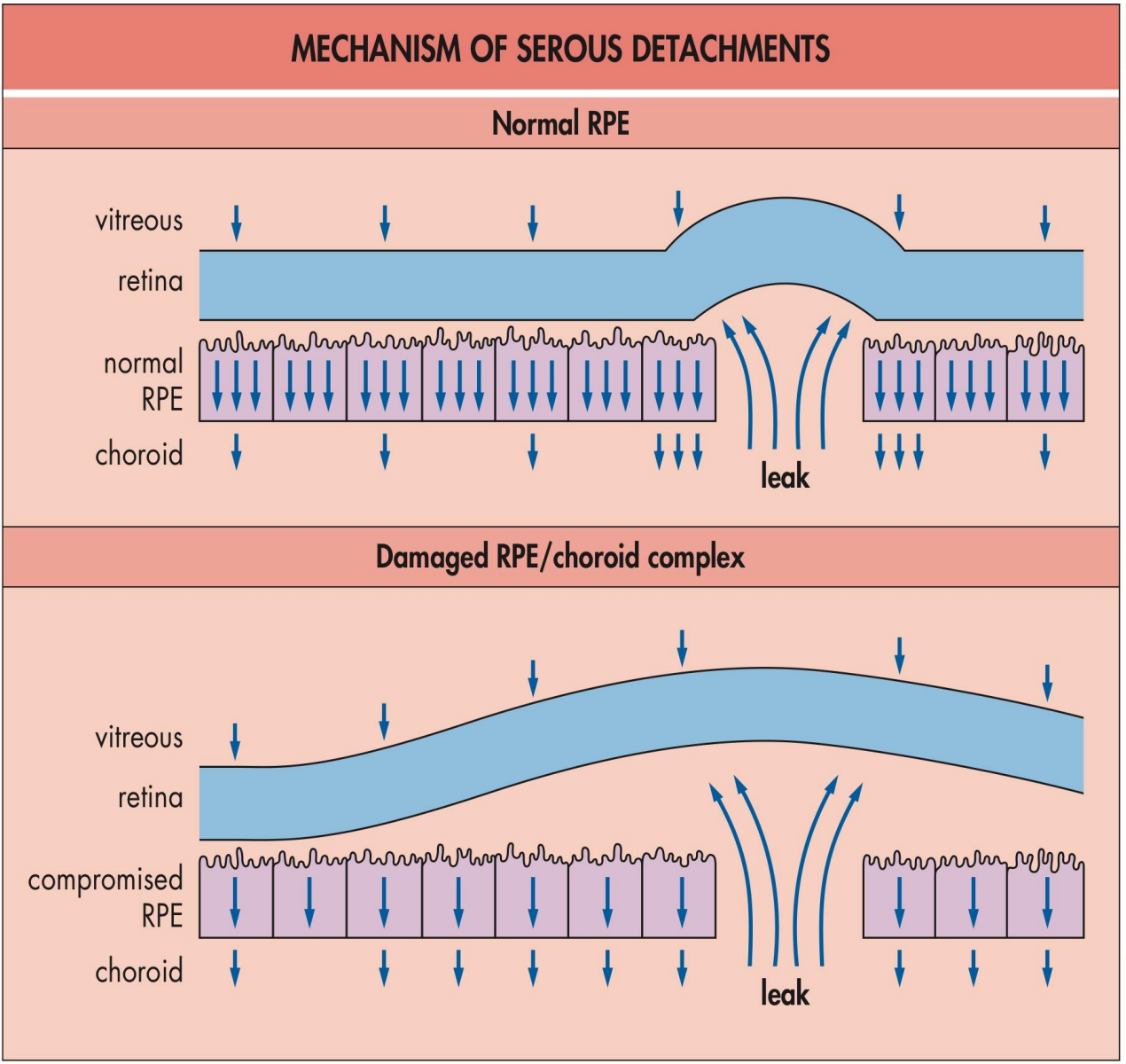


Fig. 6-2-2 Mechanism of serous detachment. When the retinal pigment epithelium (RPE) is normal, no serous detachment occurs beyond a focal site of leakage. When the RPE is compromised by choroidal or RPE disease that impairs outward fluid transport, a serous detachment forms until absorption across the exposed RPE balances the inward leak.

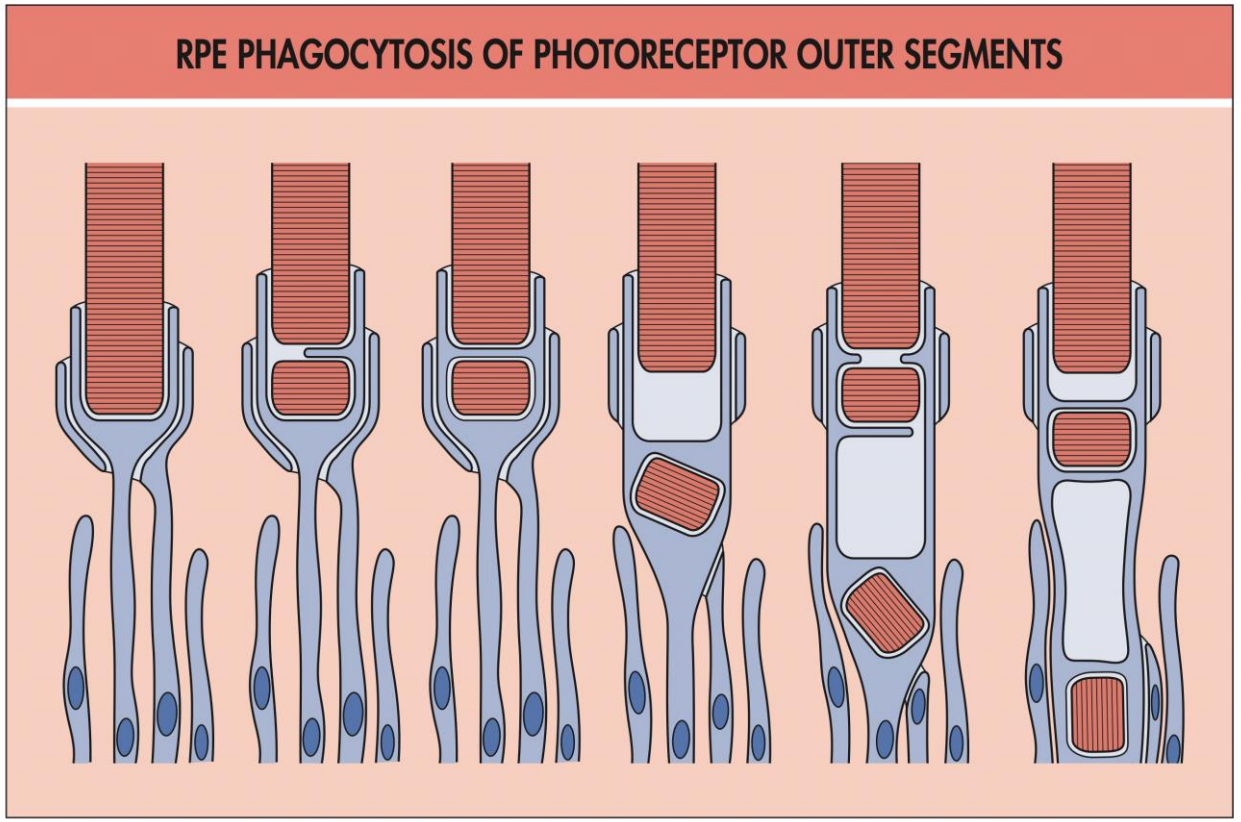
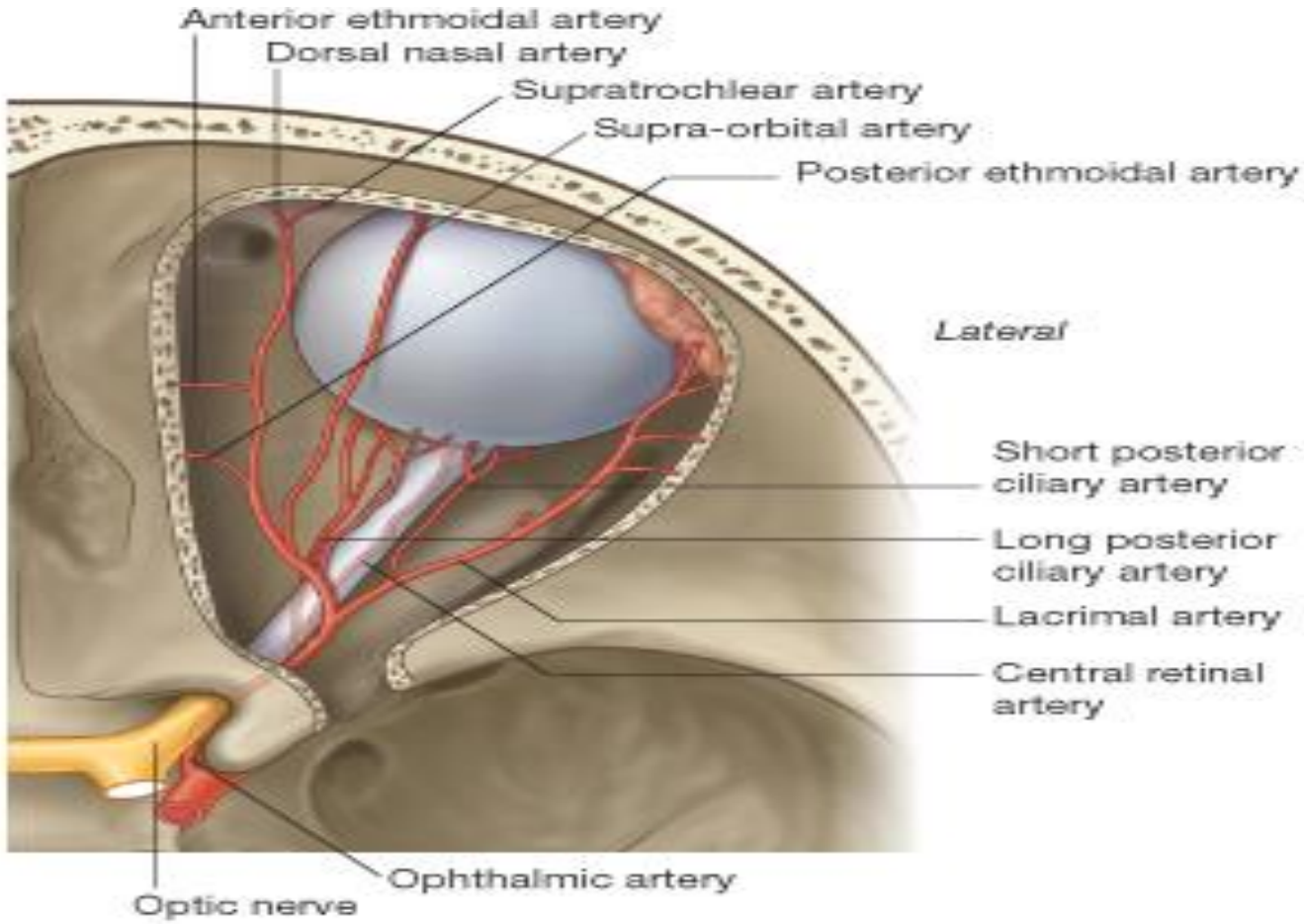
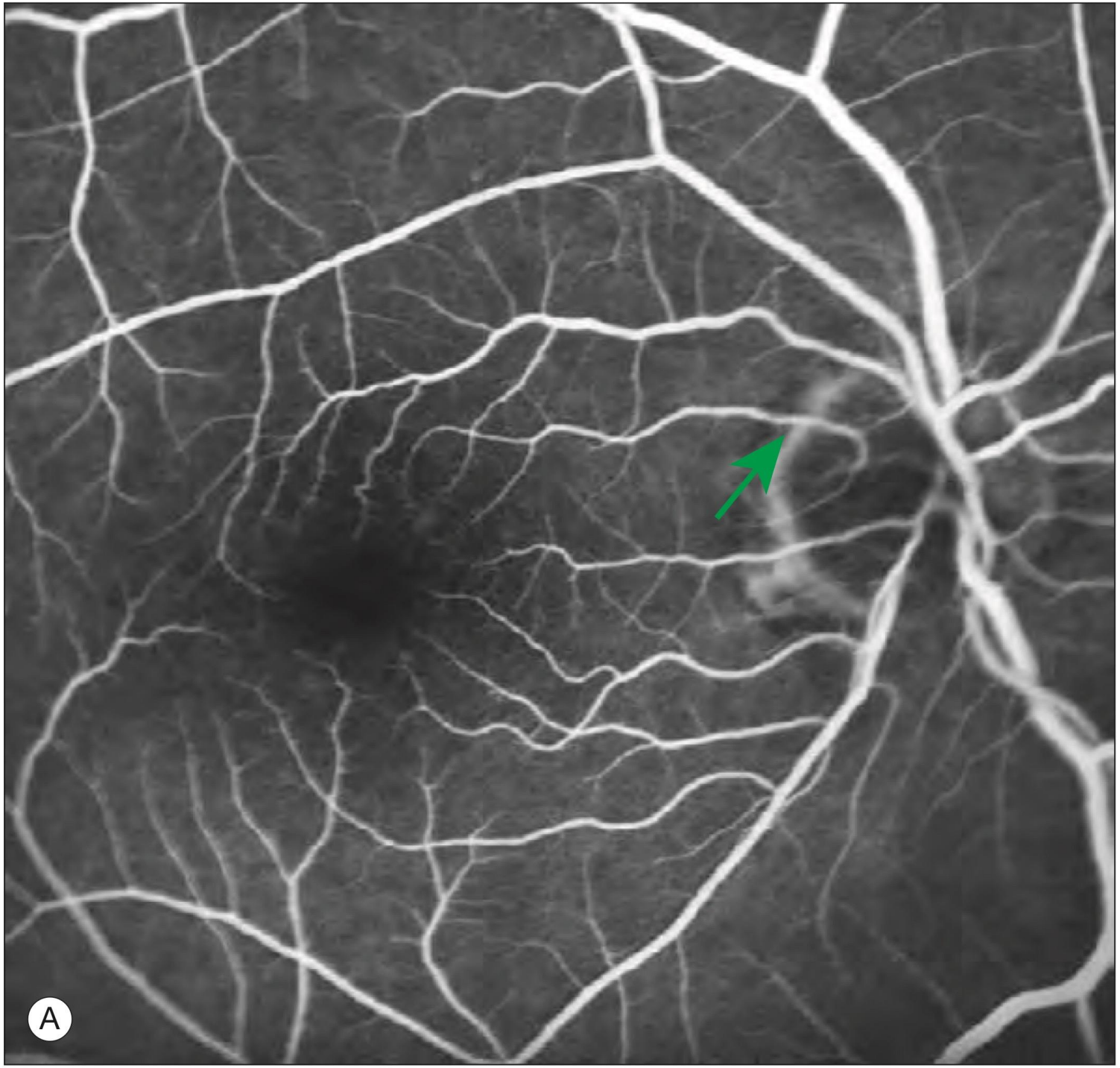


Fig. 6-2-3 Retinal pigment epithelium (RPE) phagocytosis of photoreceptor outer segments. The phagosome, containing the ingested material, enters the RPE cytoplasm, where it merges with lysosomes to facilitate digestion of the outdated membranes. (Adapted from Steinberg H, Wood I, Hogan MJ. Pigment epithelial ensheathment and

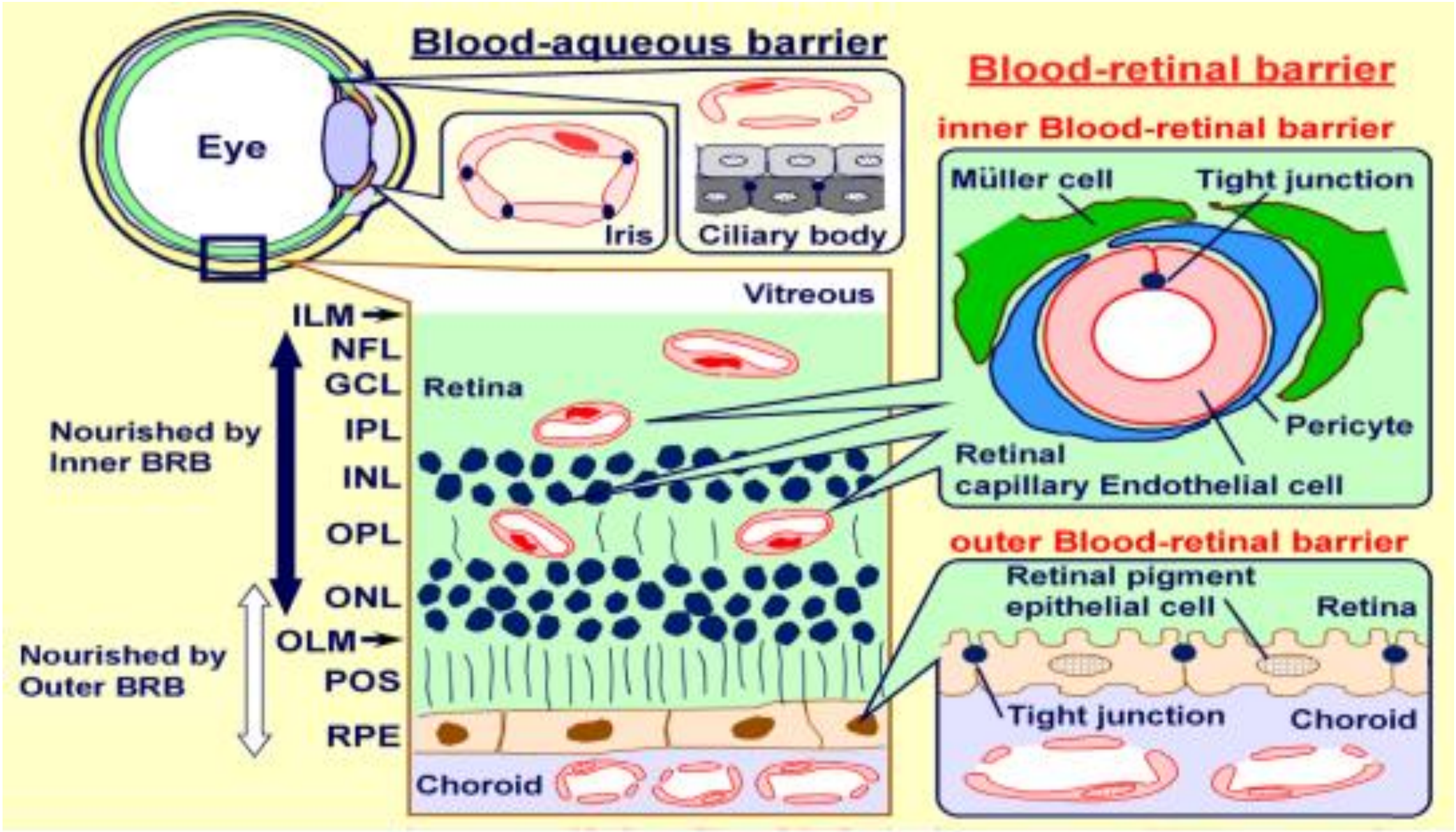
RETINAL BLOOD SUPPLY




Ophthalmic
Central
Retinal
Superior



Normal fluorescein angiogram shows the normal filling of retinal arteries and veins



