
# Diabetic and Hypertensive Retinopathy

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# Diabetic Retinopathy

- Diabetic retinopathy (DR) is a microvascular disorder occurring due to long term effects of diabetes, leading to vision-threatening damage to the retina, eventually leading to blindness.

- It is the most common cause of severe vision loss in adults of working age groups in the western world. Early detection and timely intervention is the key to avoid blindness due to diabetic retinopathy.

- The usefulness of strict glycemic control was clearly seen in clinical trials like the UK Prospective Diabetes Study (UKPDS) and Diabetes Control and Complication Trial (DCCT).

# Diabetic retinopathy

Uncontrolled diabetes can lead to many ocular disorders:

- Cataract.
- Glaucoma.
- ocular surface disorders.
- non-arteritic anterior ischemic optic neuropathy.
- diabetic papillopathy.
- **diabetic retinopathy.**

diabetic retinopathy is the most common and severe ocular complication.

# Etiology

- Diabetic retinopathy affects people with diagnosed or undiagnosed diabetes mellitus.

- The propensity of developing diabetic retinopathy is directly proportional to the
    - age of the patient
    - duration of diabetes
    - poor glycemic control and fluctuation
    - blood pressure level

# Risk factors

Non-modifiable:

- Puberty
- Pregnancy

Modifiable:

- Hypertension
- Obesity
- Dyslipidemia
- Poor glycemic control
- Nephropathy

Newer risk factors:

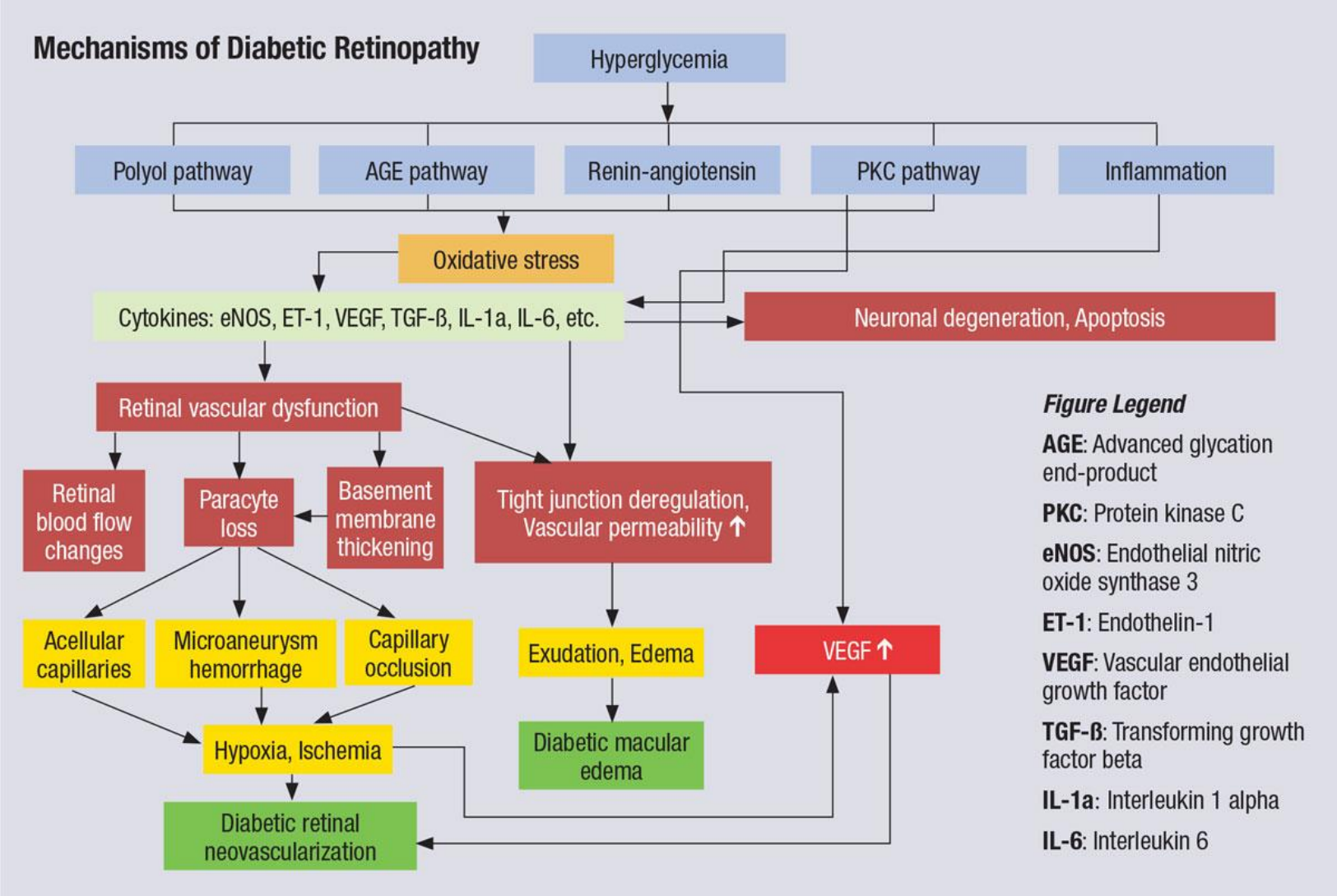
- Inflammation
- Apolipoprotein
- Hormonal influence- Leptin and Adiponectin
- Vitamin D deficiency
- Oxidative stress
- Genetic factors

# Epidemiology

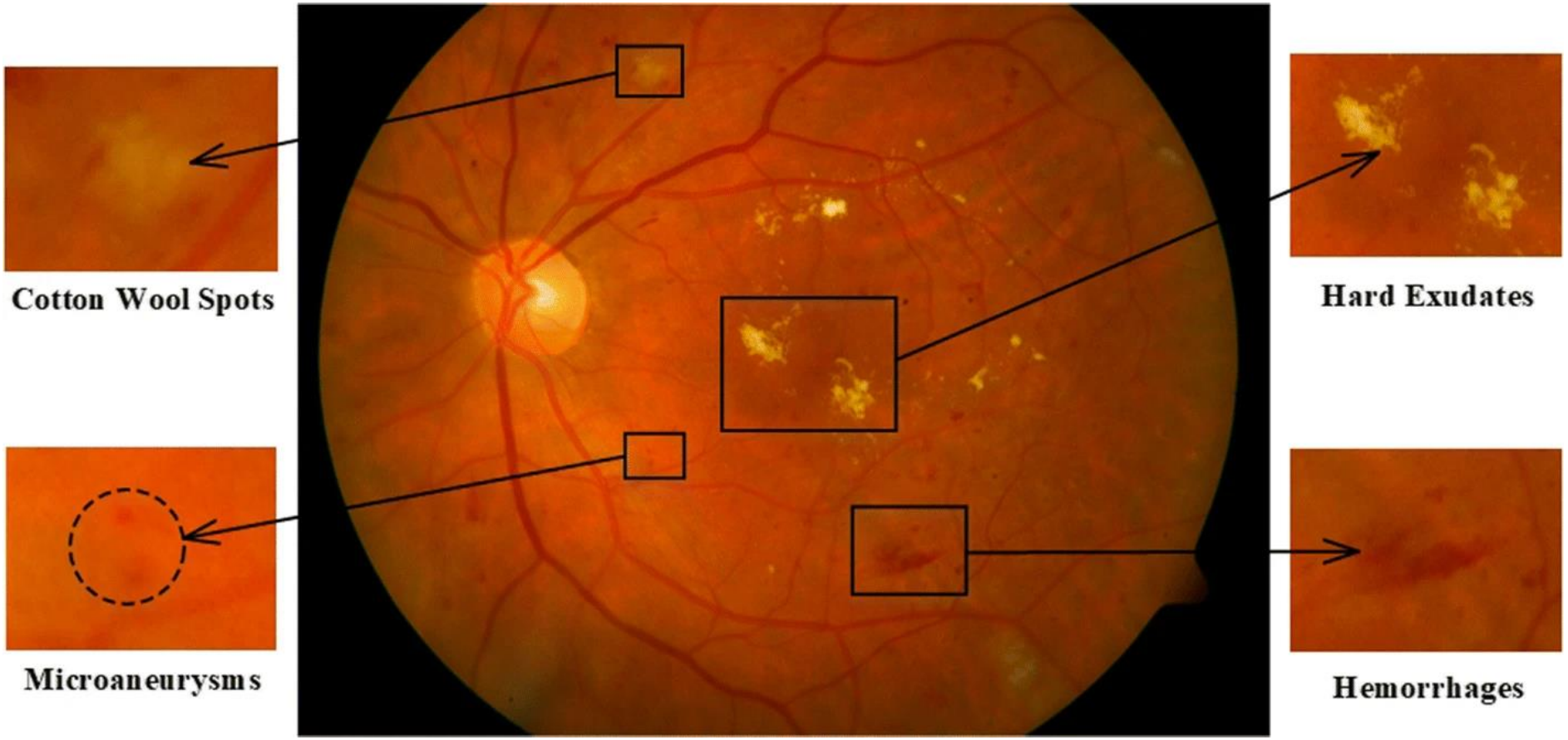
- Diabetic retinopathy is one of the major neurovascular complications of diabetes.
- **93 million** people are globally affected by **diabetic retinopathy**.
- Prevalence of diabetic retinopathy is **77.3% in type 1 diabetes** patients and **25.1% in type 2 diabetes patients**, out of which approximately 25% to 30% are expected to develop vision-threatening diabetic macular edema.
- Between 5% and 8% of patients with diabetic retinopathy need laser treatment. As many as 0.5% of patients will require vitrectomy surgery.