Schematic diagram of the blood-ocular barrier

Classification of disease affecting the ocular circulation :

- Diabetic retinopathy
- Central retinal artery occlusion
- Branch retinal artery occlusion
- Central retinal vein occlusion
- Branch retinal vein occlusion
- Hypertensive retinopathy
- Retinopathy of prematurity
- Sickle cell retinopathy
- Abnormal retinal blood vessels

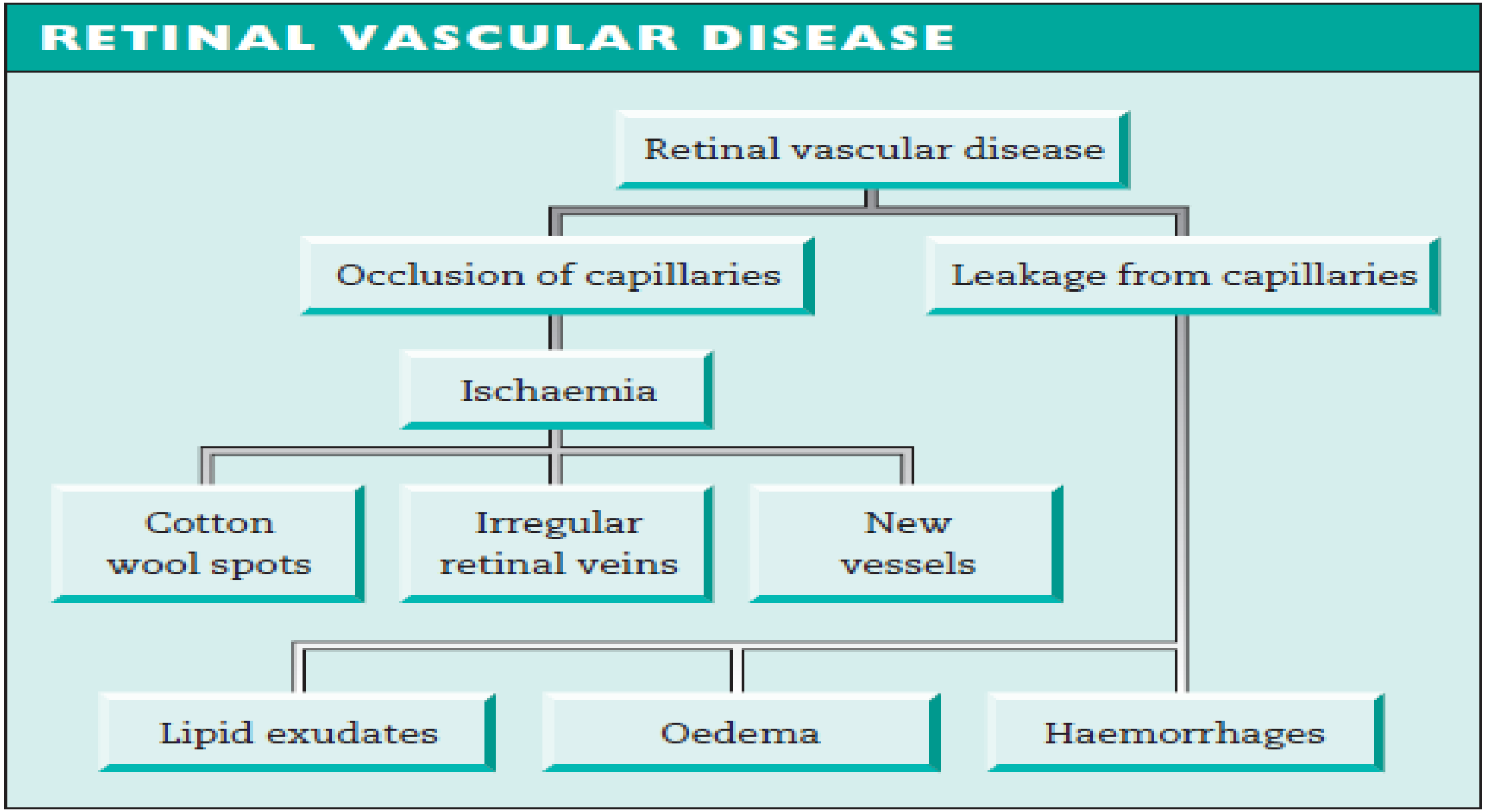


Fig. 12.1 Diagram showing the building blocks of retinal vascular disease.

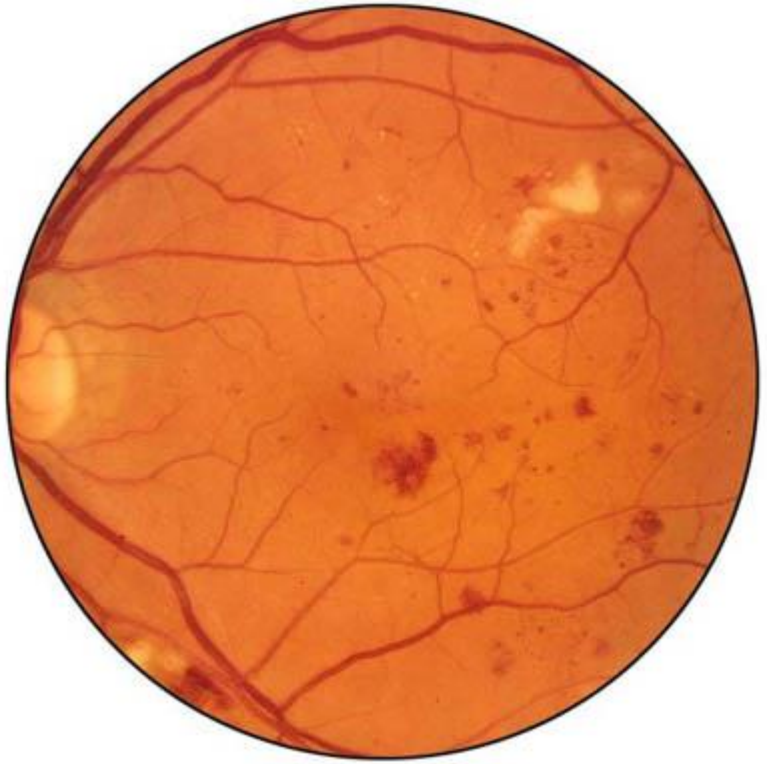
1-LEAKAGE FROM THE MICROCIRCULATION

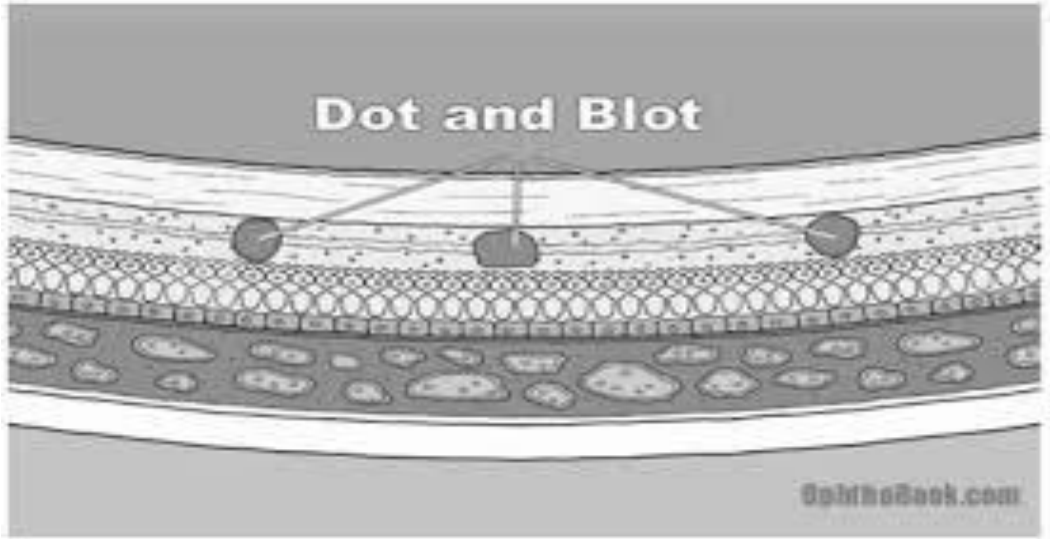
This results in:

- **1-*haemorrhages*** caused by leakage of blood from damaged vessels;
- **2-*edema* of the retina,** the result of fluid leakage from damaged vessels
- ***3-exudates*** formed by lipids, lipoprotein and lipid containing macrophages. These are yellow in color, with well-defined margins.

HEMORRHAGE

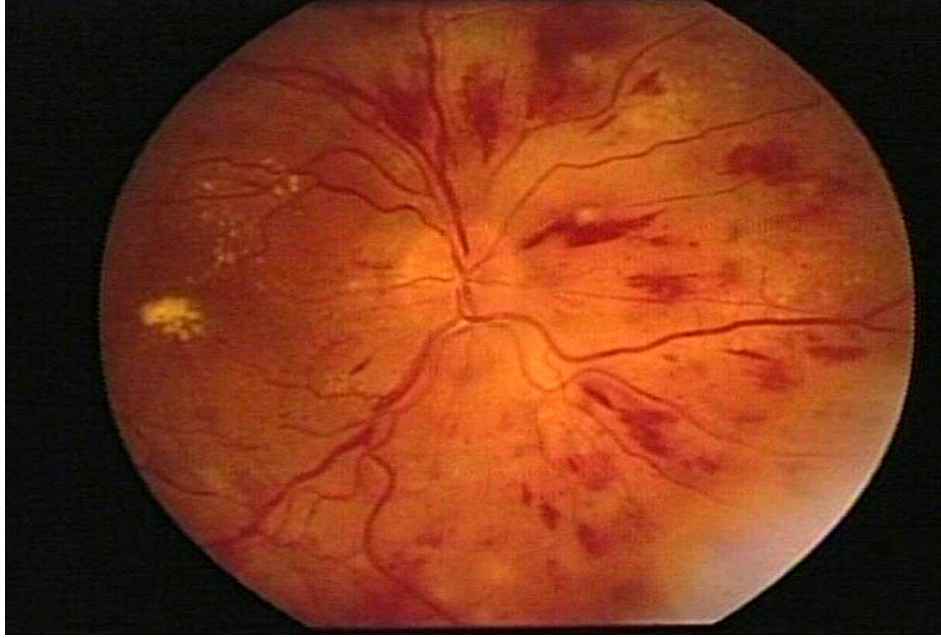
Dot –blot hemorrhage (intra-retinal hemorrhage association with DR

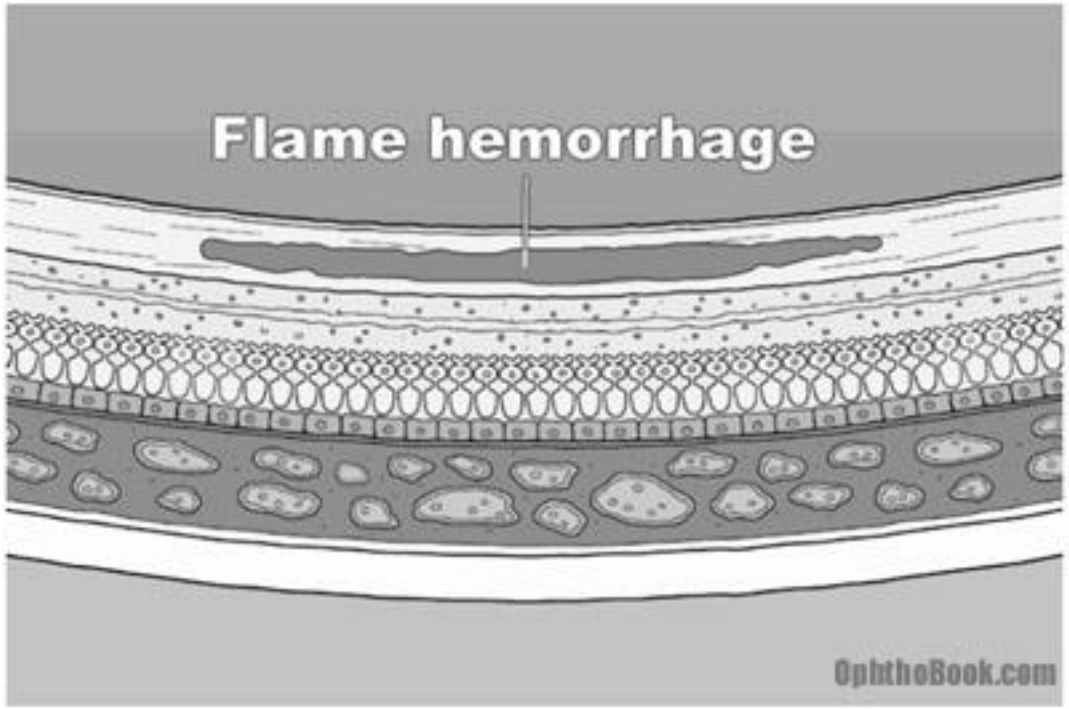




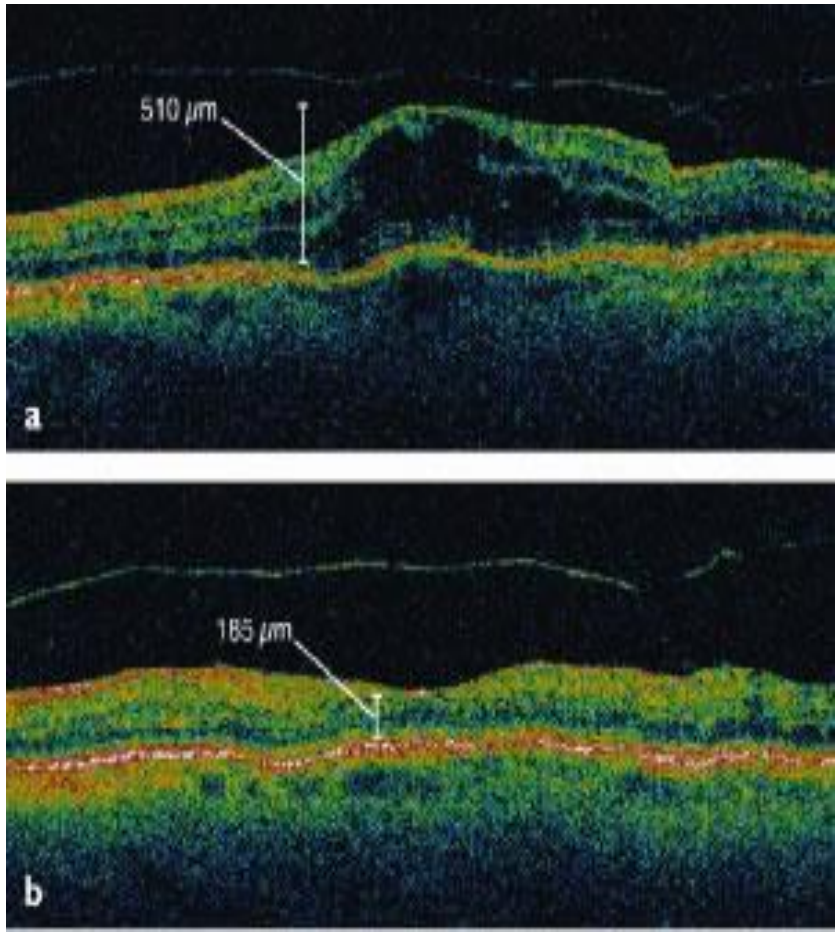
HEMORRHAGE

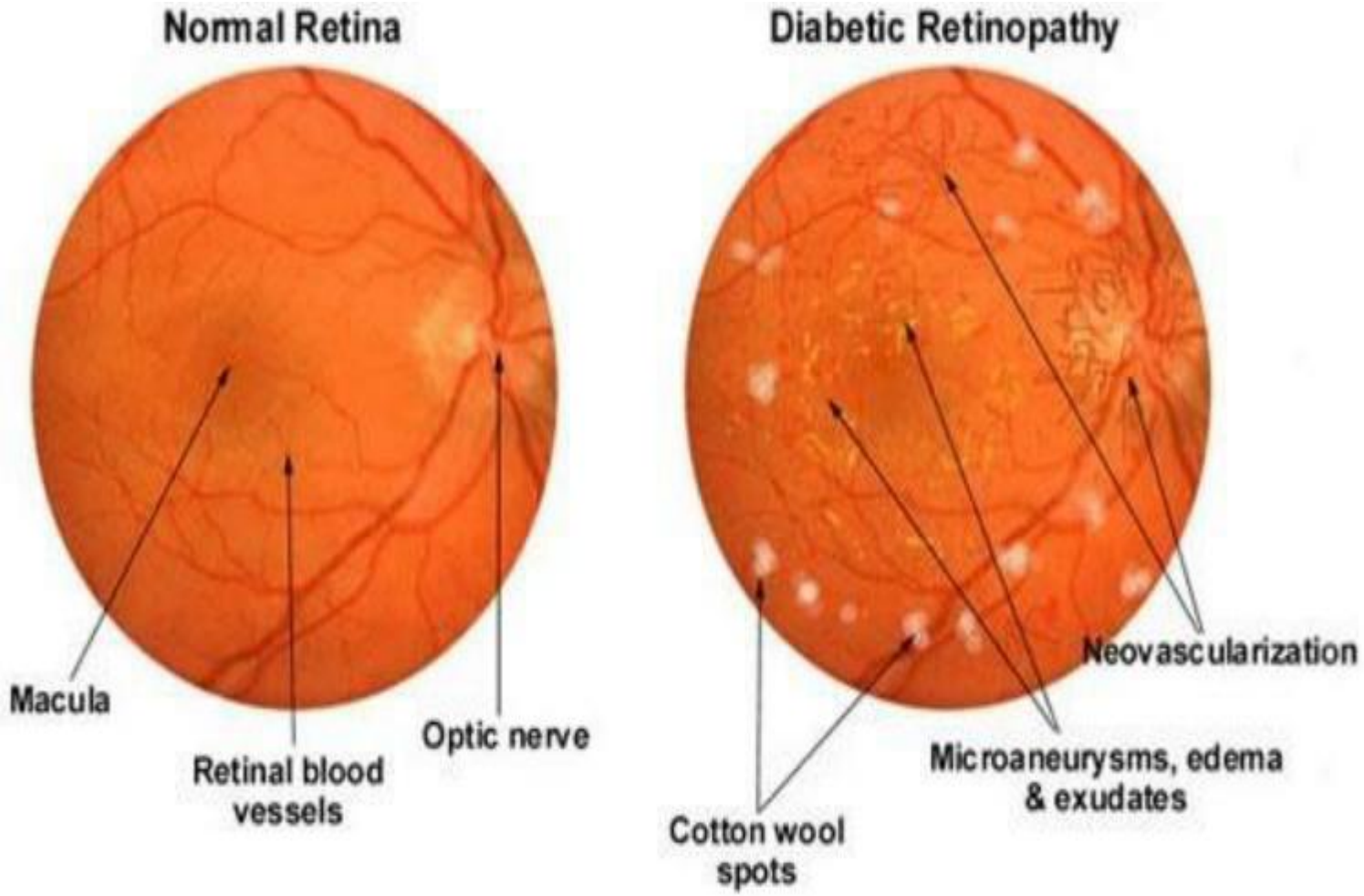
Flame hemorrhage association with HTN & venous stasis



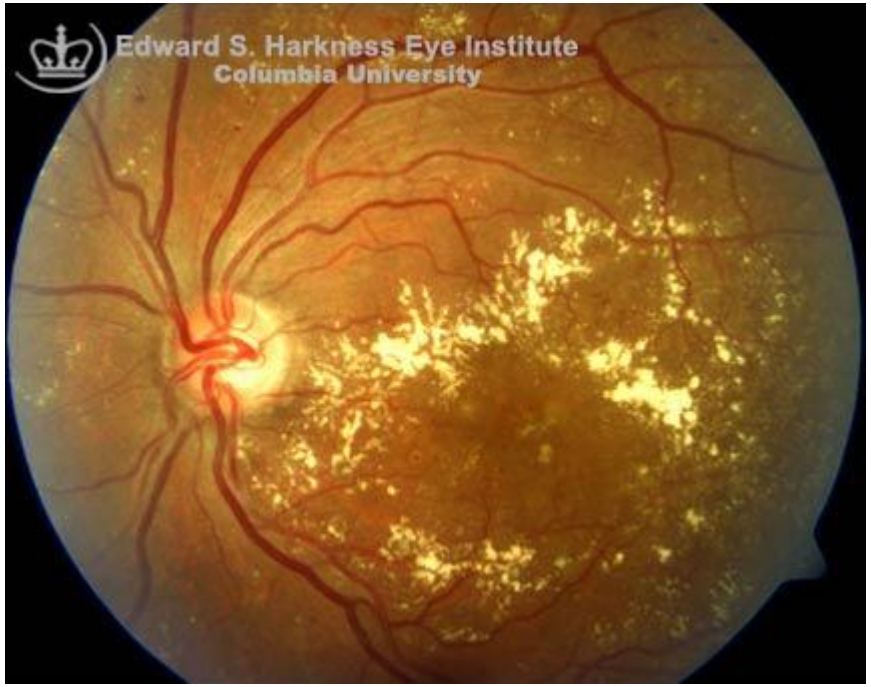


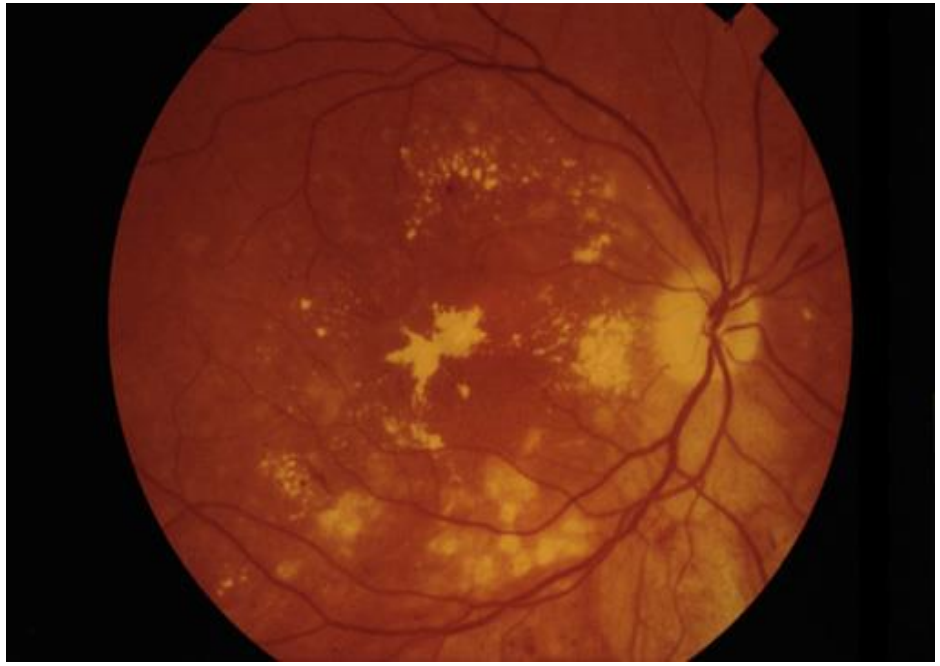
RETINAL EDEMA



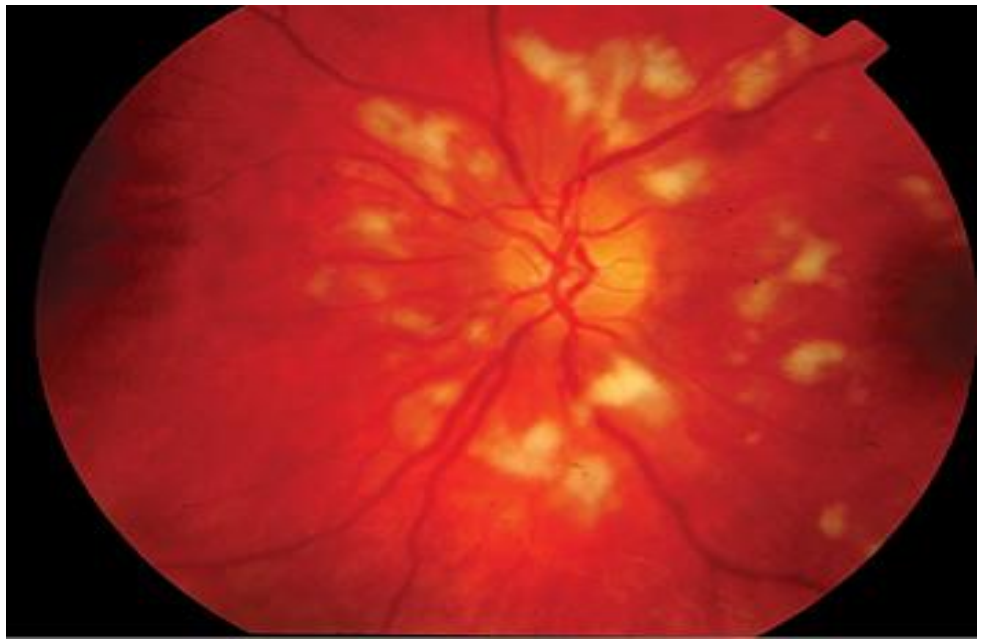


HARD EXUDATE





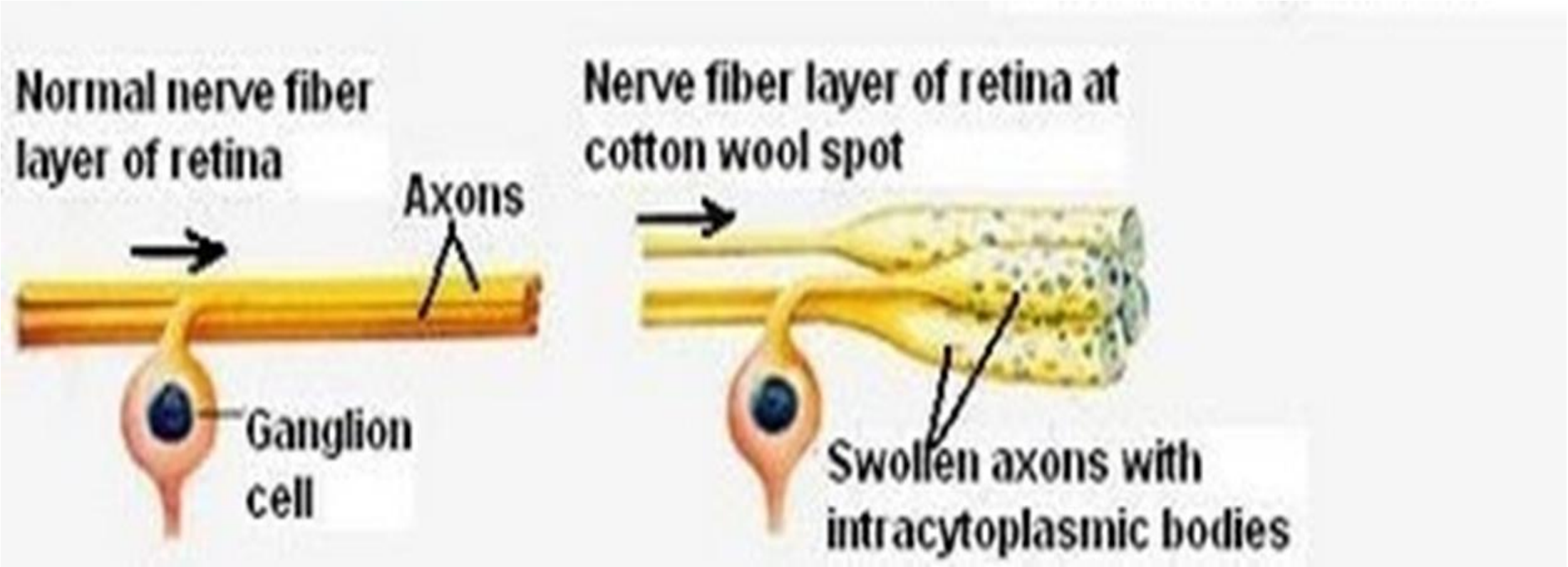
OCCLUSION OF THE MICROCIRCULATION :



1-Cotton wool spots **(previously termed *soft exudates*)**

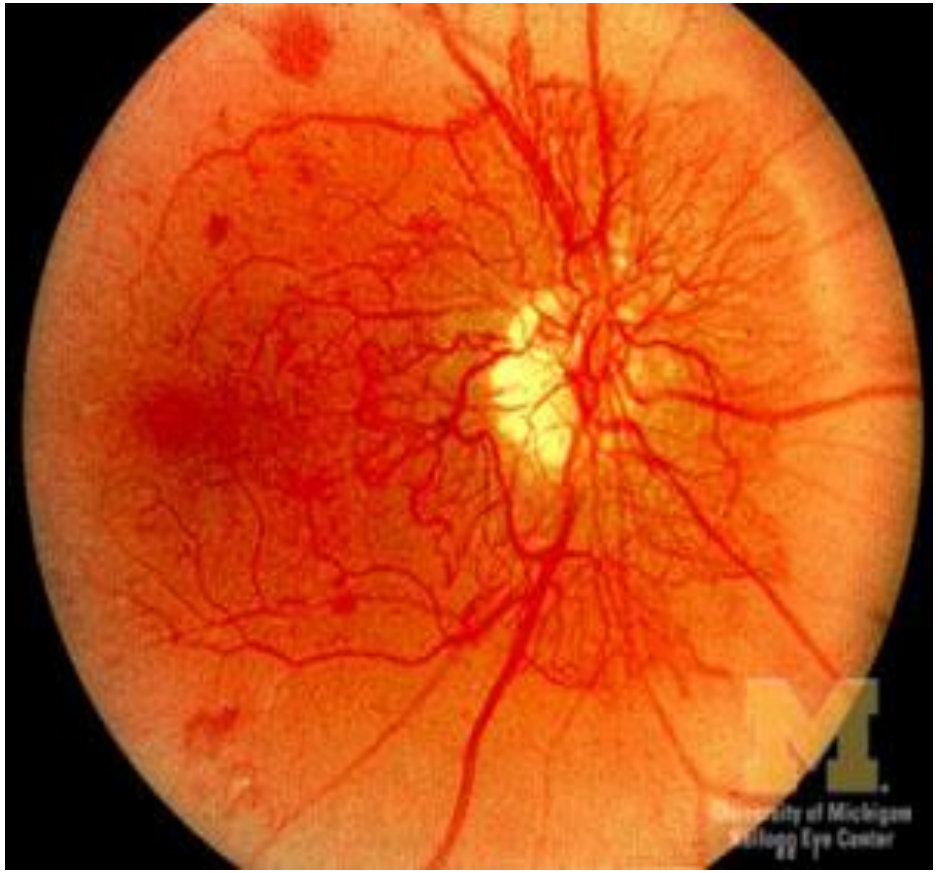
Nerve fiber layer infarctions from occlusion of precapillary arterioles; they are frequently bordered by microaneurysms and vascular hyperpermeability

Their visibility depends on nerve fiber layer thickness so that they are seen close to the optic disc, where the nerve fiber layer is thick, and not in the periphery where the nerve fiber layer is thin .They are white in color with indistinct borders.



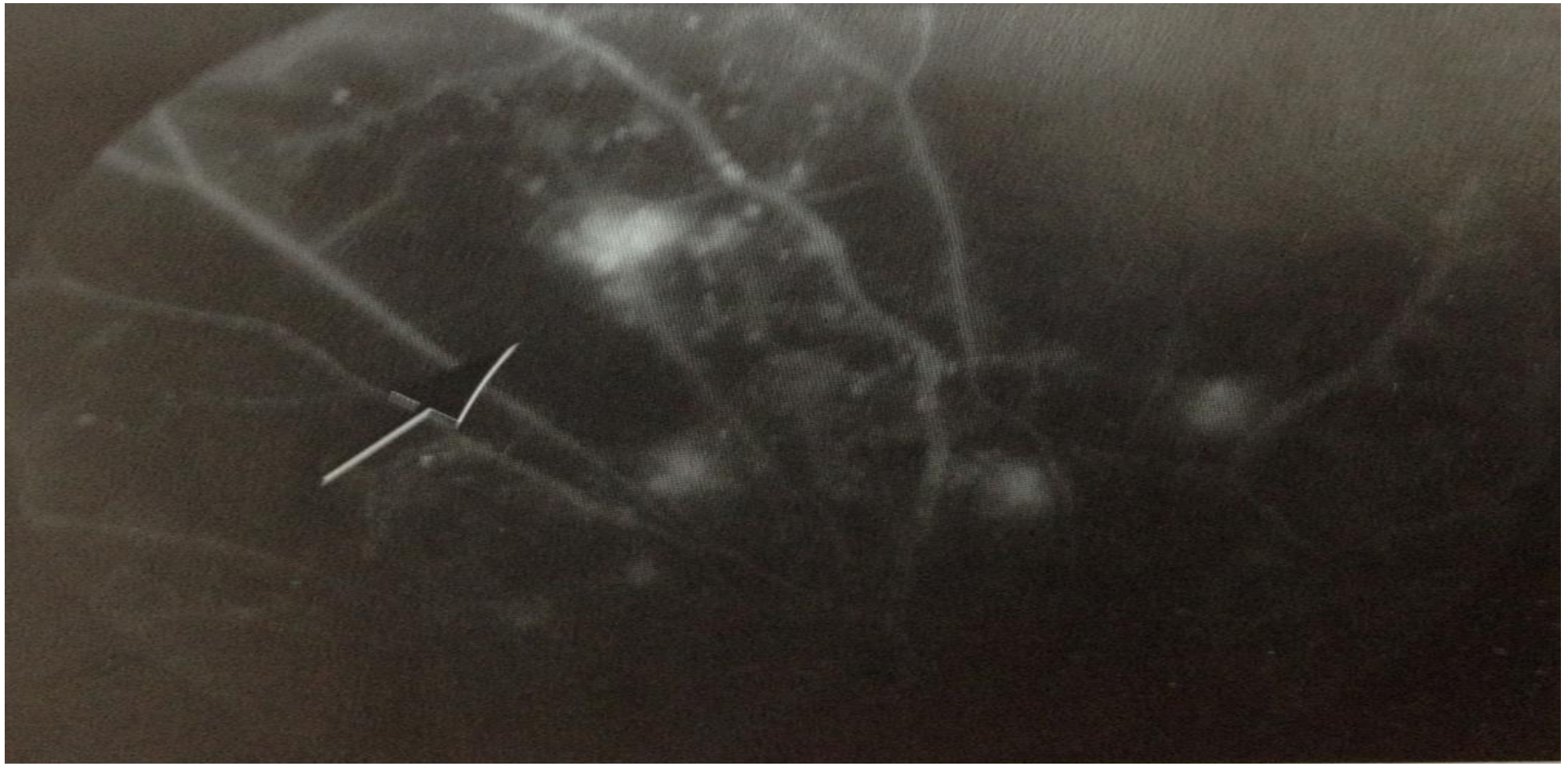
- These are caused by a build-up of axonal debris in the nerve fiber layer of the retina. This results from a hold-up in exoplasmic transport due to ischemia. Cotton wool spots are found at the margins of ischemic infarcts.

OCCLUSION OF THE MICROCIRCULATION :