1. Wilkinson-Berka JL, Miller AG. Update on the treatment of diabetic retinopathy. ScientificWorldJournal. 2008 Feb 06;8:98-120. [PMC free article13.
2. Moutray T, Evans JR, Lois N, Armstrong DJ, Peto T, Azuara-Blanco A. Different lasers and techniques for proliferative diabetic retinopathy. Cochrane Database Syst Rev. 2018 Mar 15;3:CD012314. [PMC free article]
3. Gupta V, Arevalo JF. Surgical management of diabetic retinopathy. Middle East Afr J Ophthalmol. 2013 Oct-Dec;20(4):283-92. [PMC free article]

# Pathophysiology



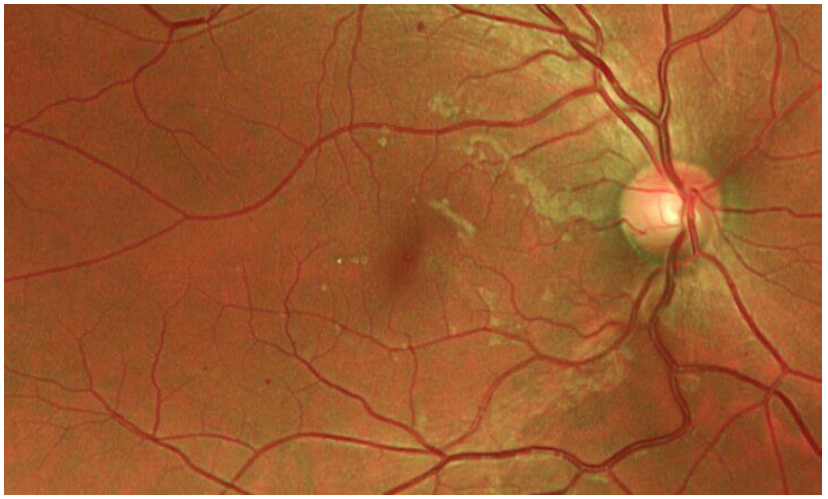
# Fundus picture of patient with diabetic retinopathy

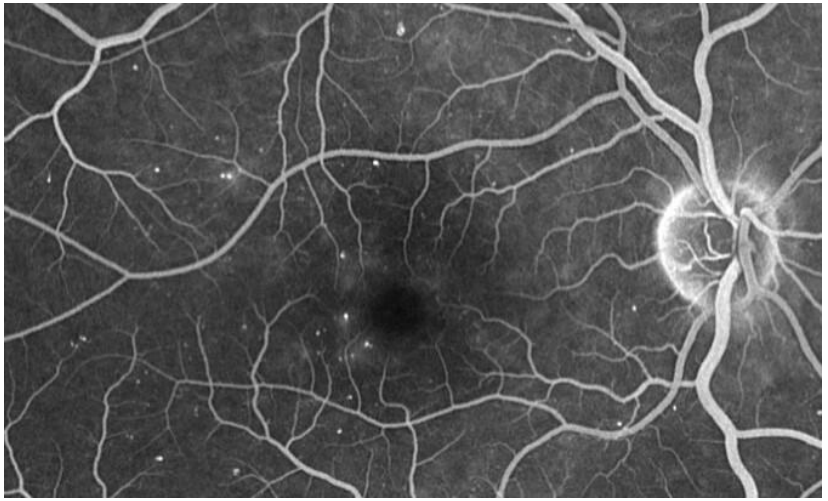


# Retinal changes in diabetic retinopathy

**Microaneurysms:**

- Are the earliest clinically detectable lesions.
- Clinically identified by ophthalmoscopy as tiny, round, red dots with a sharp regular margin.
- A diameter of 15- 60 µm (less than 125 µm). Microaneurysms with a diameter of less than 30 µm may not be detectable clinically.
- Initially appear temporal to the fovea.
- May disappear with time.
- Microaneurysms are differentiated from dot hemorrhages by FFA (fundus fluorescein angiogram) wherein microaneurysms show tiny hyperfluorescent points whereas dot hemorrhages show blocked fluorescence. Dot hemorrhages are clinically larger and may have an irregular margin.

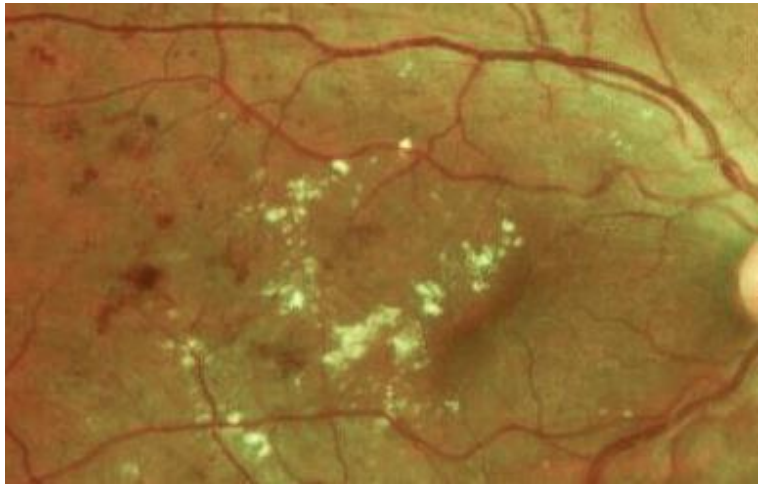


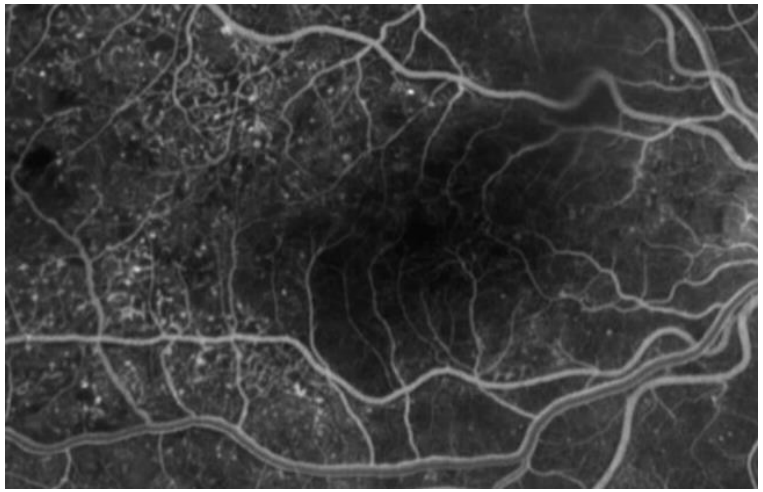


# Retinal changes in diabetic retinopathy

**Hemorrhages:**

- Weakened capillary wall ruptures leading to intraretinal dot hemorrhages.
- Superficial or flame-shaped hemorrhages arises from the precapillary arterioles located in the retinal nerve fiber layer.
- Deep hemorrhages or dot and blot hemorrhages are located in the inner nuclear and outer plexiform layers of the retina.

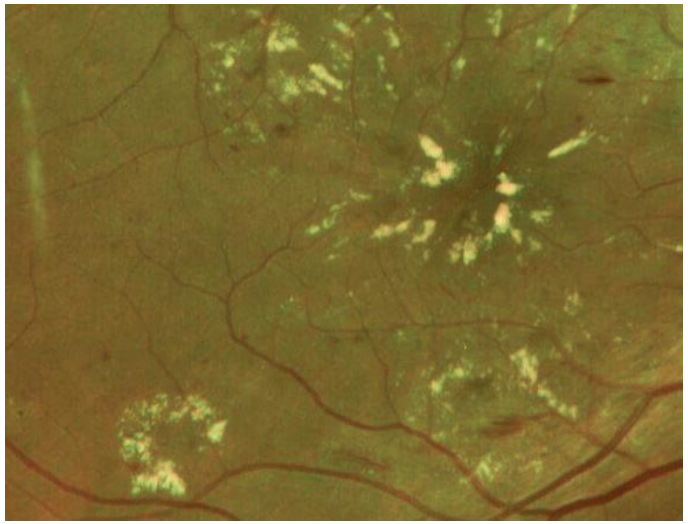




# Retinal changes in diabetic retinopathy

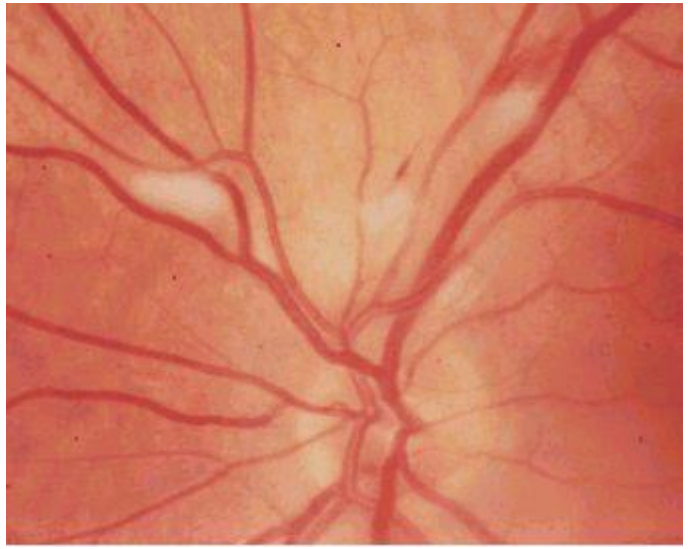
**Hard exudates:**

They are composed of lipoprotein and lipid-filled macrophages located in the outer plexiform layer. They develop at the junction of the edematous and non-edematous retina.