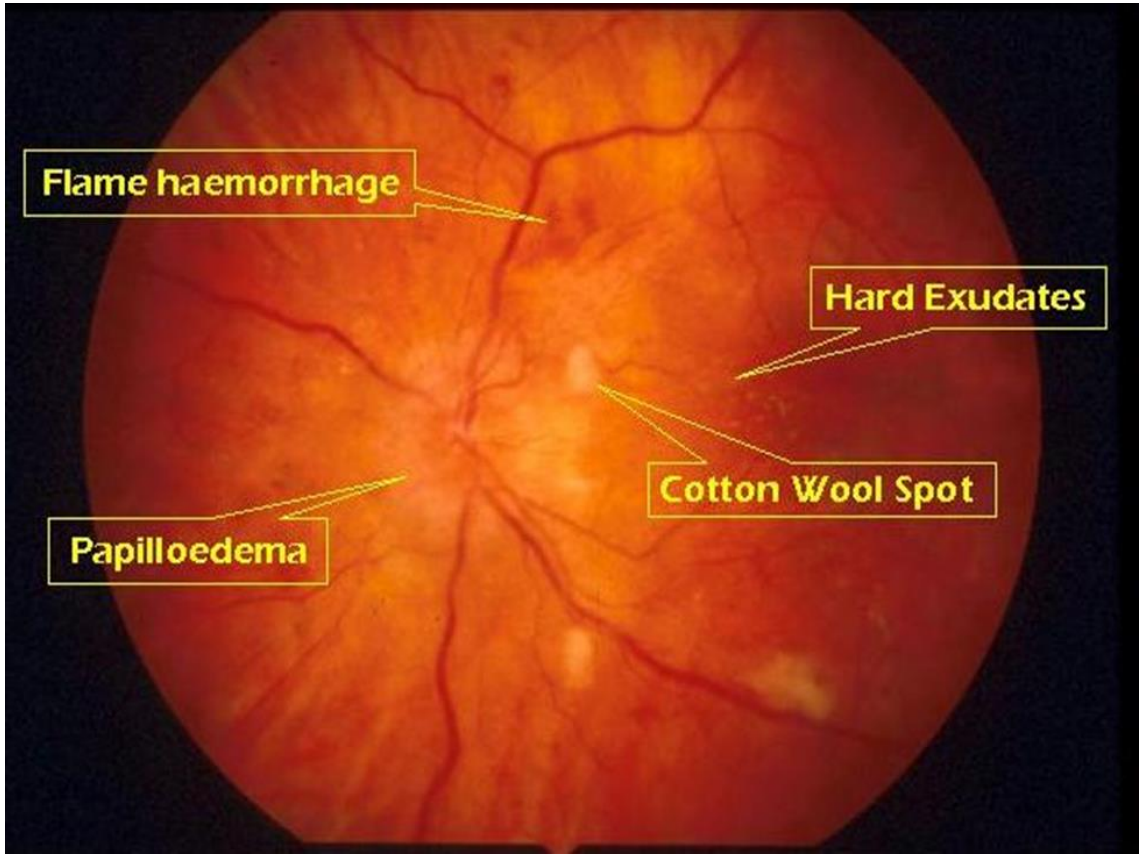


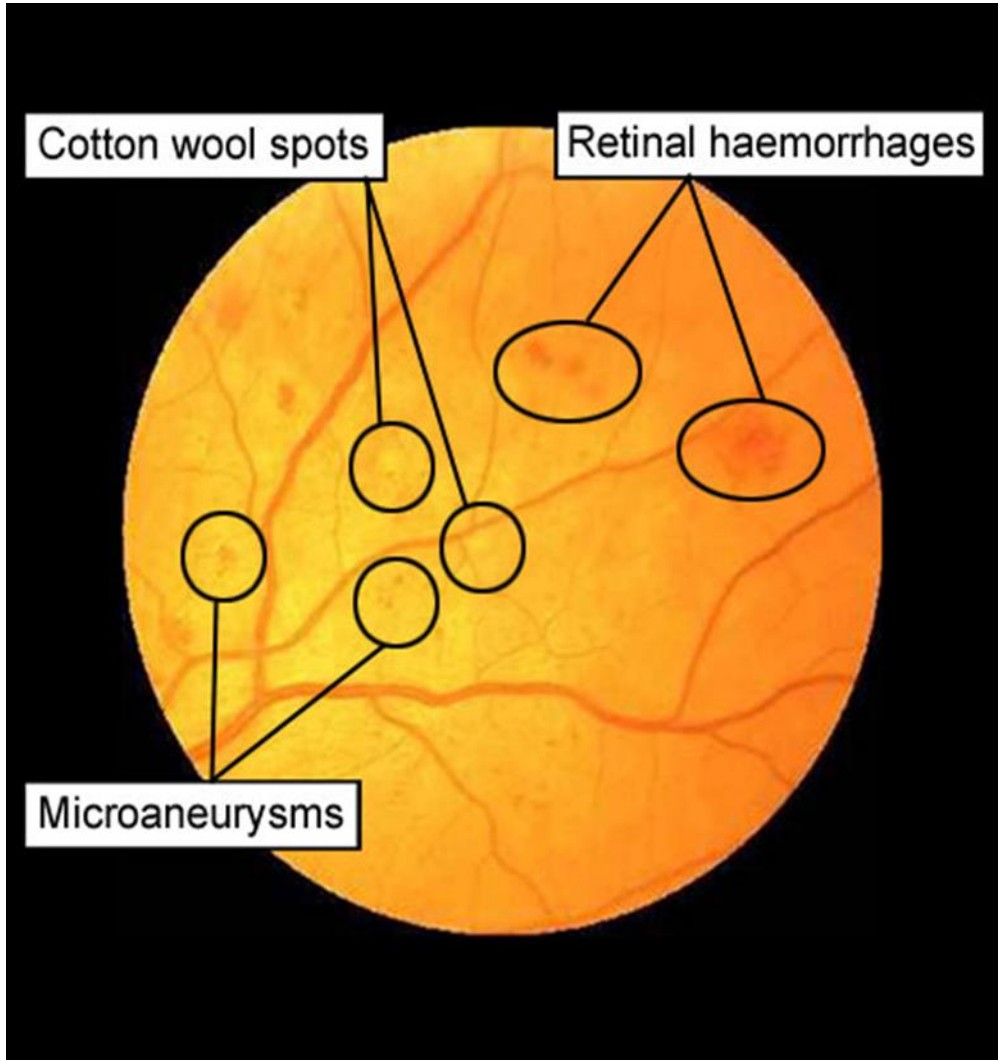
2-new vessels

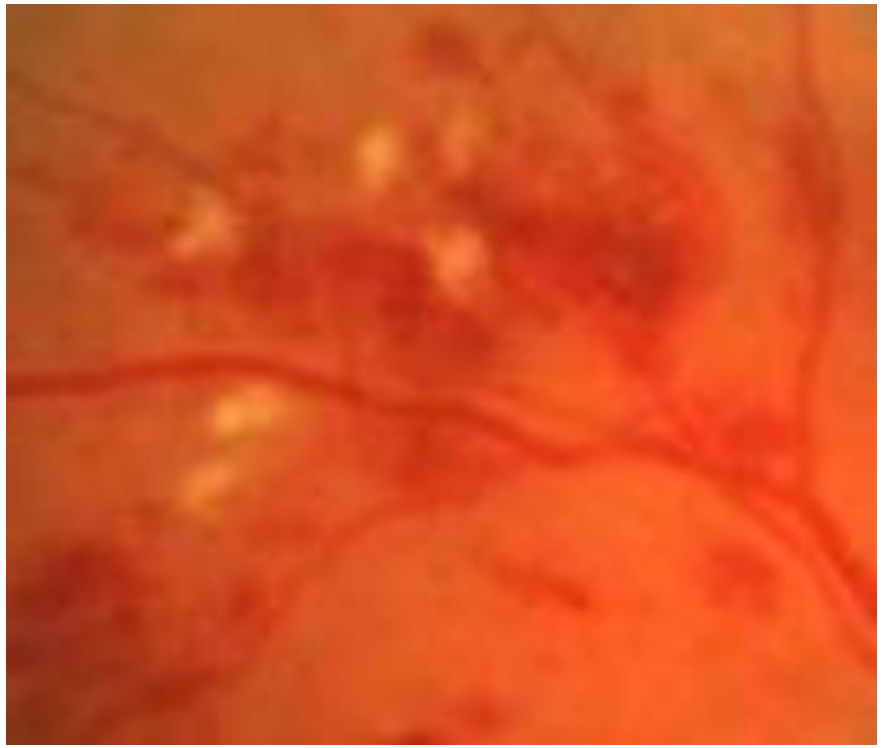
An ischemic retina releases vasogenic factors (e.g.VEGF) which result in the growth of abnormal blood vessels and fibrous tissue onto the retinal surface and forward into the vitreous. These intravitreal vessels are much more permeable than normal retinal vessels, and their abnormal position predisposes them to break and bleed

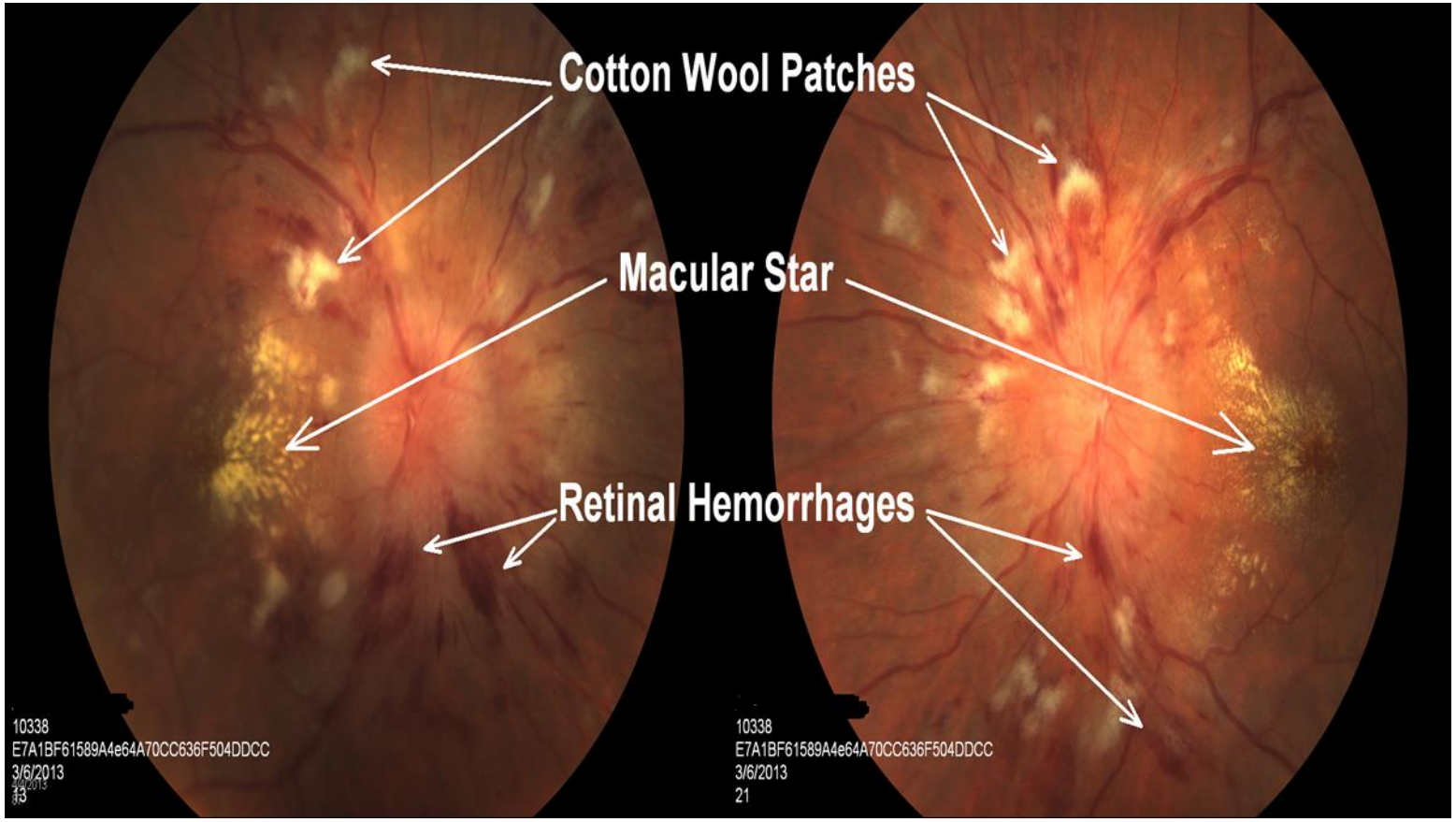


The new vessels are more permeable than the normal ones so they leak dye during retinal fluorescein angiography.


Flame haemorrhage
Hard Exudates
Cotton Wool Spot
Papilloedema

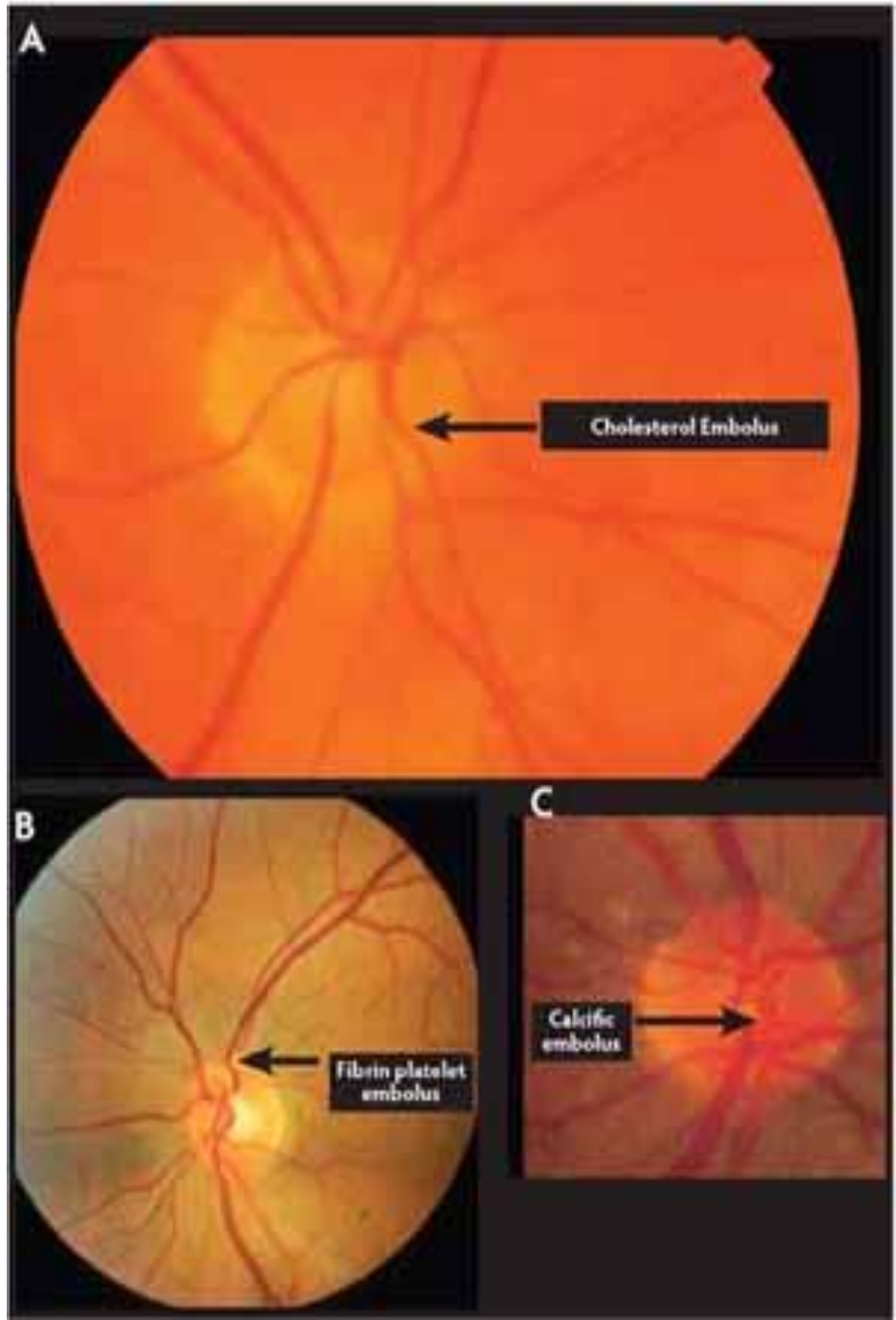

Cotton wool spots
Retinal haemorrhages
Microaneurysms




Cotton Wool Patches
Macular Star
Retinal Hemorrhages
10338
E7A1BF61589A4e64A70CC636F504DDCC
3/6/2013
10338
E7A1BF61589A4e64A70CC636F504DDCC
3/6/2013
21

ARTERIAL OCCLUSION

- **PATHOGENESIS**
- Central and branch retinal artery occlusions are usually embolic in origin.
- Three types of emboli are recognized:
- **1-*fibrin-platelet* emboli** commonly from diseased carotid arteries
- **2-*cholesterol* emboli** commonly from diseased carotid arteries
- **3-*calcific* emboli** from diseased heart valves.



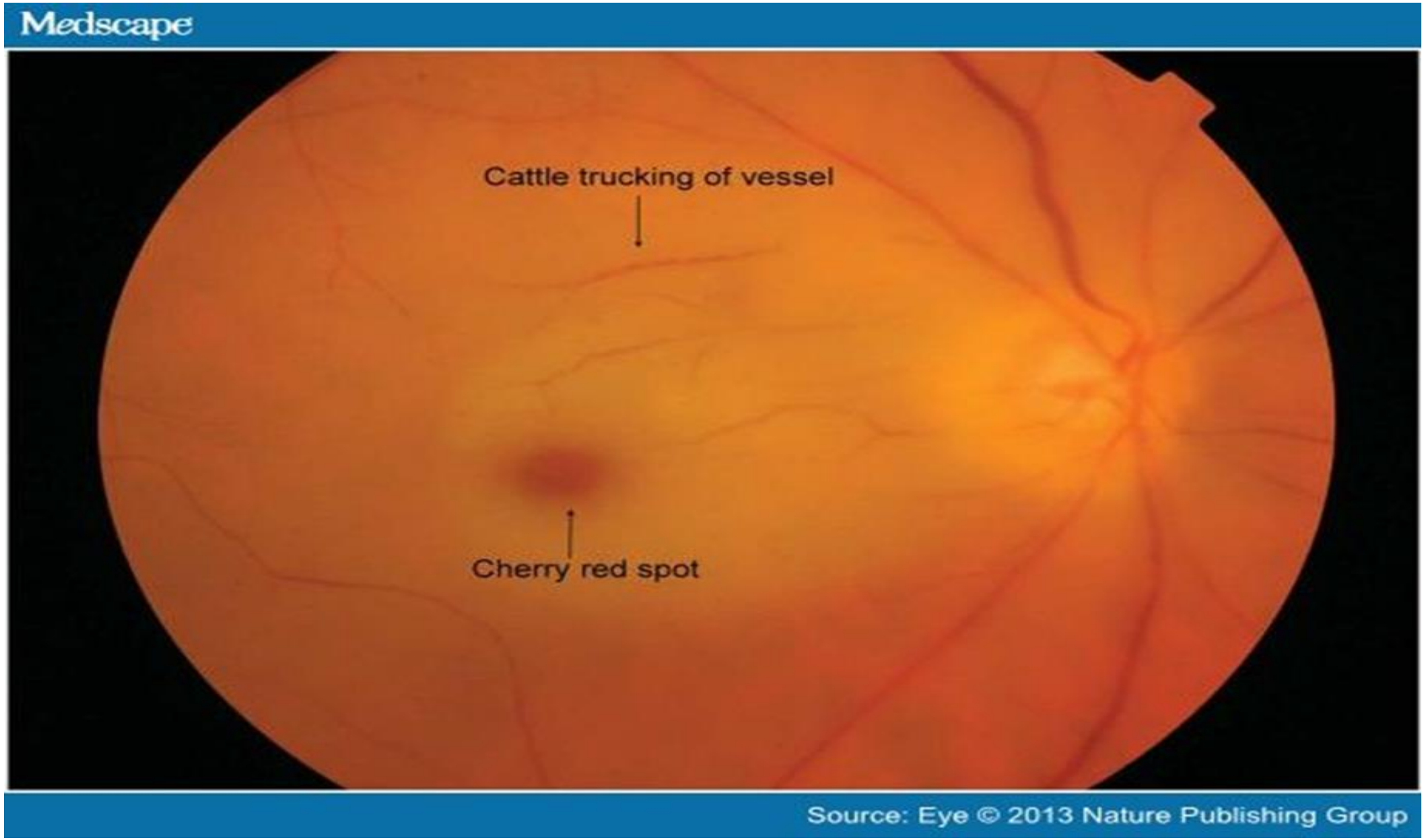
HISTORY

The patient complains of a sudden painless loss of all or part of the vision.

- Fibrin platelet emboli typically cause a fleeting loss of vision as the emboli passes through the retinal circulation (*amaurosis fugax*).
- Amaurosis fugax is a transient episode of complete or partial monocular blindness, lasting for a period of less than 10 minutes. A history of amaurosis fugax is elicited in 9-15% of patients with OIS.
- This may last for some minutes and then clears.
- Cholesterol and calcific emboli may result in permanent obstruction with no recovery in vision (they may also be seen in the retinal vessels of asymptomatic individuals).
- A central retinal artery obstruction is frequently caused by an embolus, although as it lodges further back in the arterial tree behind the optic nerve head, it cannot be seen.
- In young patients, transient loss of vision may be caused by migraine.

SIGNS

- Occasionally, a series of white platelet emboli can be seen passing rapidly through a vessel; more often a bright yellow, reflective cholesterol embolus is noted occluding an arterial branch point.
- The **acutely affected retina is swollen and white (*edematous*),** while the fovea is red **(*cherry red spot*)** as it has no supply from the retinal circulation, is not swollen, and the normal choroid can be seen through it.
- After several weeks the **disc becomes pale (*atrophic*)** and the arterioles attenuated. The condition may also occasionally be caused by vasculitis, such as giant cell arteritis


Medscape
Cattle trucking of vessel
Cherry red spot
Source: Eye © 2013 Nature Publishing Group

INVESTIGATIONS

vascular work-up since disease in the eye may reflect systemic vascular disease.

- **1- A search for carotid artery disease** should be made by assessing the strength of carotid pulsation and listening for bruits
- **2-Ischemic heart disease,** peripheral claudication and hypertension may also be present.
- **3- A carotid endarterectomy** may be indicated to prevent the possibility of a cerebral embolus if a stenosis of the carotid artery greater than 75% is present.
- **Doppler ultrasound allows non-invasive imaging of both the carotid and vertebral arteries to detect such a stenosis.**

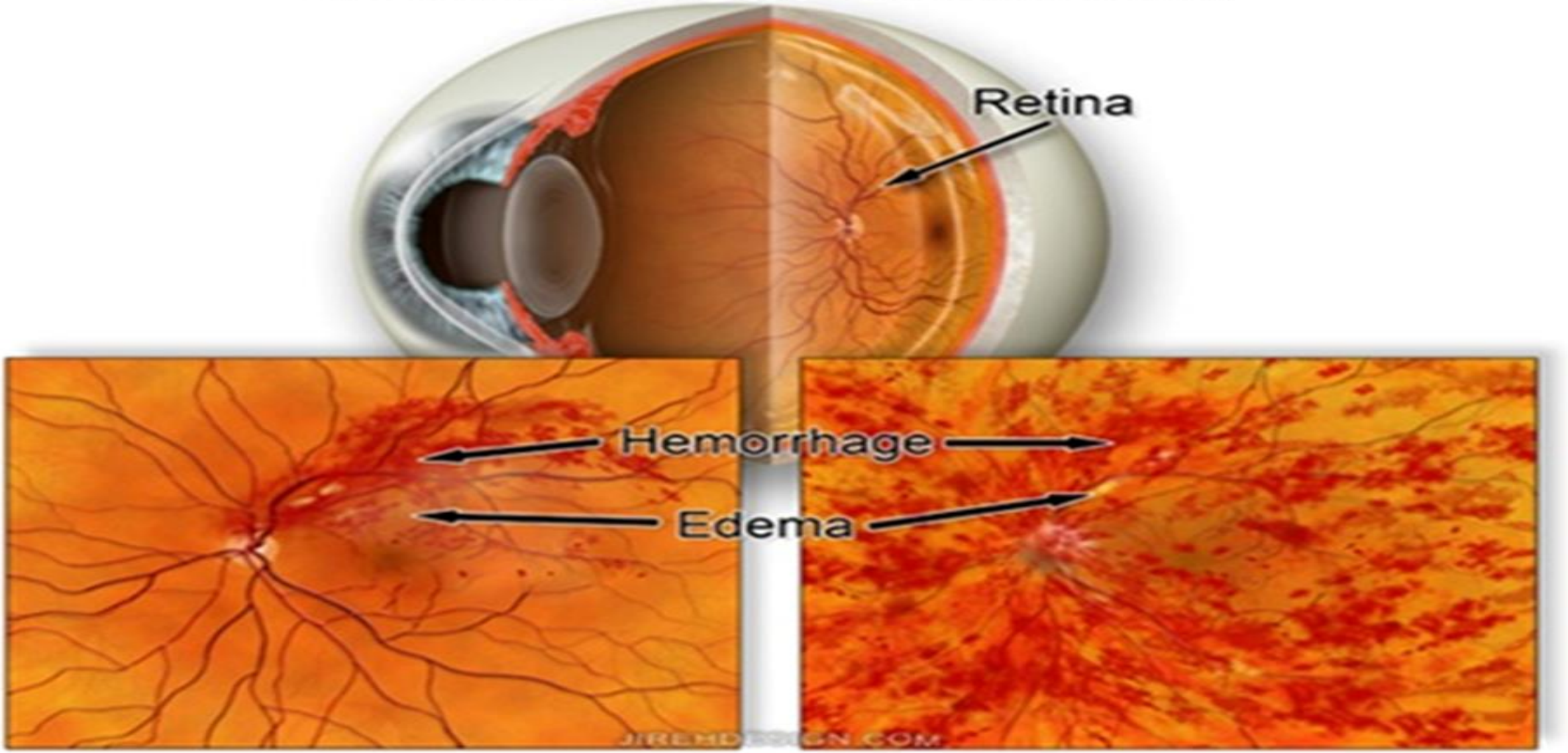
TREATMENT

- **TREATMENT**
- Acute treatment of central and branch artery occlusions is aimed at dilating the arteriole to permit the embolus to pass more distally.
- Results are usually disappointing although a trial is worthwhile if the patient is seen within 24 hours of onset of the obstruction.
- The patient is referred to an eye unit where the following measures may be tried : 1-lowering the intraocular pressure with intravenous acetazolamide;
- 2-ocular massage, 3-paracentesis (a needle is inserted into the anterior chamber to release aqueous and lower the intraocular pressure rapidly)
- getting the patient to rebreathe into a paper bag firmly applied around the mouth and nose to use the vasodilatory effect of raised carbon dioxide levels.

PROGNOSIS

- **Full visual recovery occurs with amaurosis fugax but more prolonged arterial occlusion results in severe unrecoverable visual loss.**

Retinal Vein Occlusion



VENOUS OCCLUSION

- **PATHOGENESIS**
- Central retinal vein occlusion (CRVO) may result from:
- **1-abnormality of the blood itself** (the hyper viscosity syndromes and abnormalities in coagulation)
- **2-an abnormality of the venous wall (inflammation)**
- **3-an increased ocular pressure.**

PREDISPOSING FACTORS:

1) **Advancing age** - over 50% of cases occur in patients over 65 years old, although up to 15% may affect individuals under the age of 45.
2) Systemic conditions such as **hypertension, hyperlipidemia, diabetes, smoking and obesity**
3) **Raised intraocular pressure**
4) **Inflammatory diseases** such as sarcoidosis, Behçet's syndrome
5) **Hyper viscosity states such as myeloma**
6) **Thrombophilic disorders** (to be considered in patients <45 years old) such as hyperhomocysteinemia, lupus anticoagulant, anticardiolipin antibodies.

TYPE 1 :CENTRAL RETINAL VEIN OCCLUSION

Types:

- ***Non-ischemic CRVO (*75% of CRVOs).** It is the milder form of the disease, and may resolve fully with good visual outcome or progress to the ischemic type.

- ***Ischemic CRVO;*** It is the severe form of the disease. Patients may be left with neovascular glaucoma and a painful blind eye.

HISTORY

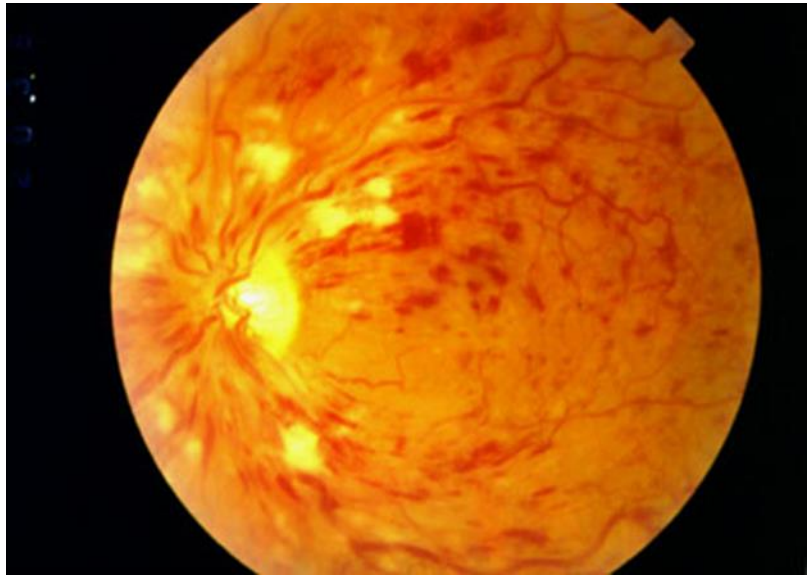
- **The patient complains of a sudden partial or complete loss of vision although onset may be less acute than that of arterial occlusion**

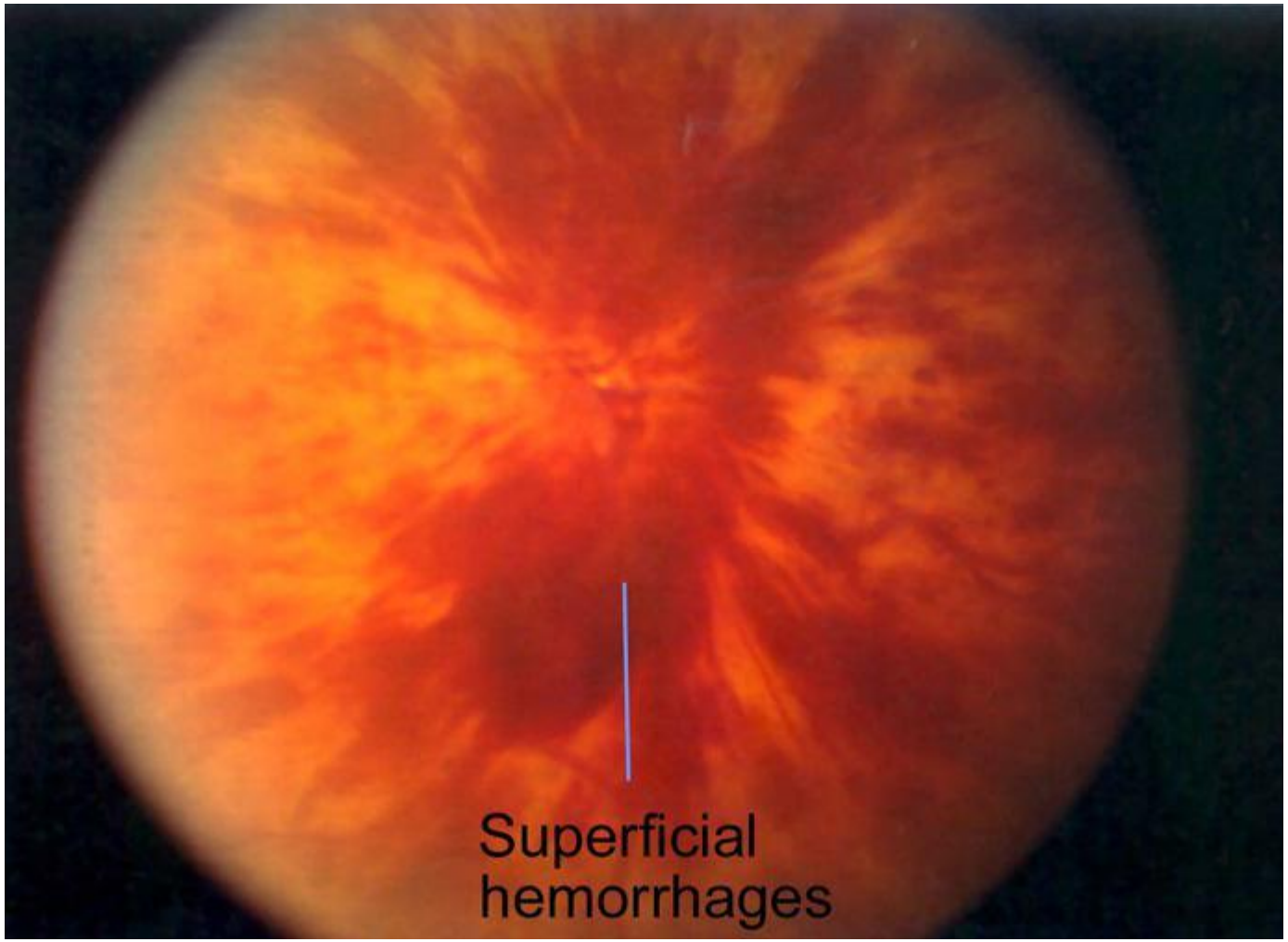
SIGNS

1- There is marked hemorrhage

2- great tortuosity and swelling of the veins.

2-The optic disc appears swollen.





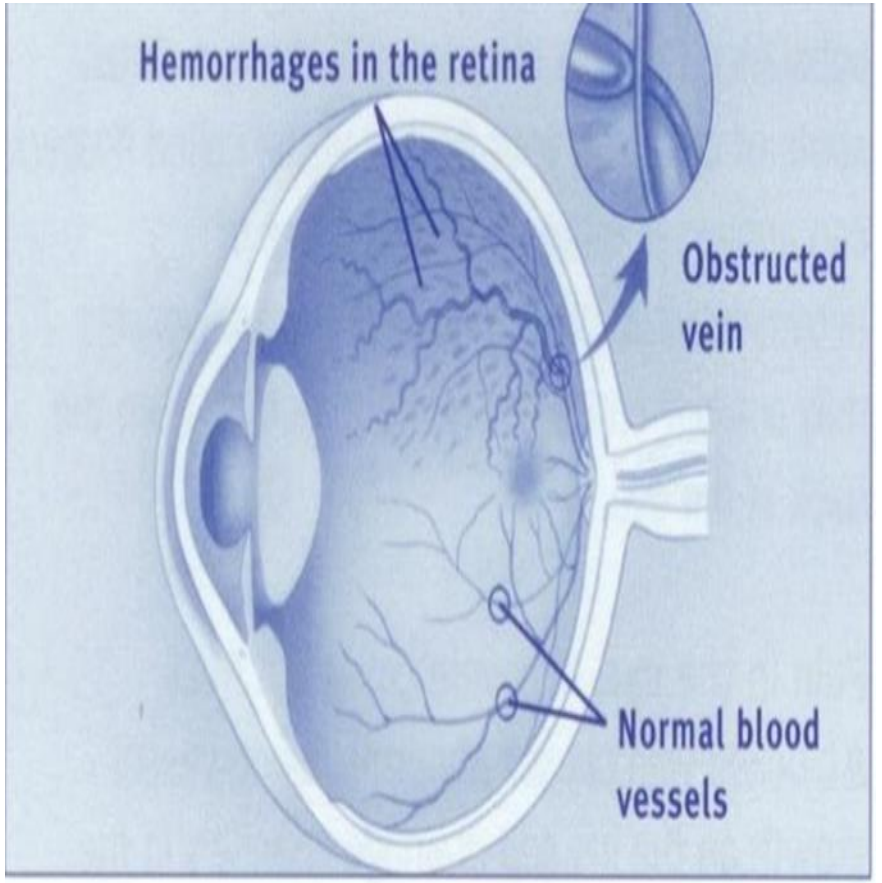
Recent onset central retinal vein occlusion, showing extensive hemorrhages in the posterior pole and giving the "**blood and thunder appearance.**"

INVESTIGATION

- Investigation of a CRVO includes **vascular and hematological work-up to**
- exclude increased blood viscosity. **Central retinal vein occlusion is also associated with raised ocular pressure, diabetes and hypertension**
- **Fluorescein angiography ;** Fluorescein angiography is the investigation of choice in CRVO. It evaluates retinal capillary non-perfusion, neovascularization and macular edema. It is not often necessary in BRVO.

TYPE 2 BRANCH RETINAL VEIN OCCLUSION

- It is three times more common than CRVO , BRVO Also has ischemic and non-ischemic types



Branch retinal vein occlusion (BRVO): A smaller branch of vessels attached to the main vein is blocked, causing bleeding in parts of the retina.

PATHOGENESIS

- **1-Hypertensive, atherosclerotic, inflammatory, or thrombophilic** conditions may lead to retinal endothelial vascular damage.
- **2-In eyes with an anatomical predisposition**, intravascular thrombus formation may occur.
- **3-Eyes with arteriovenous crossings appear to be at risk for BRVO**. In these eyes, the artery is anterior to the vein in most cases. The artery and the vein share a common adventitial sheath. Increased arterial stiffness may be a mechanical factor in the pathogenesis of BRVO.

1- Abnormal new vessels may grow on the retina and optic disc, causing **vitreous hemorrhage**. (This happens if there is an ischemic retinal vein occlusion)

2- In ischemic retinal vein occlusion abnormal new vessels may grow on the iris (rubeosis) causing **rubeotic glaucoma.**

COMPLICATIONS OF BRANCH RETINAL VEIN OCCLUSION THAT THREATEN VISION:

- **1-Macular edema.**
- **2-Macular ischemia or non-perfusion (lack of blood supply).**
- **3-Neovascularization (vitreous haemorrhage, rubeotic glaucoma).**

Symptoms:

- The most common presentation is unilateral, painless blurred vision,
- metamorphopsia (image distortion) ± a field defect (scotoma).
- Peripheral occlusions may be asymptomatic.
- Visual acuity depends on the degree of macular involvement.

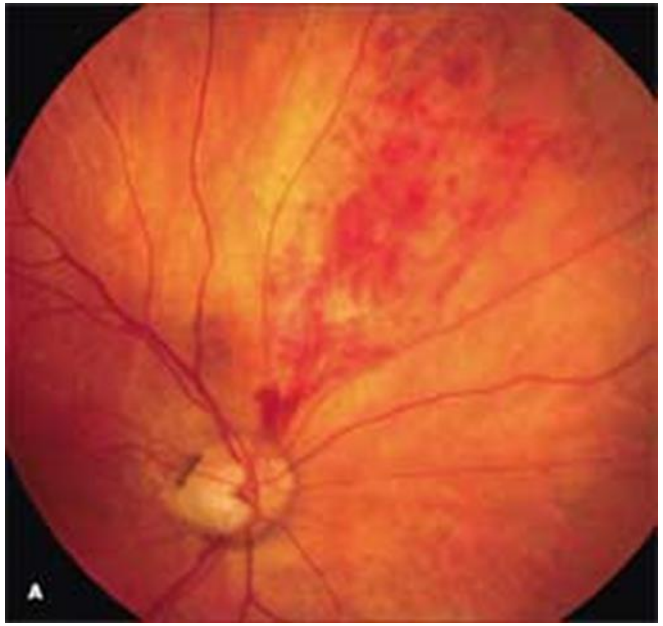
signs:

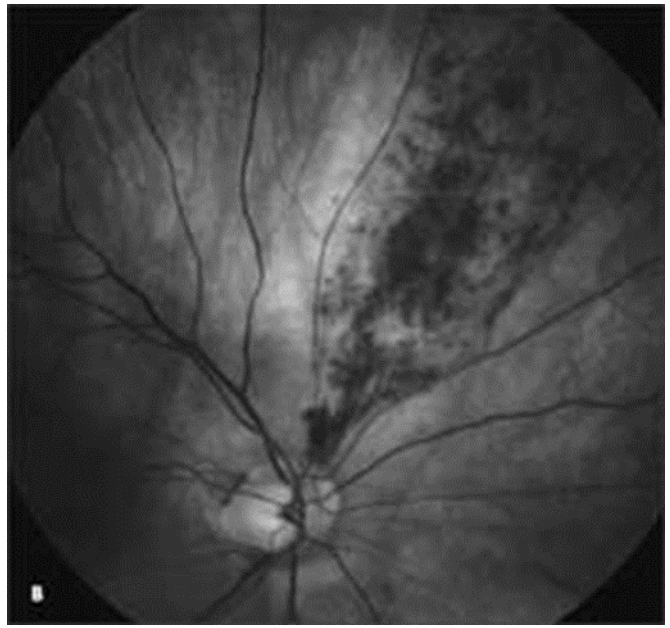
vascular dilatation and tortuosity of the affected vessels with associated hemorrhages in that area only

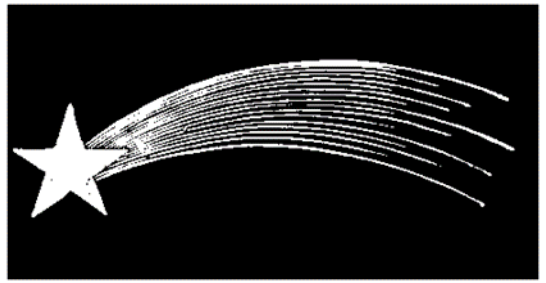
Normal Vision

Metamorphopsia
(Distortion)