**Cotton wool spots/soft exudates:**

They are located in the retinal nerve fiber layer (axoplasmic debris) and represent focal infarcts of the precapillary arterioles.

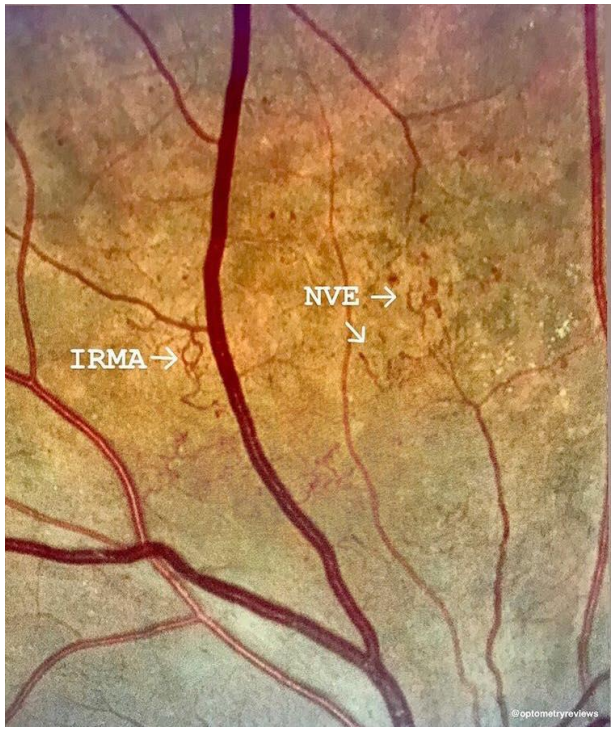


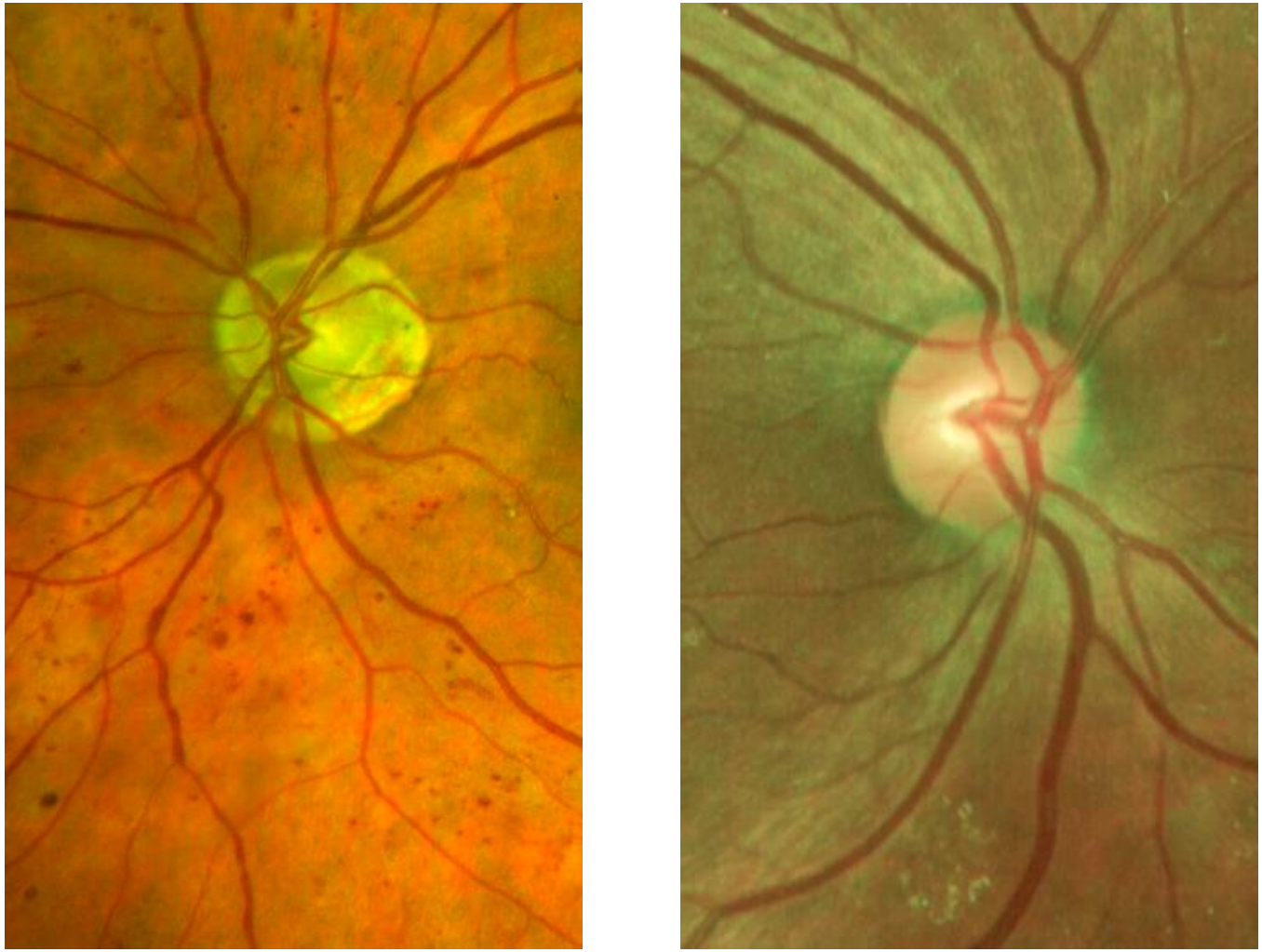
# Vascular changes in diabetic retinopathy

**IRMA (intraretinal microvascular abnormalities):**
IRMA's are intercommunications between retinal arteriole and venules, which bypass the capillaries and are seen near the areas of capillary closure. IRMA's are intraretinal in location, do not cross the major vessels, and do no leak on fluorescein angiography.

**Venous changes:**
- Dilatation
- Looping
- Beading
- Sausage-like segmentation

**Arterial changes:**
- Peripheral narrowing
- Silver-wiring
- Obliteration



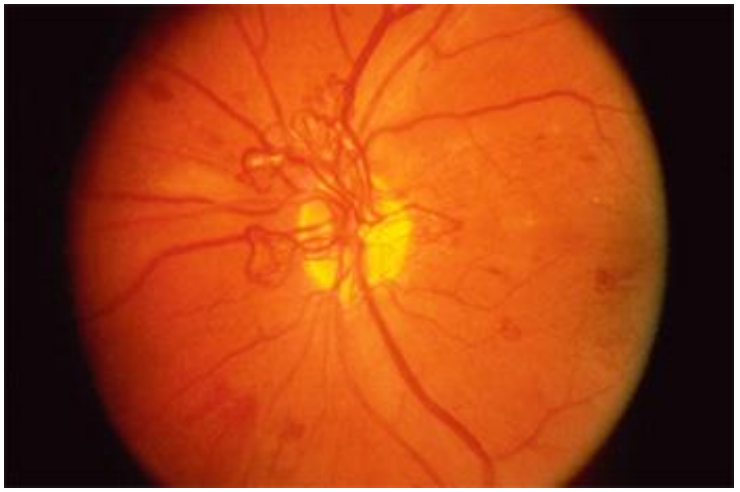


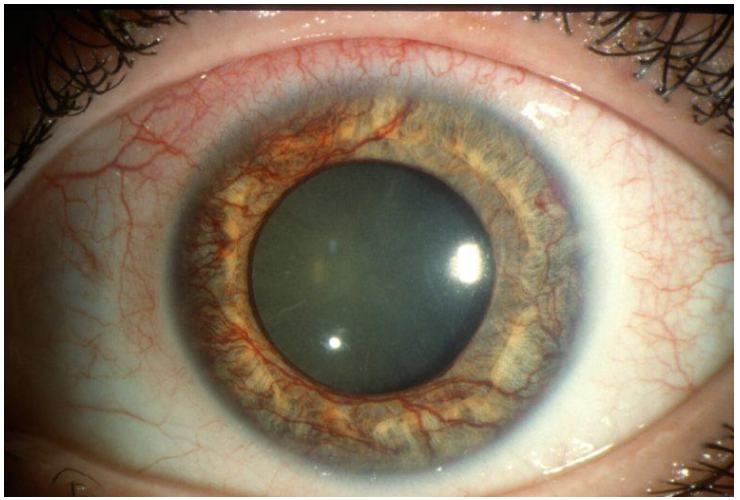
Photos showing venous dilatation and beading

# Vascular changes in diabetic retinopathy

**Neovascularization:**

- Neovascularization (new vessels) at the disc (NVD)- neovascularization at or within one disc diameter of the optic disc
- Neovascularization elsewhere (NVE)- new vessels away from one disc diameter of the optic disc.
- Neovascularization of Iris- It is a marker of poor prognosis and is associated with the propensity to develop neovascular glaucoma





# Classification ETDRS

Early treatment diabetic retinopathy study **(ETDRS)** classification of diabetic retinopathy:

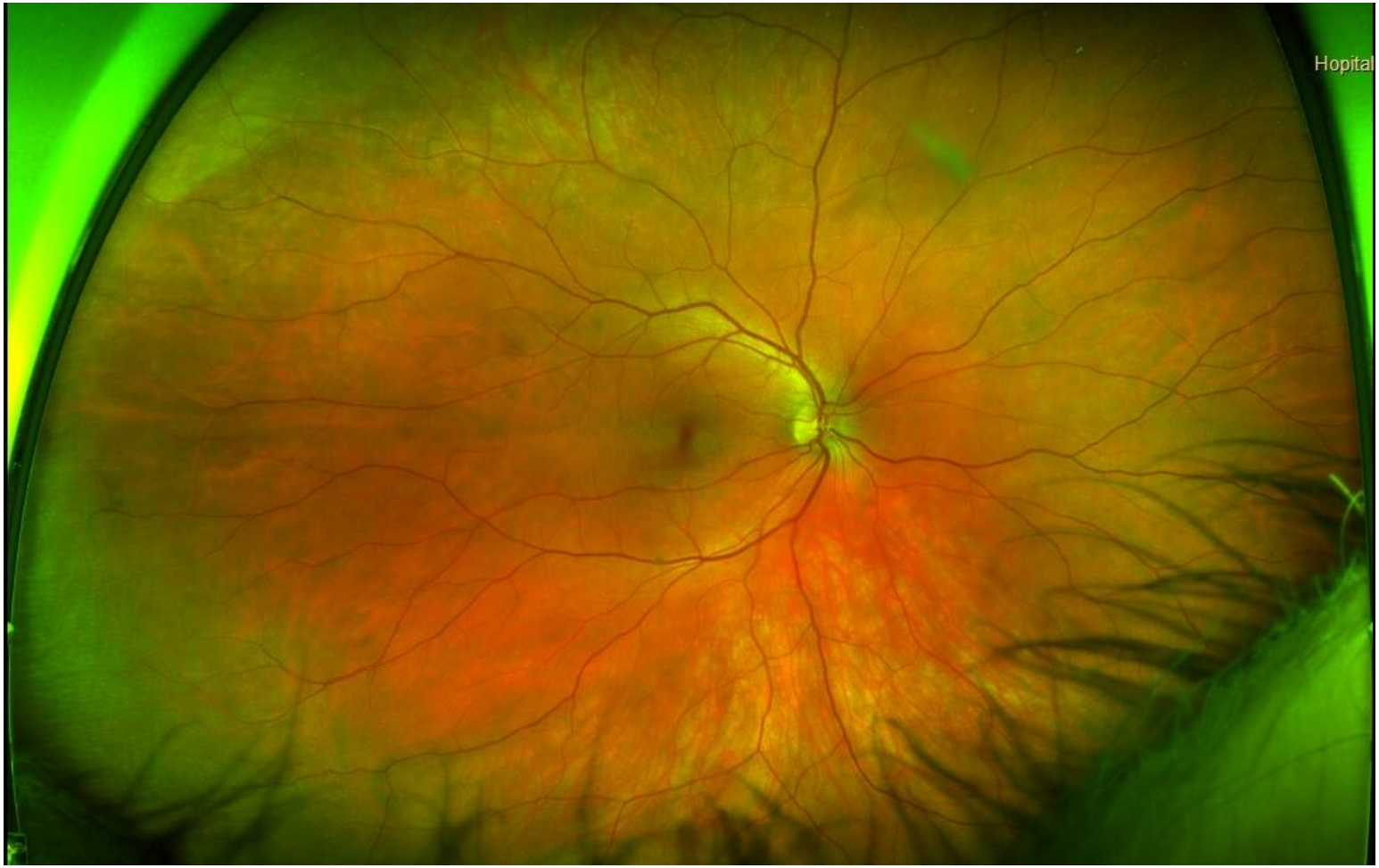
<u>Nonproliferative Diabetic Retinopathy:</u>

- No retinopathy: No retinal lesions
- Very mild NPDR: Microaneurysms only
- Mild NPDR: A few microaneurysms, retinal hemorrhage & hard exudates
- Moderate NPDR: Retinal hemorrhages (about 20 medium-large per quadrant) in 1-3 quadrant + cotton wool spots (between the grades mild and severe NPDR)
- Severe NPDR: fulfilling one rule of 4-2-1 rule.

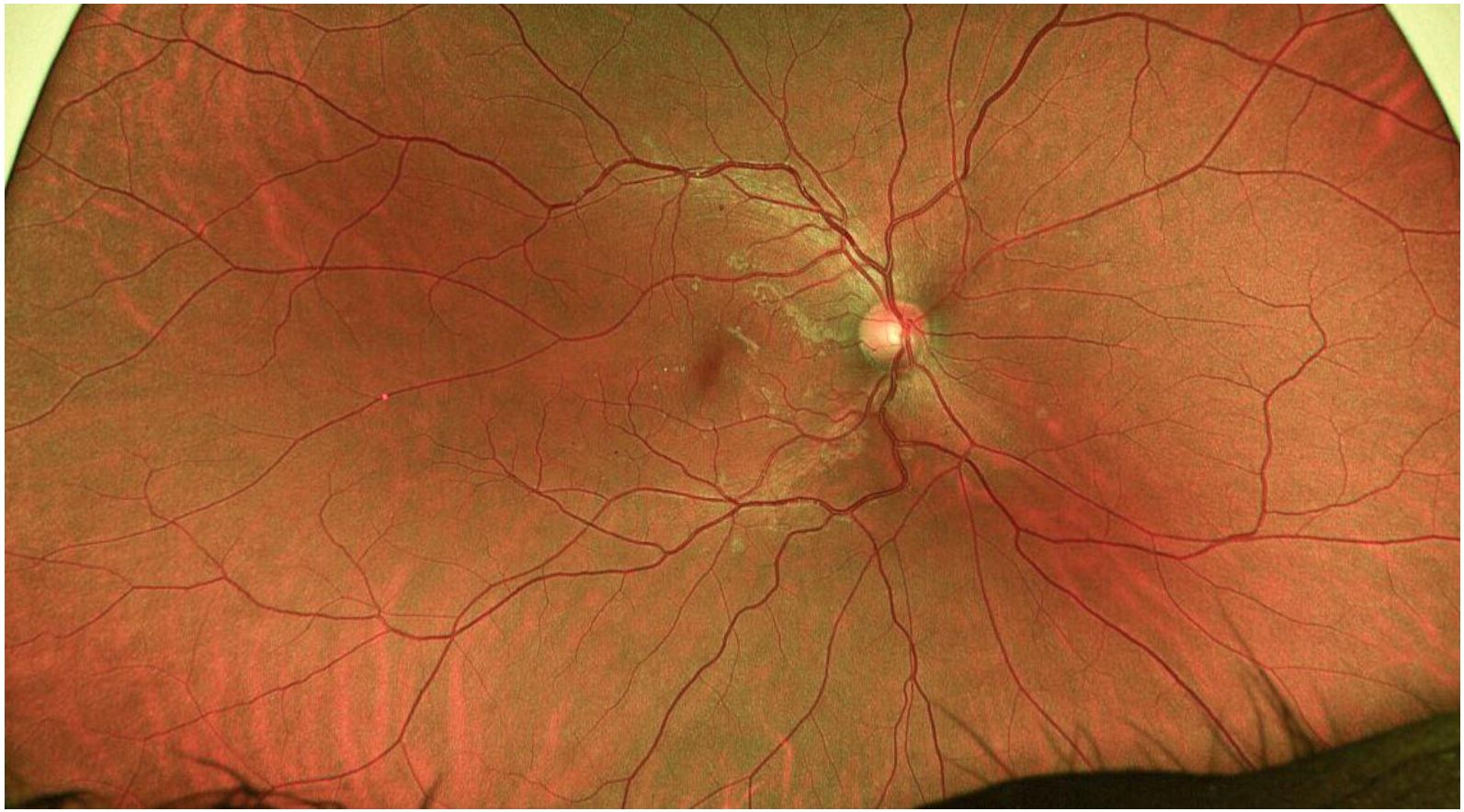
4-2-1 rule
Severe hemorrhages in all four quadrant
Venous beading in 2 or more quadrants
Moderate IRMA in 1 or more quadrants

- Very Severe NPDR: fulfilling two or more rules of 4-2-1 rule.

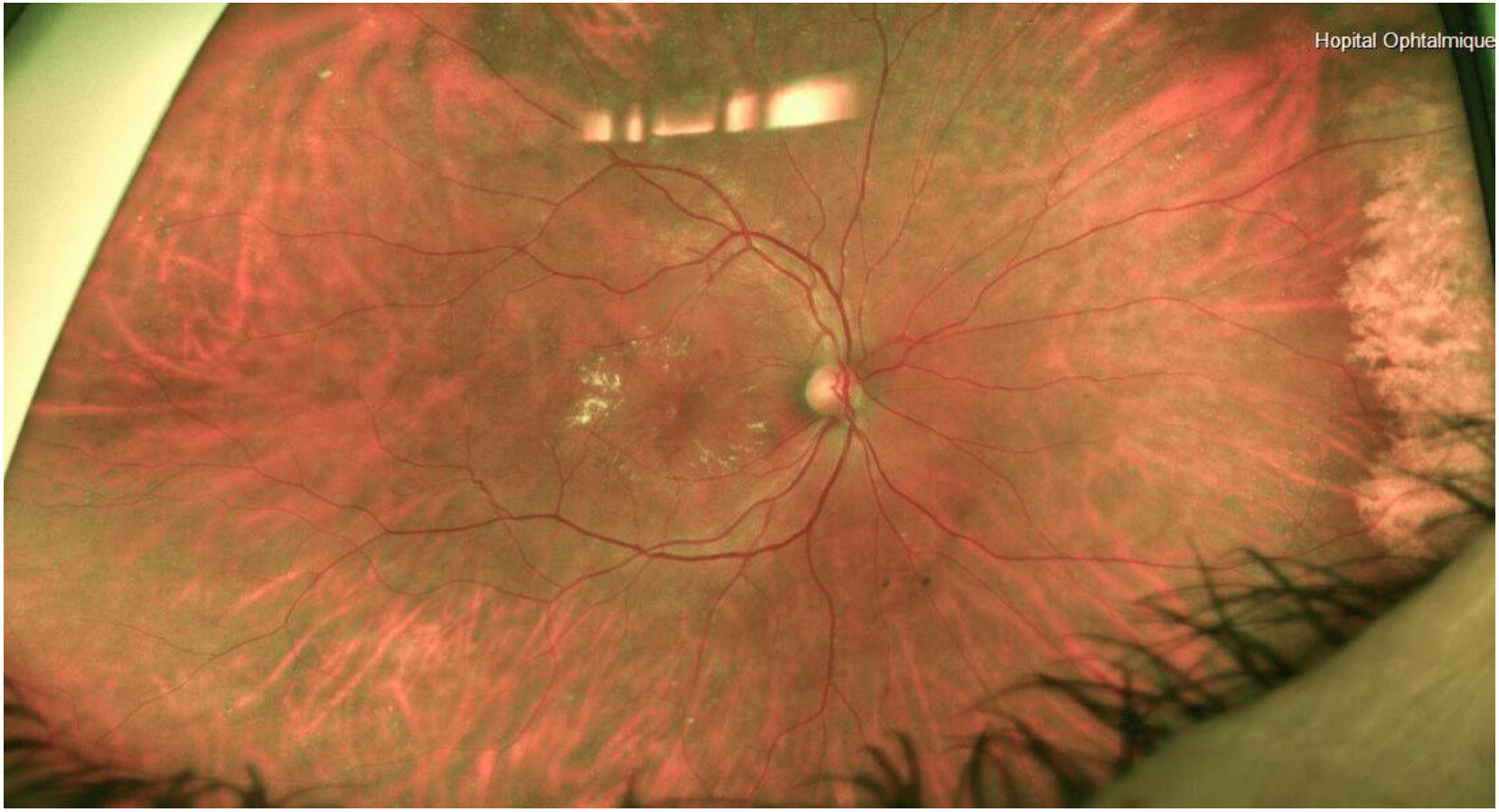
# Normal Fundus



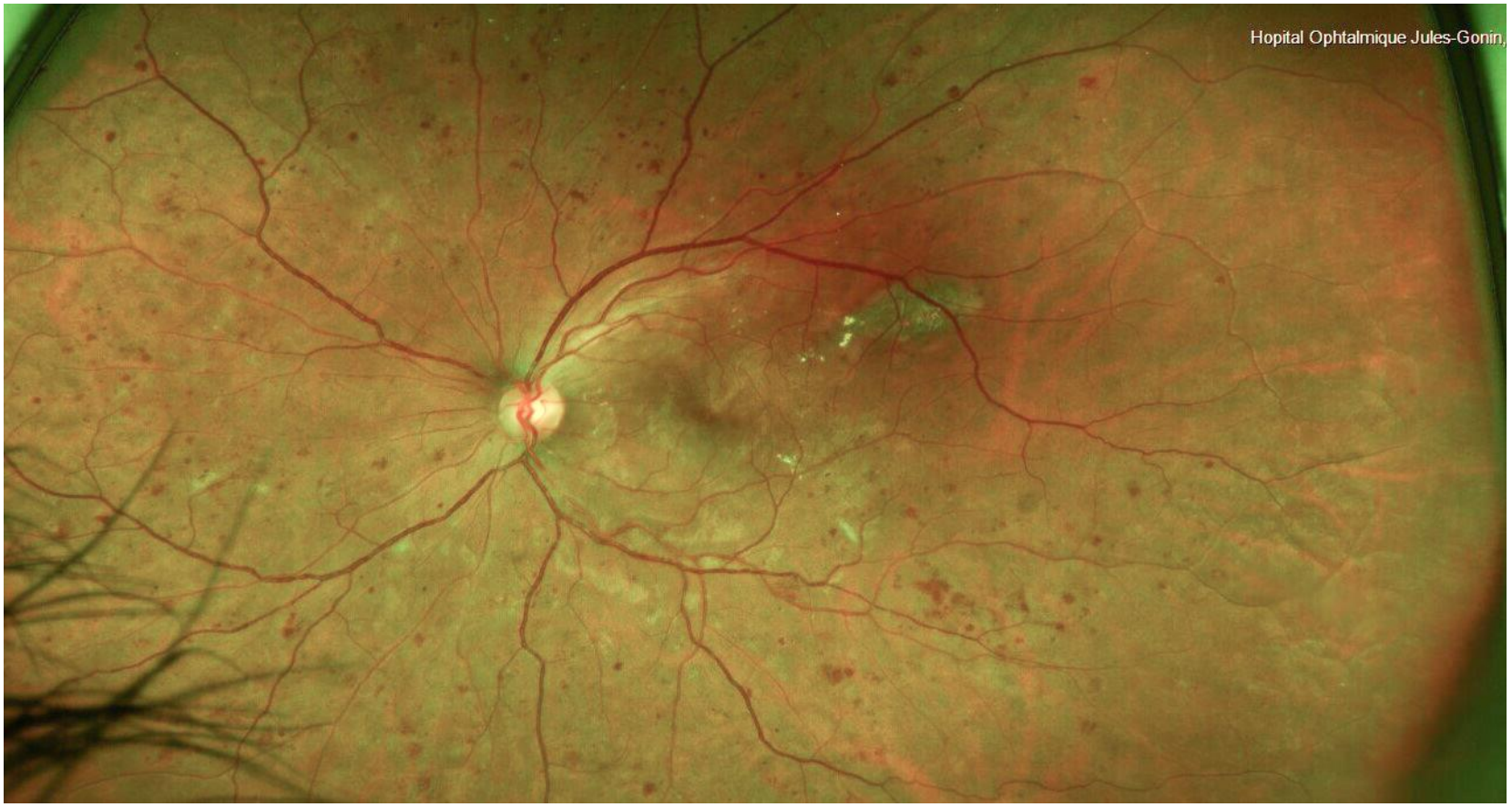
# Very mild diabetic retinopathy



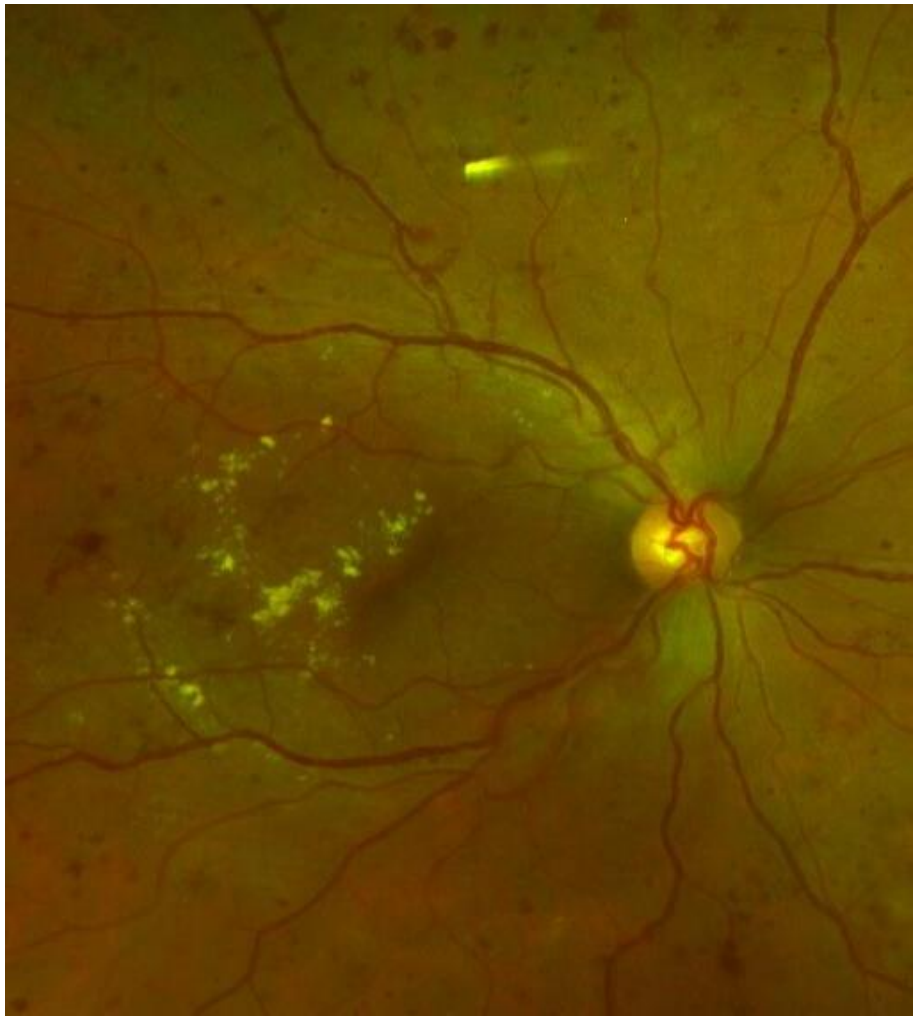
# Mild to moderate NPDR

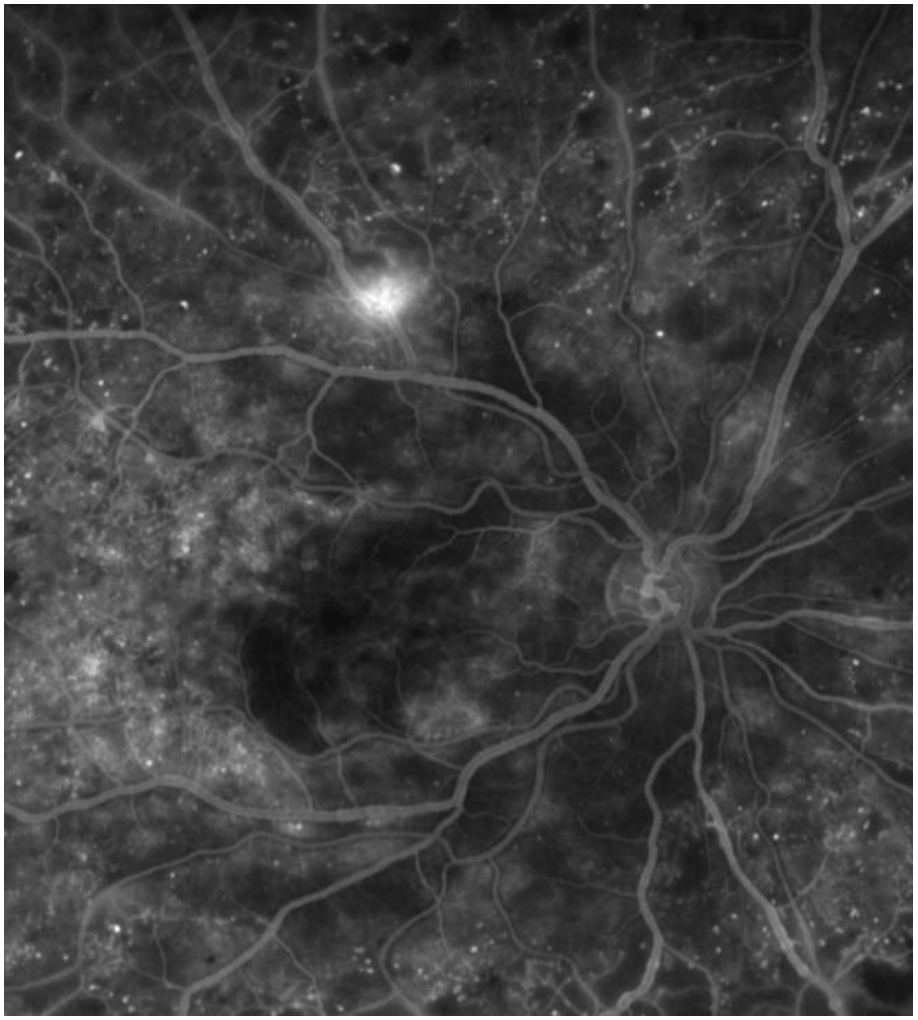


# Severe NPDR



# Proliferative Diabetic Retinopathy





# Classification ETDRS

**Proliferative Diabetic Retinopathy:**

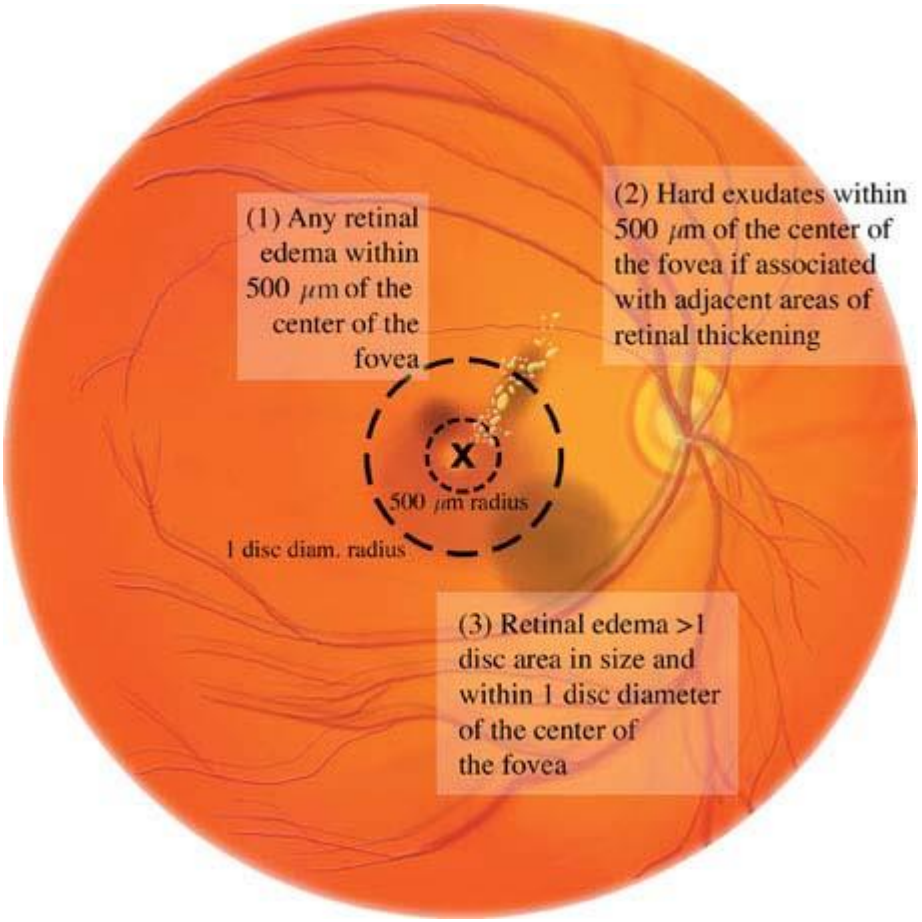
- Mild to moderate PDR:
    - NVD or NVE insufficient to meet high-risk characteristics

- High risk PDR:
    - NVD greater than ETDRS standard photograph 10A (about 1/3 disc area).
    - Any NVD with vitreous hemorrhage.
    - NVE greater than 1/2 disc area with vitreous hemorrhage.

# Diabetic maculopathy

ETDRS classification of Clinically significant macular edema (CSME):

- Retinal edema within 500 µm of the center of the fovea.