- Funduscopic will reveal vascular dilatation and tortuosity of the affected vessels with associated hemorrhages in that area only **(look for an arc of hemorrhages, like a trail left behind a cartoon image of a shooting star).**







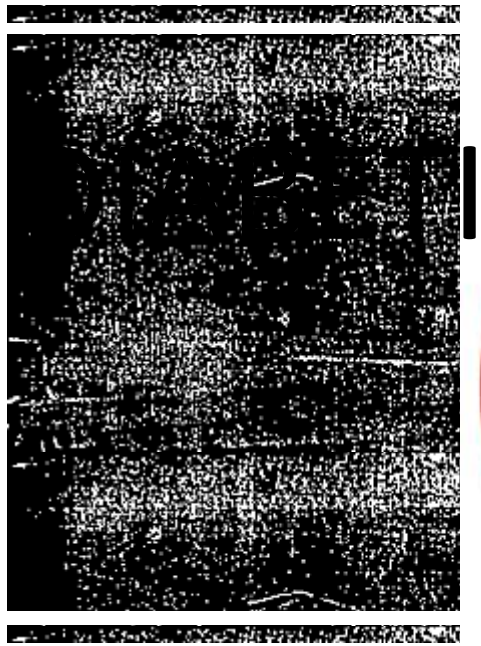
TREATMENT

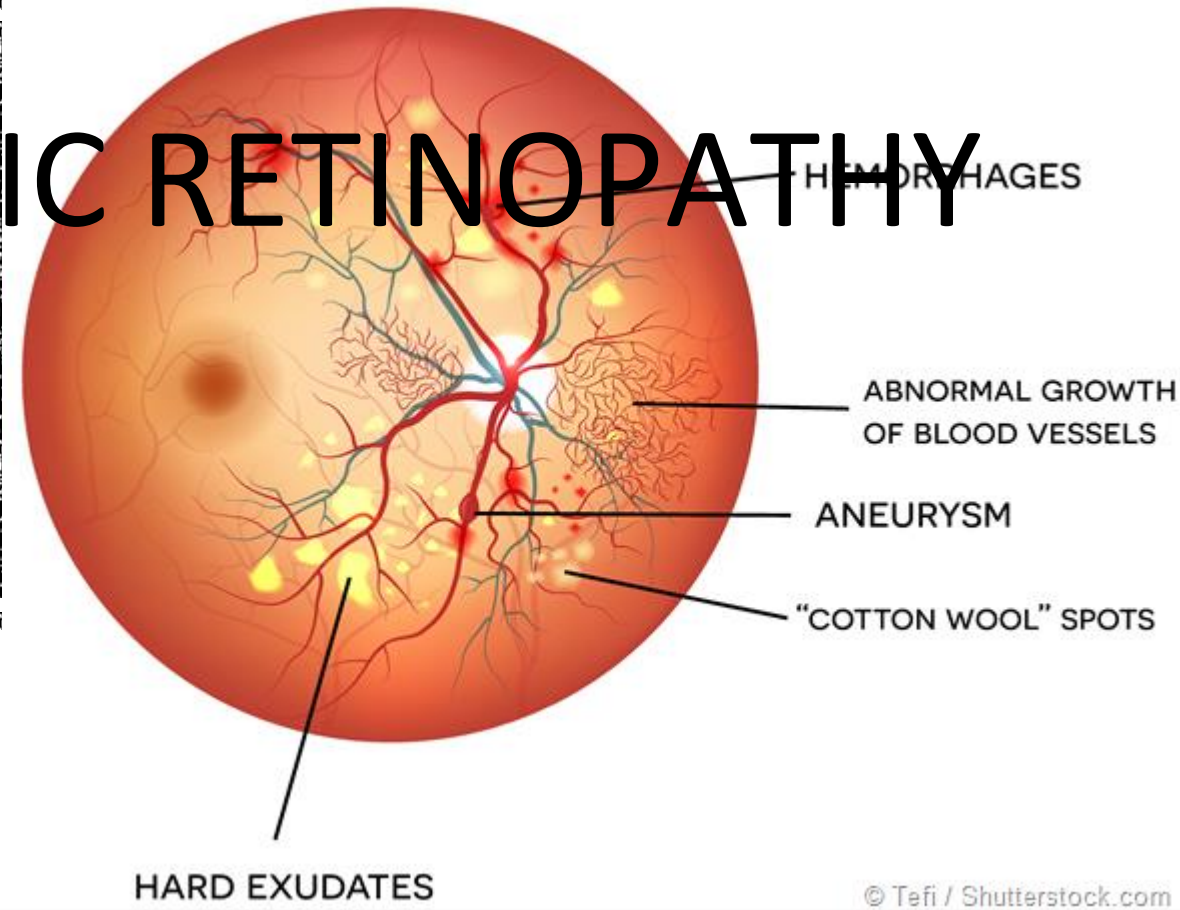
- **Retinal laser** treatment is given if the retina is ischemic to prevent the development of retinal and iris new vessels
- Laser treatment may improve vision in some patients with a branch retinal vein occlusion by reducing macular edema.
- **For macular edema; intravitreal injection of anti-VEGF, or retinal laser**

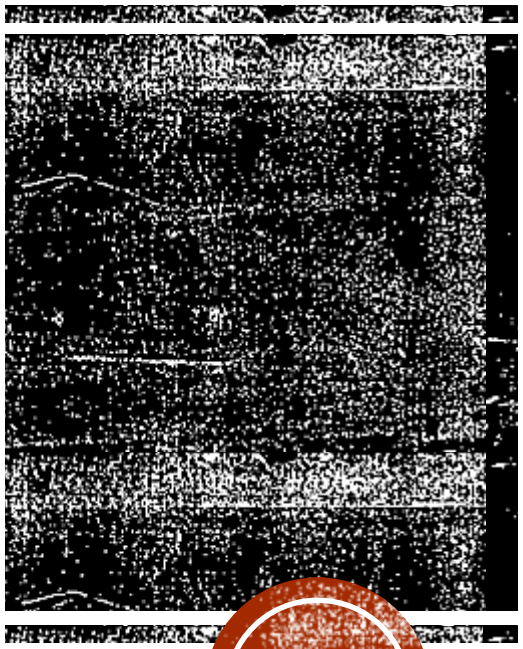
PROGNOSIS

- The vision is usually severely affected in central, and often in branch, vein occlusion and usually does not improve.
- Younger patients may fare better and there may well be some visual improvement.

IC RETINOPATHY







**retinopathy (damage to the retina) caused by complications of diabetes mellitus

EPIDEMIOLOGY

- UK : diabetic eye disease is the commonest reason for blind registration in the 30– 65 age group
- Type I diabetes : 5 years after onset
- Type II diabetes : at presentation

**DR : 1st chronic complication to develop in diabetes

Diabetes can associated with eye diseases:

Retinopathy

Cataract

Glaucoma

Extraocular muscle palsy

Risk Factor

- Duration of diabetes: 80% have retinopathy after 20 years of disease
- Poor Diabetic control.
- Coexisting diseases particularly hypertension
- Pregnancy
- Nephropathy
- Other risk factors: hyperlipidemia, smoking, cataract surgery, obesity and anemia.

PATHOGENESIS

- **Hyperglycemia → Microangiopathy**

1. **Cellular damage:** intracellular sorbitol accumulation, oxidative stress due to free radical excess, accumulation of advanced glycation end products and excessive activation of several protein kinase C isoforms.

2 **Capillaropathy** is characterized by death of pericytes

3 **Neovascularization** is caused by capillary non-perfusion → hypoxia → **vascular endothelial growth factor (VEGF)**

- decrease in the number of pericytes surrounding the capillary endothelium;
- development of microaneurysms on the capillary network which allow plasma to leak out into the retina;
- development of arterio-venous shunts with closure of the capillary net resulting in areas of ischaemic retina.

Symptoms

- Often asymptomatic (should be diagnosed before it is symptomatic-late stage)
- Curtain falling- vitreous bleeding
- Floaters- resolution of vitreous bleeding
- Decreased visual acuity :Visual loss may occur gradually (due to the maculopathy) or suddenly (due to vitreous hemorrhage)

Screening

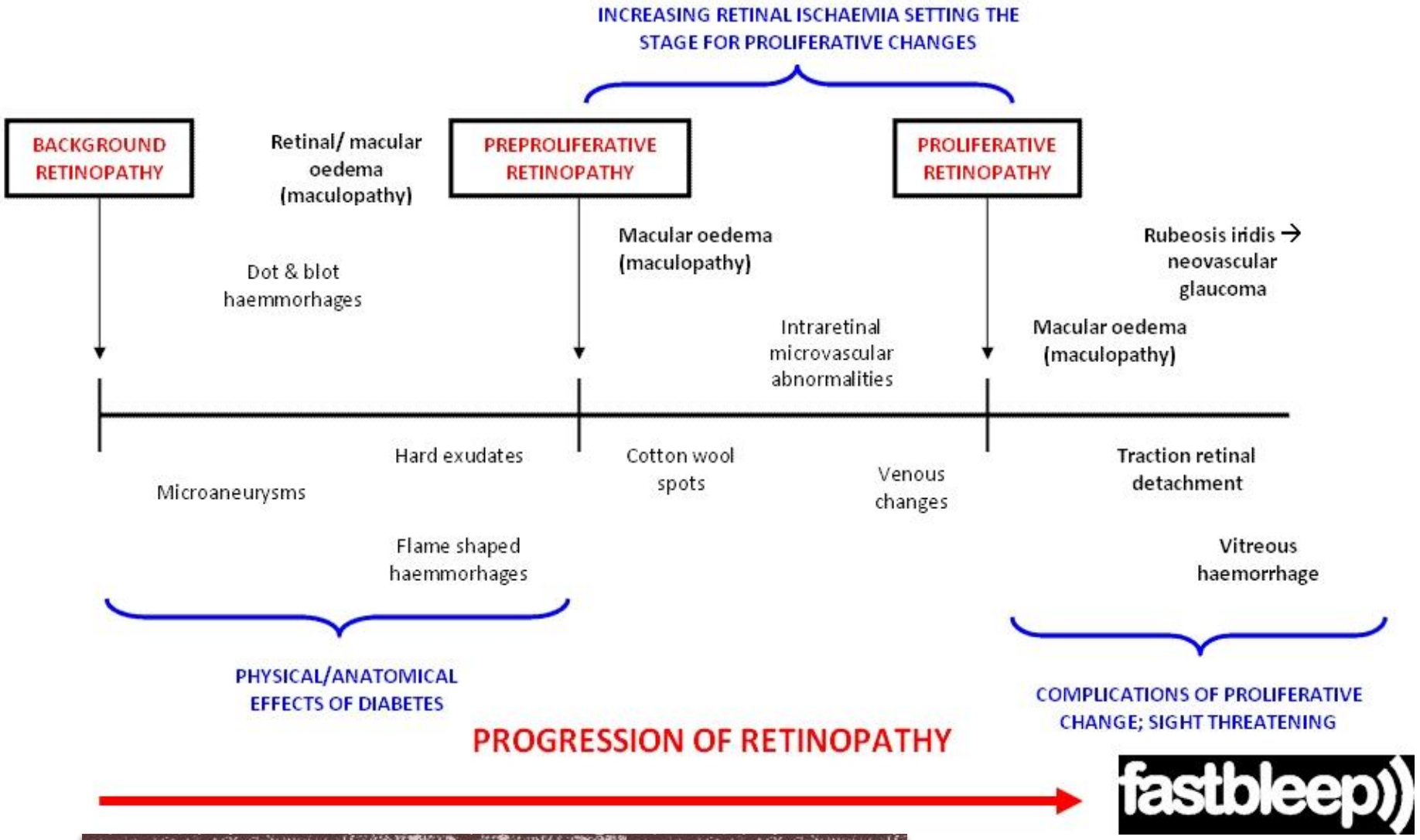
- All diabetic patient should have fundoscopy performed at least yearly
- Screening for sight threatening retinopathy (maculopathy and proliferative retinopathy) :

  Type I: 5 years after diagnosis of type 1

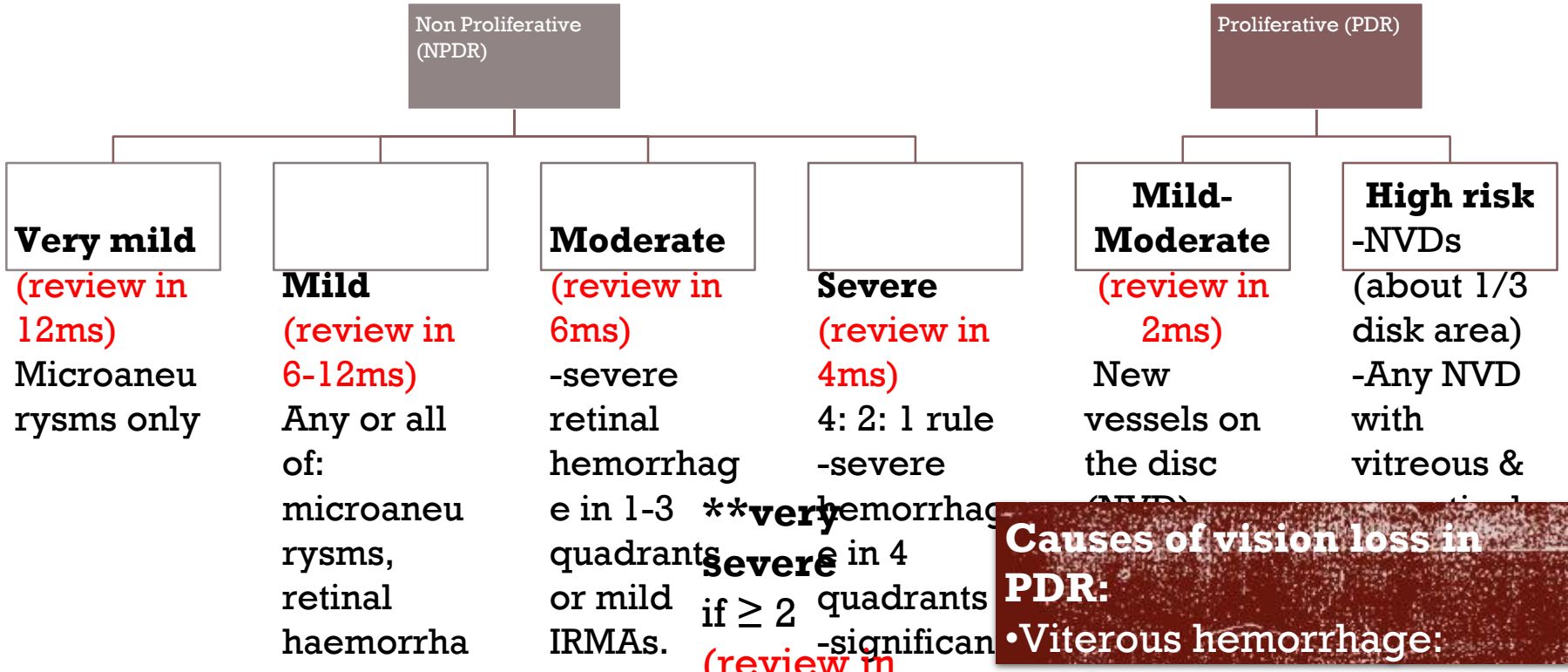
  Type II: at time of presentation

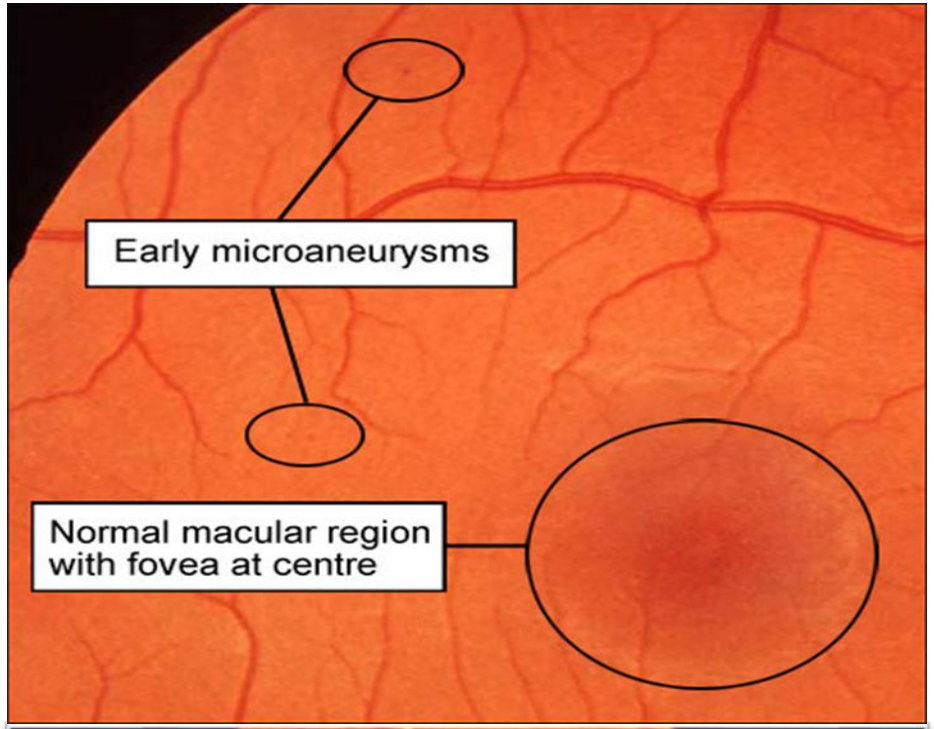
  Pregnancy: every 3 months

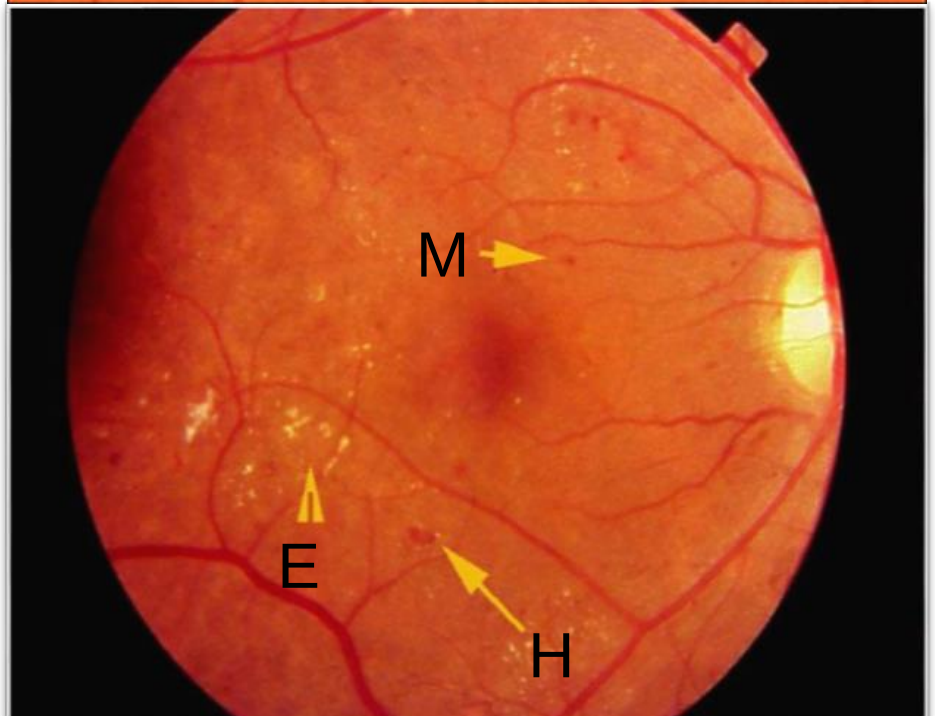
Stages/Classification



Younger patient: more likely proliferative disease
Older patient: more common develop maculopathy