- Hard exudates within 500 µm of the center of the fovea if associated with adjacent retinal thickening (which may be outside the 500 µm limit).
- Retinal edema one disc area (1500 µm) or larger any part of which is within one disc diameter of the center of the fovea.



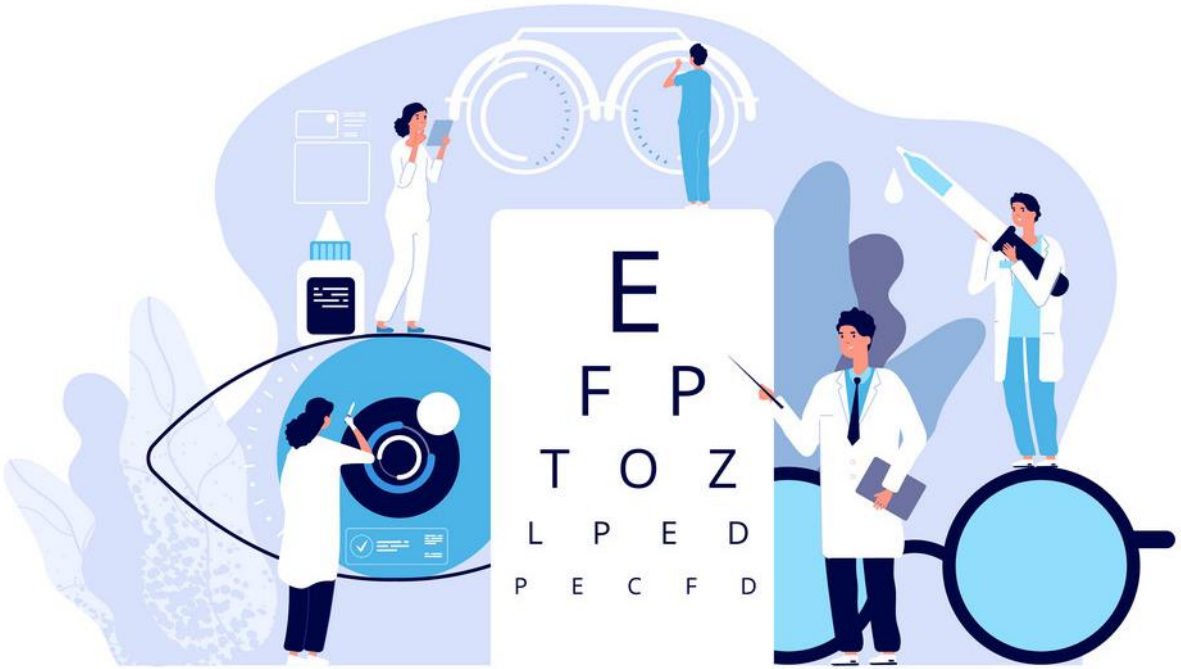
# Classification ICDRDS

**International Clinical Diabetic Retinopathy Disease Severity Scale:**

- No apparent retinopathy: No abnormality
- Mild NPDR: Microaneurysms only
- Moderate NPDR: More than just microaneurysms and less than severe disease
- Severe NPDR: No signs of PDR and any of the following:
  - 20 intraretinal hemorrhages in each of the 4 quadrants
  - Venous beading in ≥2 quadrants
  - Prominent IRMA ≥1 quadrant
- PDR: One or more of the following:
  - Neovascularization
  - Vitreous or pre-retinal hemorrhage

# Screening and Evaluation

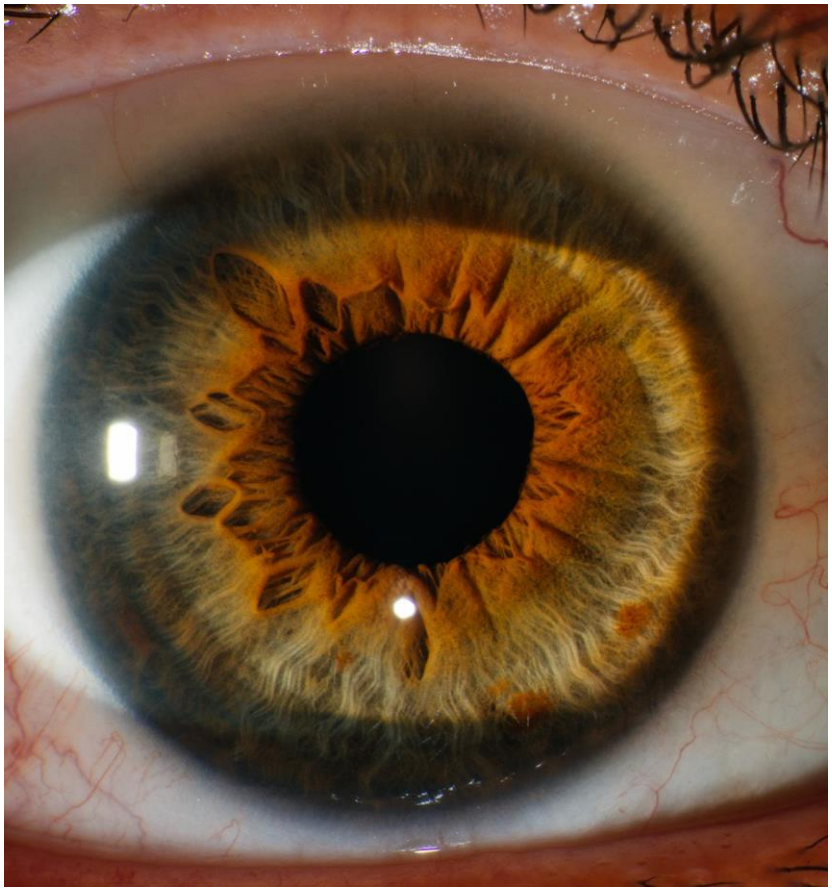
**All patients diagnosed with DM should be seen by the ophtalmlogist at least once since the time of the diagnosis**



# Evaluation

## Ocular Examination:

- Visual acuity.
- IOP measurement.
- Gonioscopy (for neovascularization of iris/angles and for raised intraocular pressure/IOP).
- Slit-lamp examination (to rule out other ocular manifestations of diabetes mellitus).
- Dilated fundus examination: for diabetic retinopathy grading.



## Fundus Photography:

- For documentation and record purposes.
- It is a very helpful tool for patient education, as well.

# Additional posterior segment investigations

## Optical Coherence Tomography (OCT):

- To evaluate retinal thickening
- Assessment and monitoring of edema after initiation of treatment
- Very helpful marker to plan for the next sitting of intravitreal injections.
- To diagnose Vitreomacular traction (VMT) and the epiretinal membrane (ERM) which might require surgery (pars plans vitrectomy)


## Fundus Fluorescein Angiography (FFA):

- For the diagnosis of ischemic maculopathy.
- To locate capillary dropout areas.
- To differentiate IRMA from neovascularization.
- To differentiate disc collaterals from disc neovascularization.
- To reveal occult new vessels that could not be detected on clinical examination
- To find out the cause of unexplained visual loss.

# Management and Treatment

# General management

General Systemic Control of Diabetes:

- Strict metabolic control of diabetes.
- HbA1C levels should be kept under 6.5%.*
- Lifestyle modifications like routine exercises and proper diabetic food diet.
- Patients should visit diabetologists for proper follow-up visits and should take timely antidiabetic medications.
- Other systemic ailments like hypertension, dyslipidemia, hypoproteinemia, anemia, nephropathy, neuropathy, cardiac ailments, and others should also be taken care of by respective medications

# Ophtalmological management

Management of Non-Proliferative Diabetic Retinopathy:

**Strict glycemic control and strict compliance of patients towards antidiabetic medication is the key to manage a case of NPDR.**

Very mild NPDR:

- followup every yearly.

Mild to moderate NPDR:

- followup 6-12 monthly.1
- 6% cases of mild NPDR and 23% cases of moderate NPDR progress to proliferative stages within four years.

Severe to Very Severe NPDR:

- Close followup within 2-4 months.
- 50% of severe NPDR and 75% of cases of very severe NPDR progress to PDR within one year.

# Treatment of Proliferative Diabetic Retinopathy (PDR)

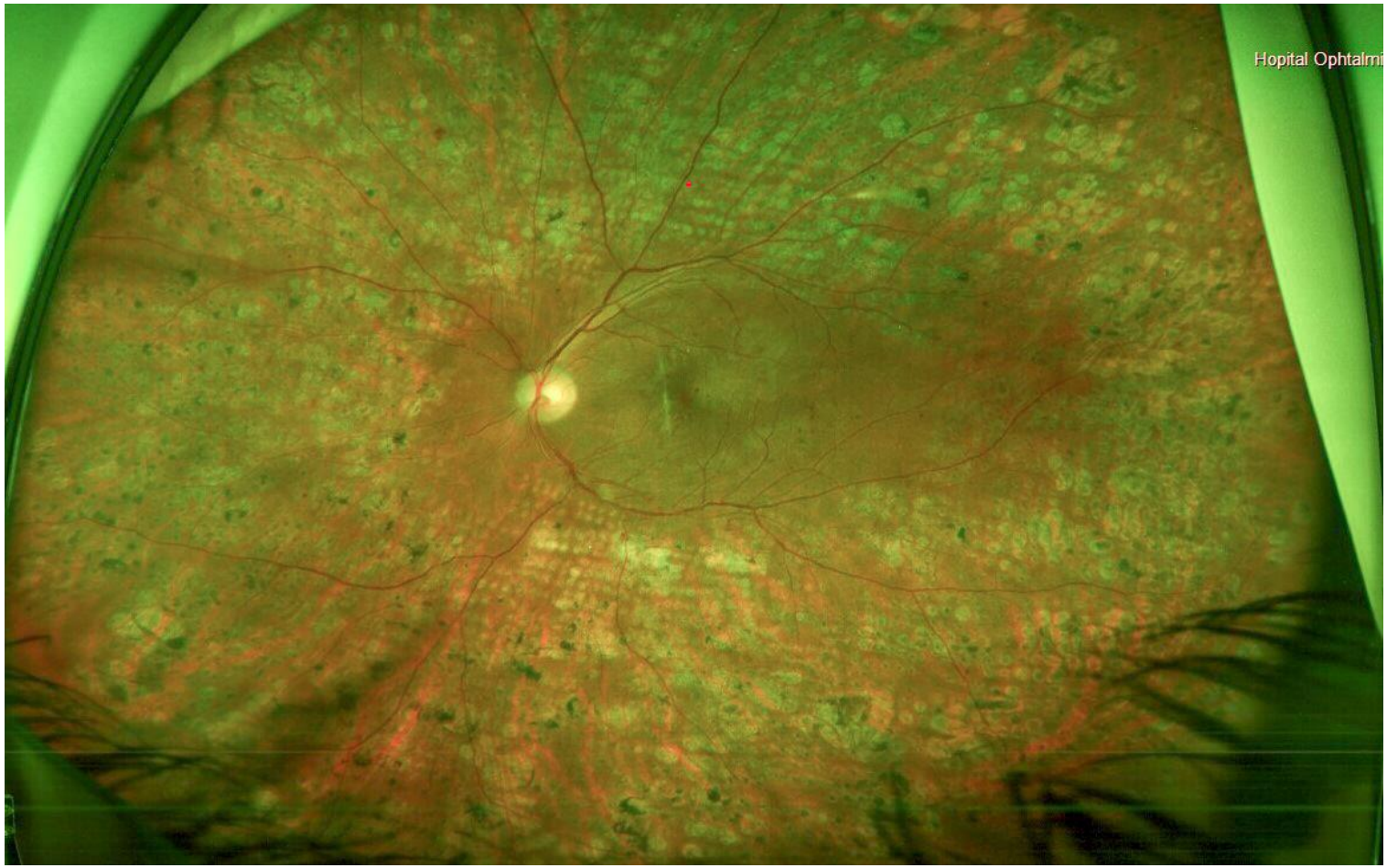
- **Panretinal photocoagulation (PRP) is considered to be the standard treatment.**
- **intravitreal anti-VEGF injections in PDR cases.**
- **A combination of intravitreal injection and pan-retinal photocoagulation.**

- Non-high-risk PDR without DME:
  - careful 2-4 months followup and immediate pan-retinal photocoagulation if high-risk PDR occurs. Some physicians perform PRP in all PDR cases.
- High-risk PDR without macular edema:
  - pan-retinal photocoagulation should be initiated.
- PDR with CSME:
  - combined intravitreal anti-VEGF injections and PRP sessions should be considered.
- High-risk PDR:
  - in which complete photocoagulation is not possible- alternatives like cryopexy or vitrectomy should be considered.