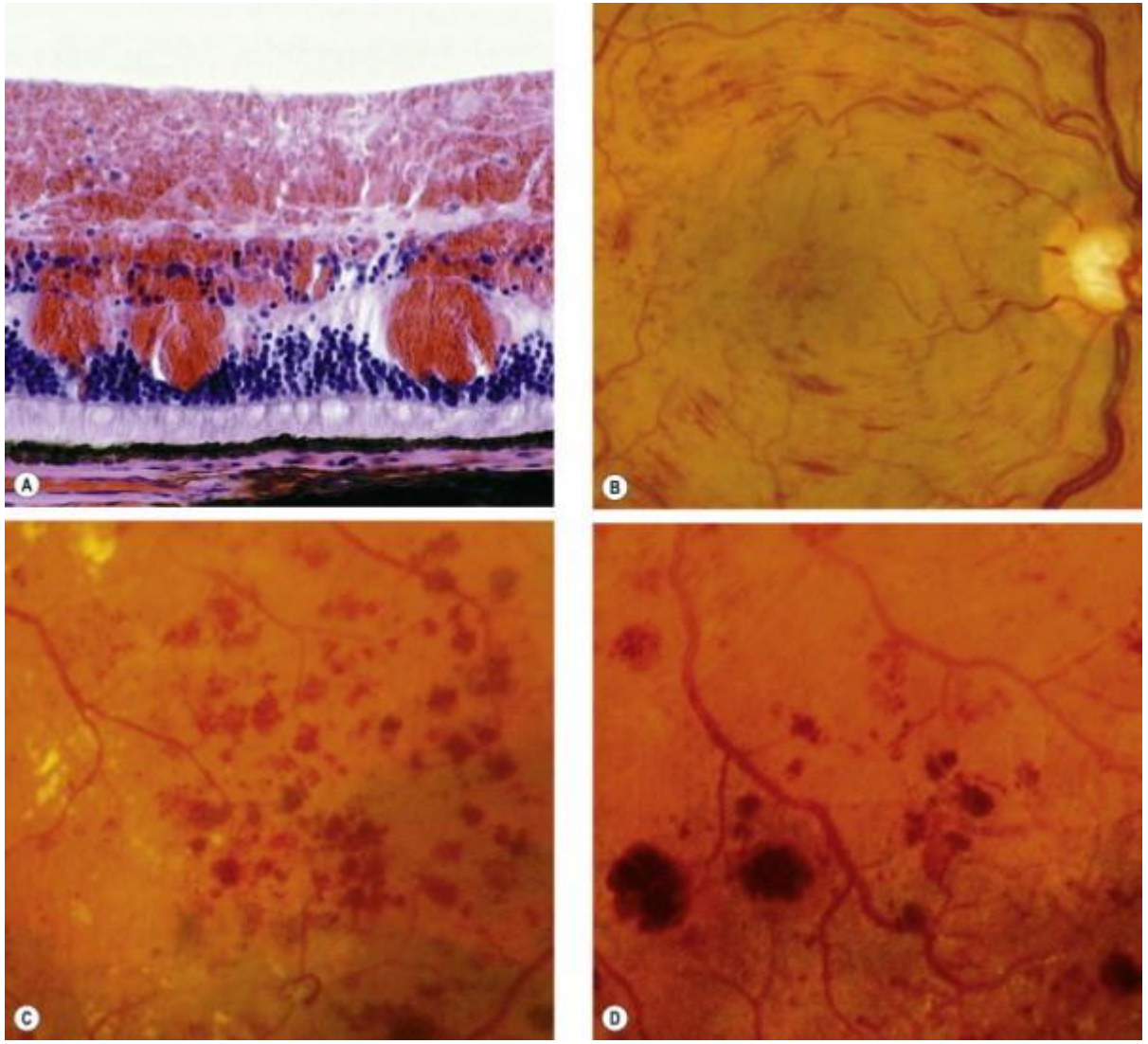

Non Proliferative (NPDR)
Proliferative (PDR)
Very mild
(review in 12ms)
Microaneurysms only
Mild
(review in 6-12ms)
Any or all of: microaneurysms, retinal haemorrhages, exudates,
Moderate
(review in 6ms)
-severe retinal hemorrhage in 1-3 quadrants or mild IRMAs.
-significant venous
**very severe
if ≥ 2
(review in 2-3ms)
Severe
(review in 4ms)
4: 2: 1 rule
-severe hemorrhage in 4 quadrants
-significan
beading in 2
Mild-Moderate
(review in 2ms)
New vessels on the disc
(NVE), but extent
High risk
-NVDs
(about 1/3 disk area)
-Any NVD with vitreous &
disc area &
vitreous or
Causes of vision loss in PDR:
•Viterous hemorrhage:
sudden
•Macular edema: gradual





Microaneurysms

- focal dilation of retinal capillaries 10 -100 μm → Red dots.
- Usually at the posterior pole (temporal to the fovea).
- 1st detectable change (due to loss of pericytes).



Retinal hemorrhages:

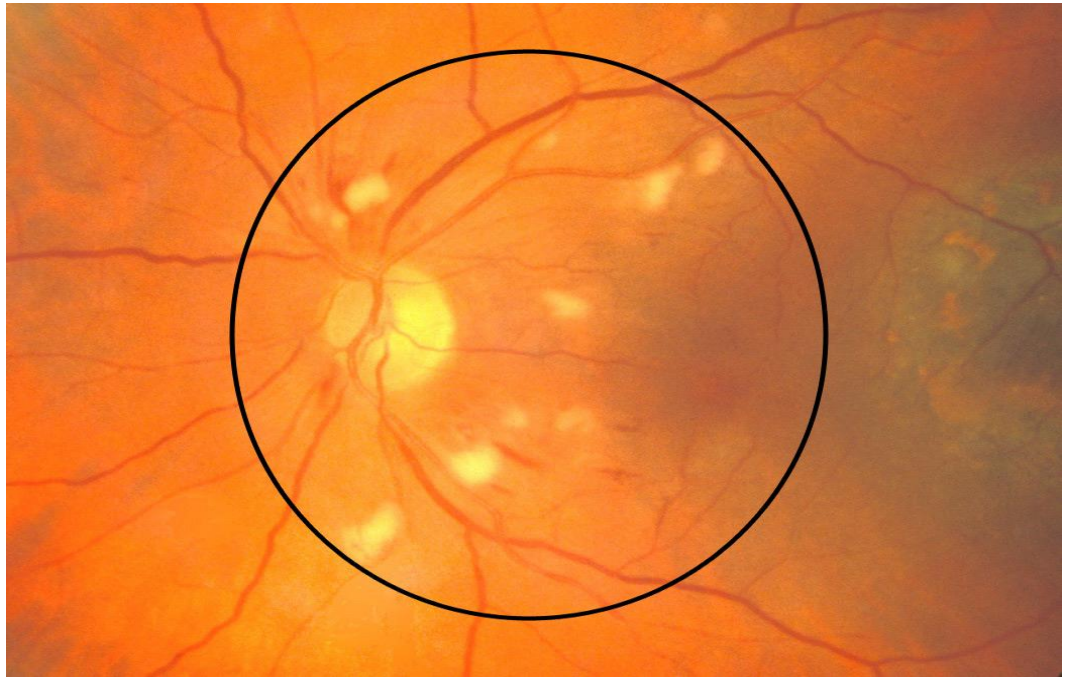
•Intraretinal hemorrhage (dot-blot hemorrhage): from venous ends of capillaries.

- Dots: bright red dots (look like microaneurysms).

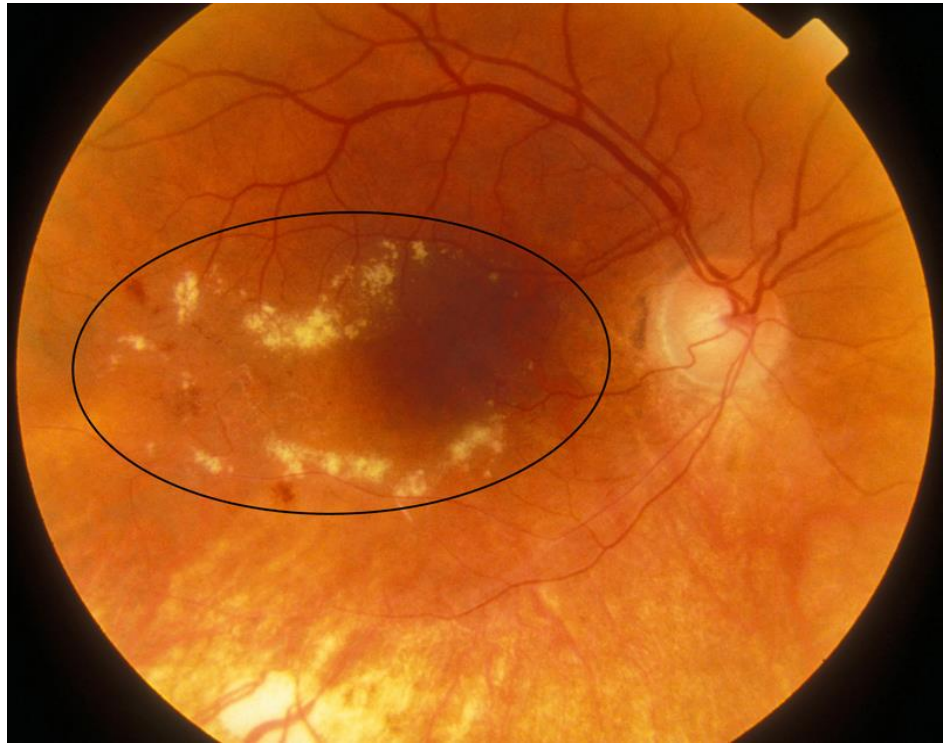
- Blots: larger, less circular; usually in mid retina or in surrounding areas of ischemia.

•Retinal nerve fiber layer hemorrhages (flame hemorrhage): from large superficial precapillary arterioles. →They are flame shaped due to the architecture of the retinal nerve fibers (also occurs in HTN).

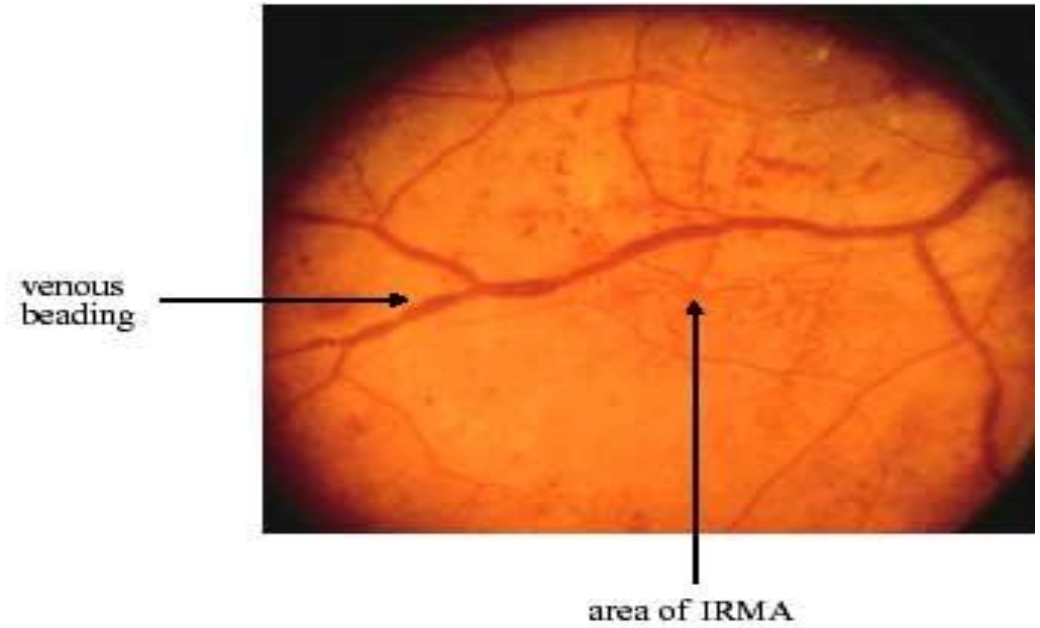
Fig. 13.5 Retinal haemorrhages. (A) Histology shows blood lying diffusely in the retinal nerve fibre and ganglion cell layers and as globules in the outer layers; (B) retinal nerve fibre layer haemorrhages; (C) deep dot and blot haemorrhages; (D) deep dark haemorrhages (Courtesy of J Harry and G Misson, from Clinical Ophthalmic Pathology, Butterworth-Heinemann 2001 – fig. A; Moorfields Eye Hospital – fig. C)

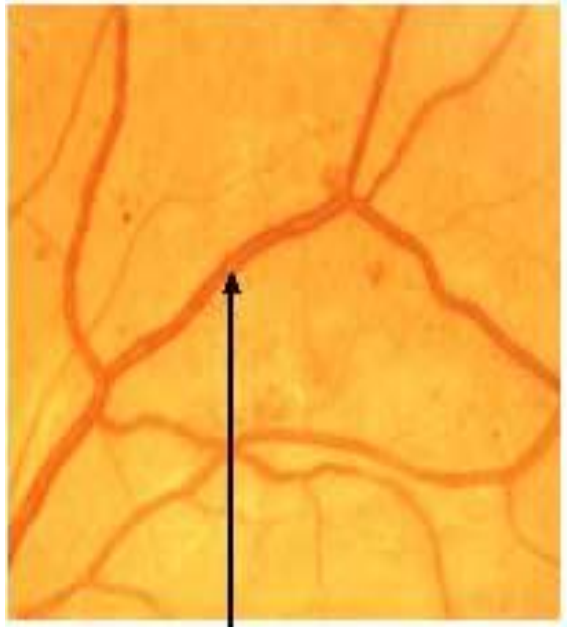


Cotton wool spots (soft exudates): occlusion of retinal precapillary arterioles supplying the nerve fiber layer & swelling of local nerve fiber axons. →White fluffy lesions (Also occurs in HTN).



Lipid Exudates "Hard exudates": yellow deposits of lipid & protein in sensory retina.
→ Distinct margins, in clumps.
↑ in hyperlipidemia (intra retinal lipid exudates).





definite venous beading

severe venous beading

Intra-Retinal Microvascular Abnormalities "IRMAs":

• remodeling of preexisting normal vessels in the retina that act as shunts; they look like new vessels, but actually are not.

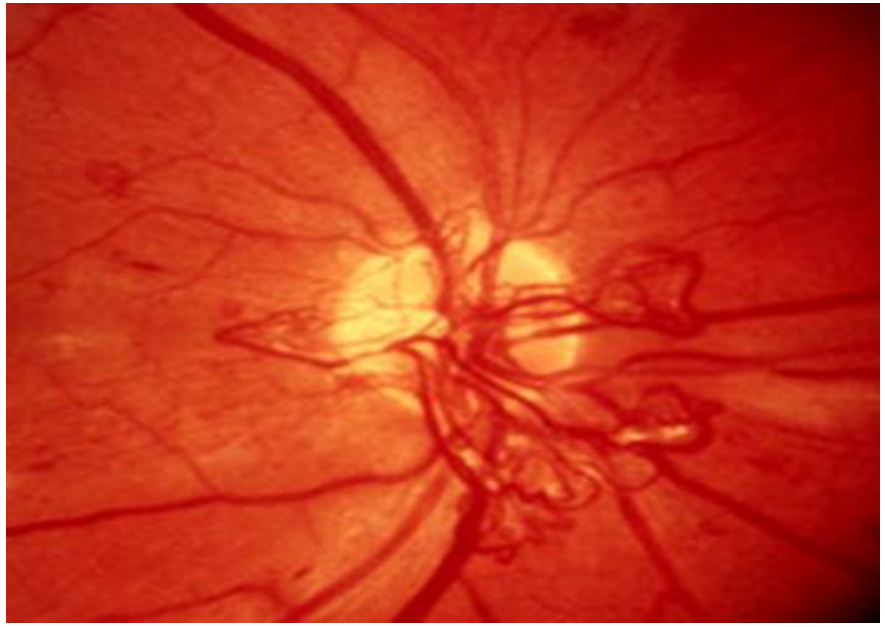
• Occurs in severe NPDR and indicates rapid progression to PDR.

• Not leaky.

Venous beading:

•Sausage shaped dilations of retinal veins.

•Occurs in severe NPDR (if 4 quadrants are involved).

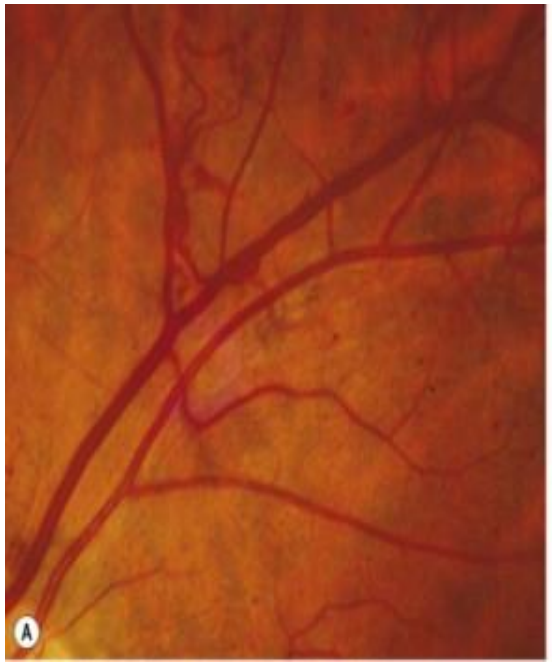


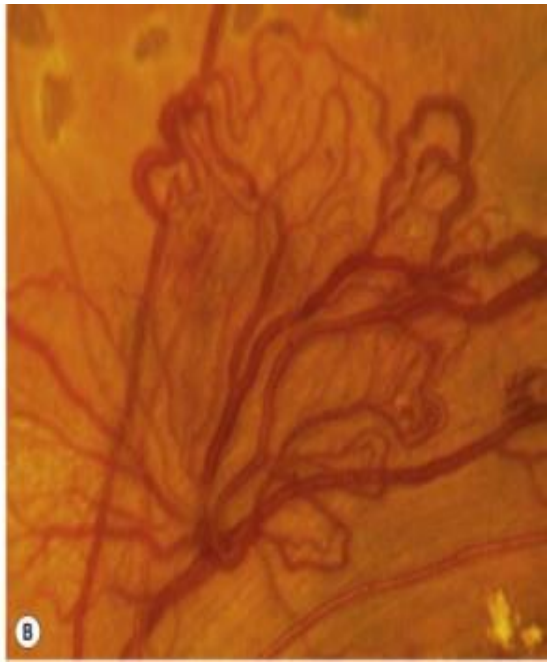
Sign in PDR

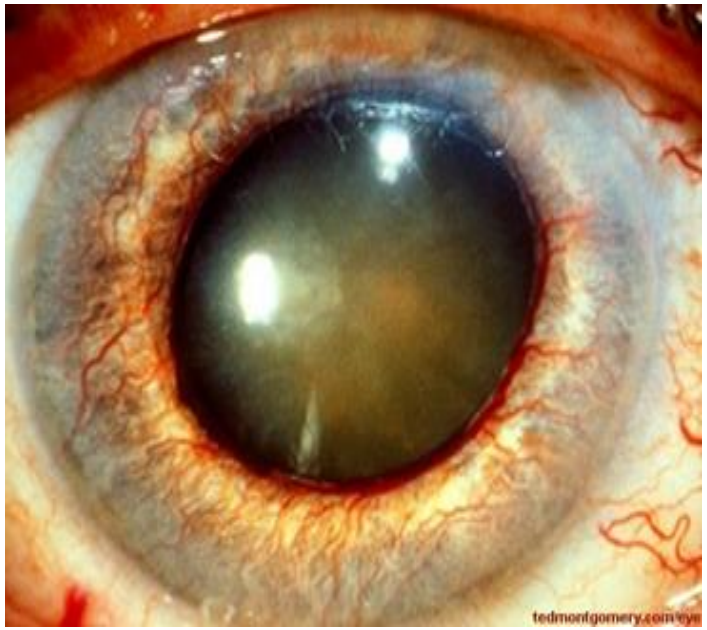
Neovascularization of the optic Disc (NVD)

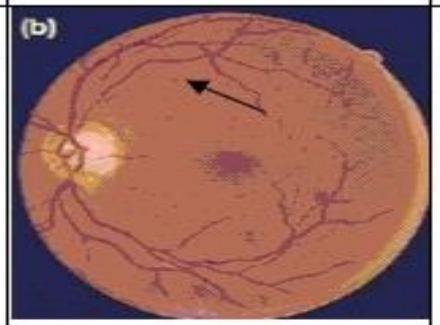
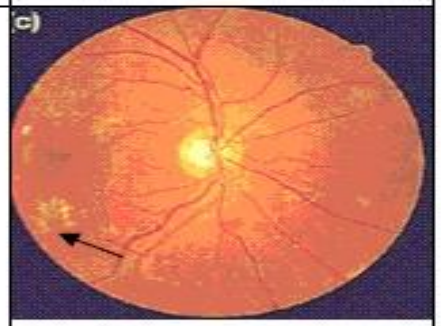
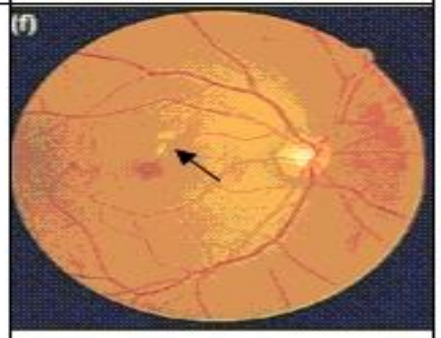
Neovascularization elsewhere (NVE).

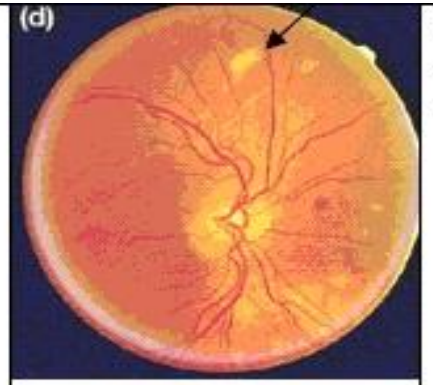
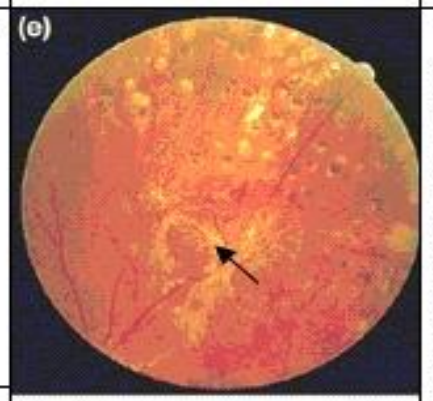
Neovascularization of iris (NVI; Rubeosis iridis) → may progress to neovascular glaucoma. (Advanced diabetic eye disease)







Grade of retinopathy	Features	Appearance	Fundoscopy	Pathophysiology
Non-proliferative	Microaneurysms	Small red dots in superficial retinal layers.		Outpouching of the capillary wall due to pericyte loss.
	Dot & blot haemorrhages	Appear similar to microaneurysms if small.		Microaneurysm rupture in the deeper retinal layers.
	Flame-shaped haemorrhages	Splinter haemmorhages		Microaneurysm rupture in superficial nerve fibre layer.
	Retinal oedema	Dull appearance to the retina.		Leakage of serum proteins, lipids & protein from vessels due to breakdown of blood-retina barrier.
	Hard exudates	Waxy, yellow lesions often arranged in clumps or rings.		
	Macular oedema	Retinal thickening at macula, hard exudates within disc width of the macula.		

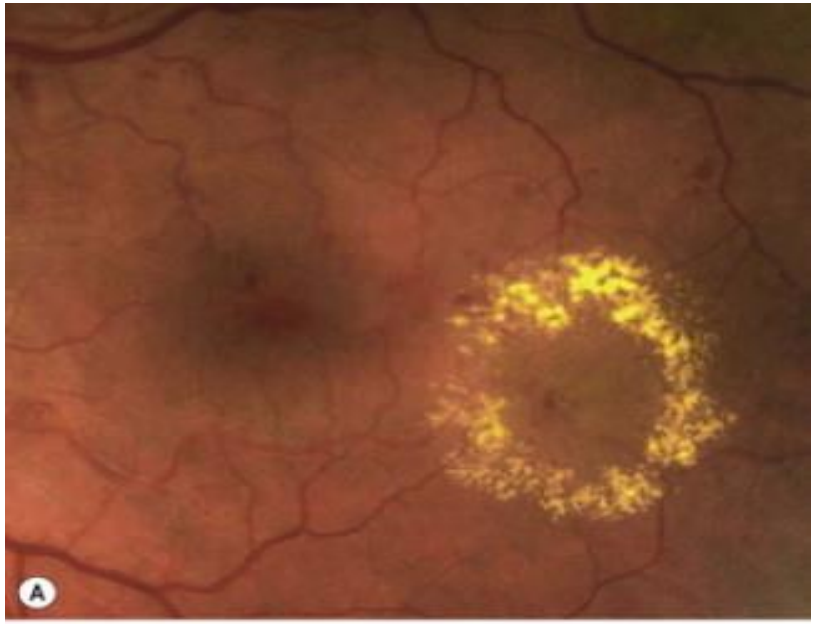
Pre-proliferative	Cotton wool spots	Small, white, fluffy superficial lesions.		Occlusion of precapillary arterioles leads to infarction of the nerve fibre layer.
	Venous changes	Dilatation, tortuosity, looping, beading, 'sausage-like' segmentation.		Indicates increasing retinal ischaemia (most significant predictor of progression to proliferative retinopathy)
	Intraretinal microvascular abnormalities	Fine, irregular red lines that run from arterioles to venules. Collateral vessels.		Not proliferative changes. Arteriovenous shunts.
Proliferative	New vessels at disc (NVD)	Neovascularisation on or within one disc diameter of the optic nerve head.		Neovascularisation in response to vasogenic factors e.g. VEGF released by ischaemic retina. Growth of abnormal blood vessels and fibrous tissue on retina and forwards into vitreous. Intravitreal vessels are more permeable than normal retinal vessels → may cause vitreous haemorrhage.
	New vessels elsewhere (NVE)	Neovascularisation further away from the disc.		

DIABETIC MACULOPATHY

- Retinal thickening & edema involving macula (foveal oedema, exudates or ischaemia)
- DR could be with or without diabetic maculopathy
- Can occur at any stage of DR
- Blurred vision

** (most common cause of visual impairment in DM patients)

- 4 types
  - Focal exudative macular edema .
  - Diffuse exudative macular edema .
  - Ischemic maculopathy .
  - Mixed types

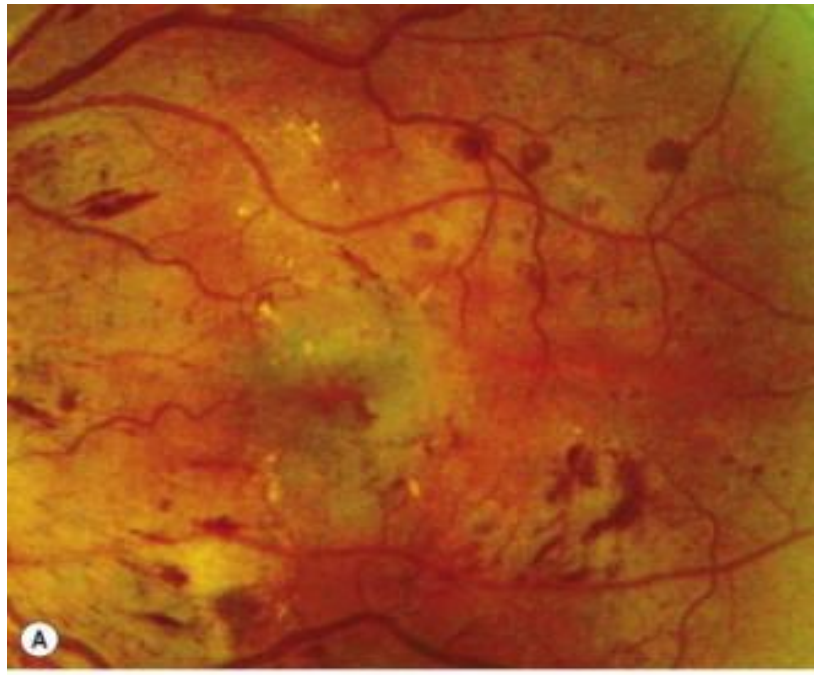


A ring of hard exudates temporal to the macula

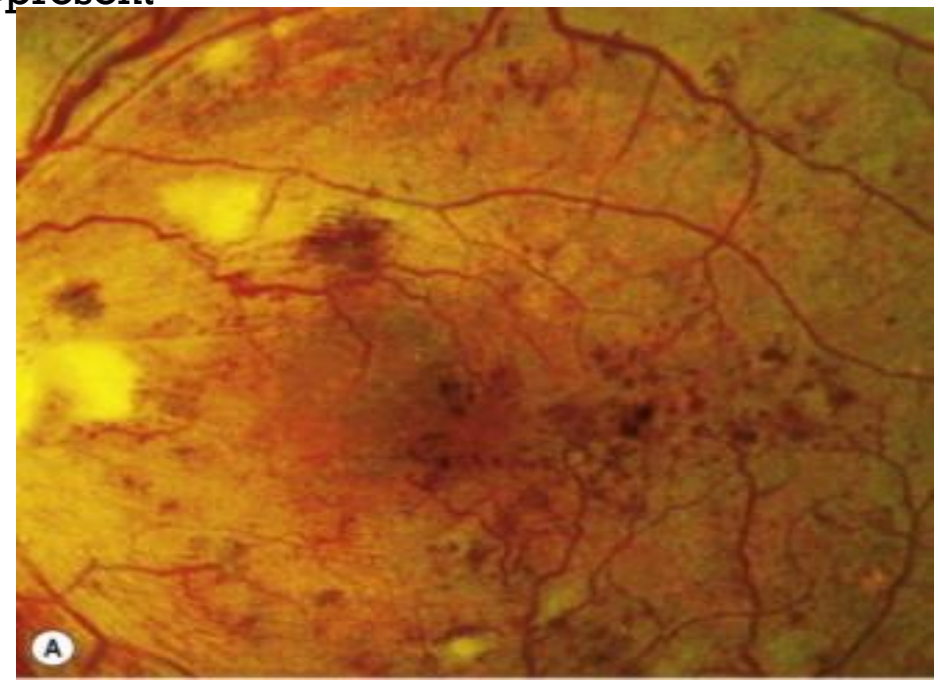
FOCAL : Well-circumscribed retinal thickening associated with complete or incomplete rings of exudates

DIFFUSE: Diffuse retinal thickening, which may be associated with cystoid changes. Landmarks are obliterated by severe oedema which may render localization of the fovea impossible

ISCHEMIC: Signs are variable and the macula may look relatively normal despite reduced visual acuity. In other cases PPDR may be present



Dot and blot haemorrhages



Dot and blot haemorrhages and cotton wool

stages of diabetic retinopathy:

1) Non-proliferative (normal vision)

• hyperglycemia → loss of pericytes→ increase permeability →Edema (hard exudate)

• weak capillary wall →micro aneurysm & dot hemorrhage

2) Pre-proliferative (normal vision)

• occlusion → infarction in nerve fiber layer → swollen ganglion cells → (cotton wool spots & IRMA(intra retinal microvascular abnormality) & hypoxia(ischemia) & venous loops

3) Proliferative (normal vision; sight threatening)

• occlusion → release of vaso-proliferative substance from the retina → growth of new vessels (on the disk (NVD) or elsewhere on the retina (NVE))

4) Advanced (reduced vision, often acutely with vitreous hemorrhage; sight threatening)

• Proliferative changes → bleeding (into vitreous or between vitreous & retina)

• Growth of new vessels → fibrous proliferation → pull the retina from its RPE(retinal pigment epithelium)

** Maculopathy (not a stage! could happen with any stage) (may reduce

Advanced diabetic eye disease:

• tractional retinal detachment.

• Significant persistent vitreous hemorrhage.

• Neovascular glaucoma. (NVI)

Investigations in DR:

•Visual acuity.

•Fundus exam.

•Fluorescent angiography. (assess the degree of retinal ischaemia and to pinpoint areas of leakage both from micro-aneurysms and new vessels)

•Slit lamp exam (before & after mydriasis).

•OCT (Optical coherence tomography)

Treatment

•NPDR: follow up according to severity (mild-moderate-severe-very severe)

•Maculopathy: 1st line is grid/focal laser (At leakage point)

2nd line is Anti-VEGF (avastin) or steroids.

**newly the first line of tt is : Anti-VEGF

•PDR:

Pan retinal photocoagulation (PRP): sparing the central macular area & optic disc.

→Eliminates ischemic retina → ↓VEGF.

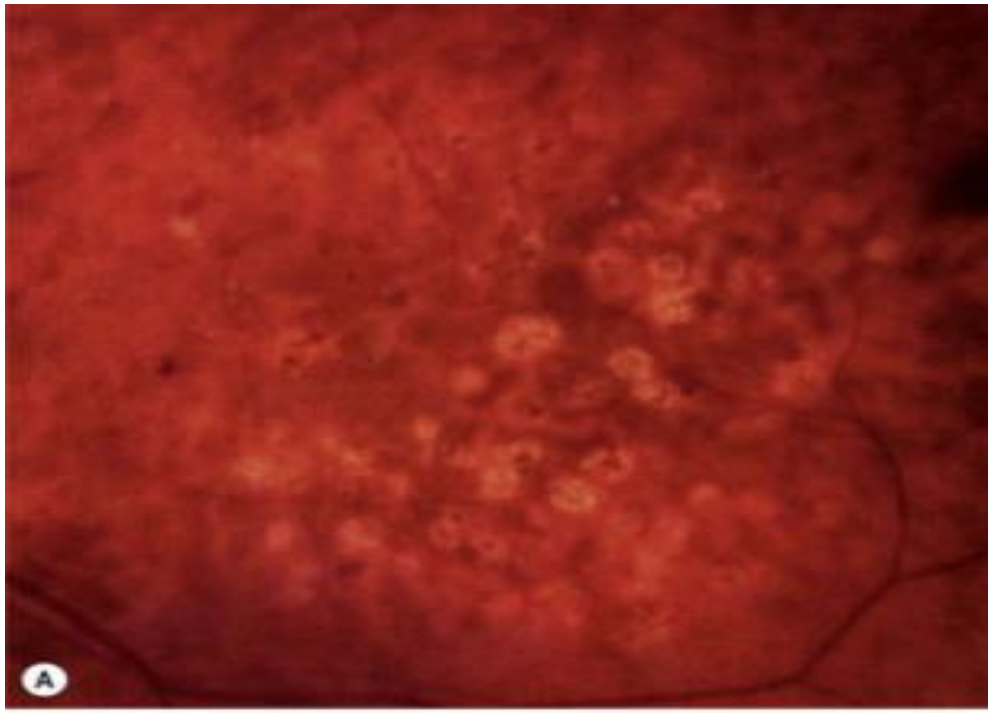
• Intravitreal anti-VEGF: temporary.

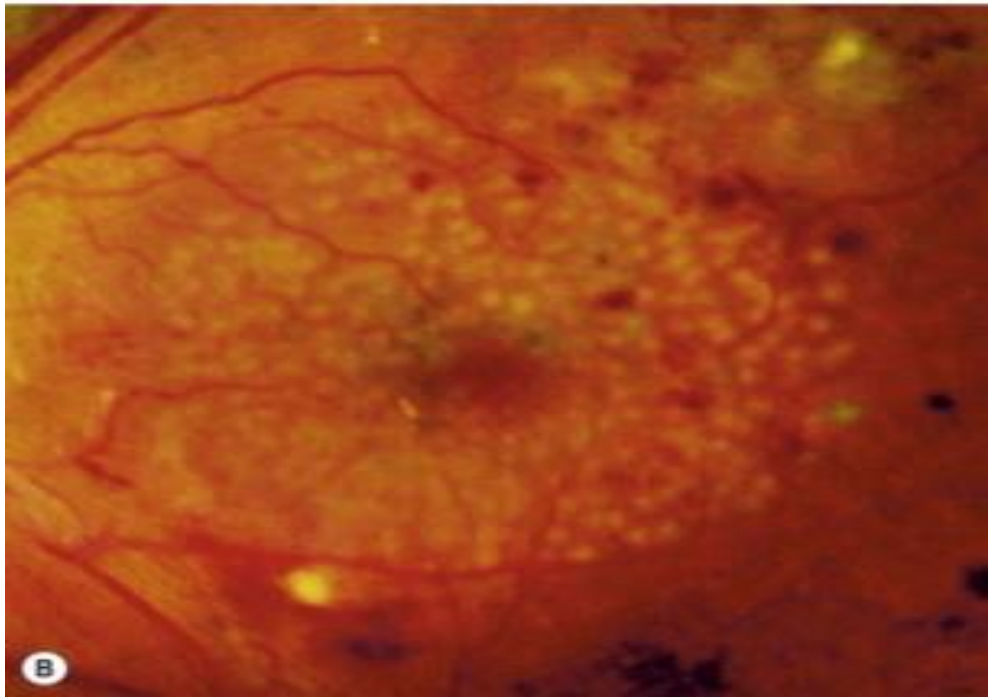
it is used when there's vitreous hemorrhage & the retina can't be seen because of blood.

-used for 2-3 months till the blood stop.

• Surgery (vitrectomy): Pars plana vitrectomy (PPV).

if viterous bleeding or fibrous traction on retina





Laser photocoagulation for clinically significant macular oedema. (A) Appearance several weeks following focal laser photocoagulation shows laser scars and absence of hard exudates; (B) appearance immediately following grid laser photocoagulation