In Protocol S of DRCR.net, a comparison of safety and efficacy of PRP to intravitreal injection of 0.5 mg ranibizumab was studied. The primary outcome of protocol S Ranibizumab 0.5 mg was non-inferior to PRP.

- High cost.
- repeated injection.
- Endophthalmitis.
- Tachyphylaxis.

# Panretinal photocoagulation (PRP)



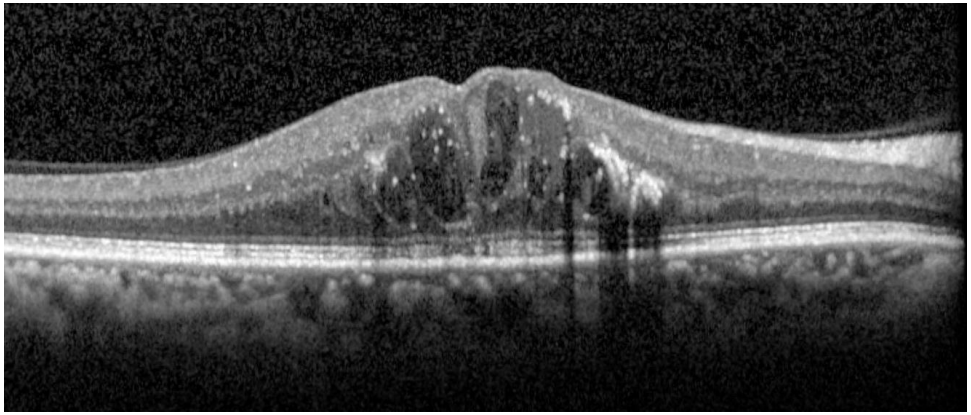
| Retinopathy stage | Findings on ophthalmoscopy | Management and review/referral timeframe |
|---|---|---|
| **No apparent retinopathy** | No abnormalities | In line with AOA, AAO, and JDC, OA recommends annual review |
| **Minimal NPDR** | Microaneurysms (MA) only | Review 6-12 months taking into consideration proximity of MA to fovea |
| **Mild to moderate NPDR** | More than just MA but less than severe NPDR. This may include:<br>• dot haemorrhages<br>• blot haemorrhages<br>• cotton wool spots<br>• intraretinal microvascular anomalies (eg venous beading) | Refer or closely monitor<br><br>Depending on level of DR present, 3-6 monthly or annually |
| **Severe NPDR** | Any of the following:<br>• more than 20 intraretinal haemorrhages in each of 4 quadrants<br>• definite venous beading in 2+ quadrants<br>• prominent IRMA in 1+ quadrant AND no signs of proliferative retinopathy | Ophthalmology referral |
| **PDR** | One of the following (or unexplained fall in VA)<br>• neovascularisation<br>• vitreous/pre-retinal haemorrhage | Urgent ophthalmology referral (days – week) |

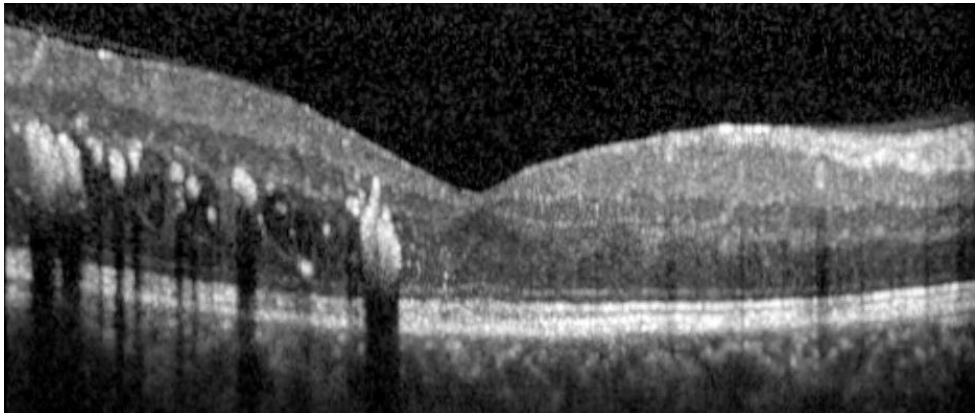
# Management of Diabetic Macular Edema (DME)

Center involving DME:
**Anti-VEGF** agents have become the first line of treatment for center involving diabetic macular edema.

- Ranibizumab.
- Aflibercept.
- Intravitreal steroid implants.
- Bevacizumab.

Aflibercept and Ranibizumab have received FDA approval for use in diabetic retinopathy associated with Macular edema





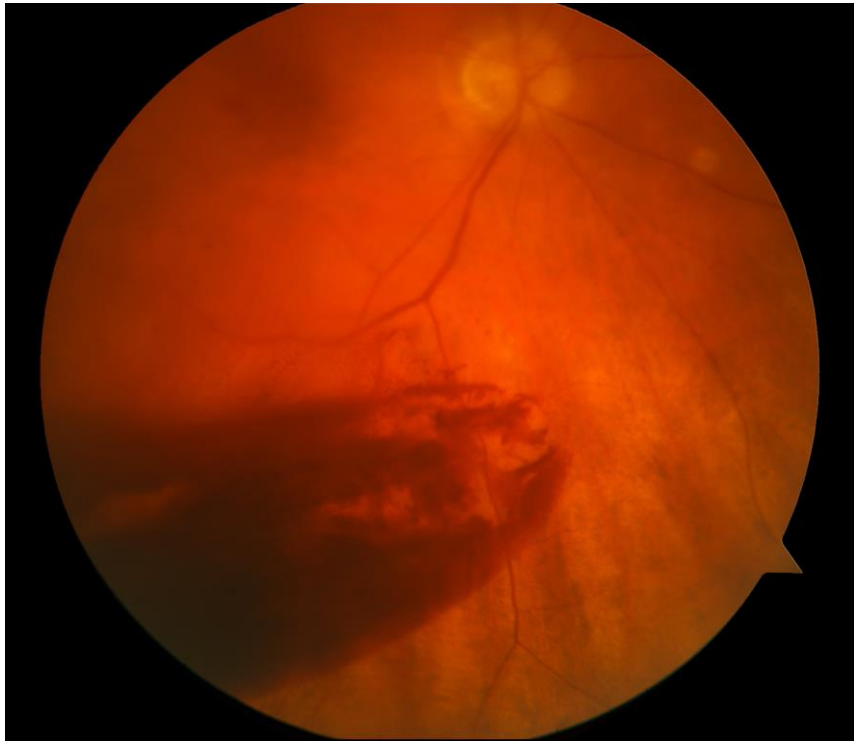
Non center involving DME:
- Observation.

Tractional DME:
VMT (Vitreomacular traction) or ERM (Epiretinal membrane).
- Vitrectomy surgery should be considered.

# Treatment of Advanced Diabetic Eye Disease

Prognosis is guarded in patients of advanced diabetic eye disease.

<u>mild vitreous hemorrhage:</u>
anti-VEGF agent following which if the hemorrhage resolves, then scattered pan-retinal photocoagulation in the visible areas can be tried.
Ultrasnogram must exclude retinal traction if such an approach is considered.



Vitrectomy should be considered in the following cases:

- Non-clearing vitreous hemorrhage (vitreous/subhyaloid/pre-macular)
- Tractional retinal detachment with macula off
- Combined tractional with rhegmatogenous retinal detachment
- Anterior segment neovascularization with the invisibility of the posterior segment
- Ghost cell glaucoma
- Thick epiretinal membrane
- Vitreomacular traction

# Prognosis

**Prognosis of diabetic retinopathy depends on:**

- the duration of diabetes.
- glycemic control.
- associated comorbid conditions.
- compliance of the patient to the appropriate line of treatment.

- Proper patient counseling is needed about his/ her retinal condition and making patients aware that delay in proper followup could lead to permanent, irreversible loss of vision.
- Initial stages of diabetic retinopathy are reversible if proper glycemic control is achieved.
- Many patients with diabetic macular edema require long term support of repeated injections of intravitreal anti-VEGF medications.
- Patients treated with pan-retinal photocoagulation may require additional supplementation of anti-VEGF medications if there is persistent macular edema and neovascularization.
- Once there is tractional macular detachment for a longer duration of time, then the visual prognosis is usually guarded as the macular anatomy is markedly distorted.

# Enhancing Healthcare Team Outcomes

- Any patient presenting with diabetic retinopathy should not receive treatment by only one health care provider. It requires a **multispecialty evaluation** by the **family doctor** and **ophthalmologist** then endocrinologist, ophthalmologist, nephrologist, cardiologist, and neurologist.

- Interprofessional communication can lead to better patient management. The patient will most often present to the primary health care provider or nurse practitioner, and these professionals should be aware of the condition as it is treatable.

- Prompt referral to an ophthalmologist is necessary. These patients can then be followed by their primary clinicians and should ensure correct dosing on the medication management aspect of the condition.

- The American Academy of Ophthalmology's current recommendation:
    - Patients with diabetes mellitus type 1 should have yearly screening for diabetic retinopathy starting at five years after the onset of diabetes.
    - Patients with diabetes mellitus type 2 should have fundus evaluation at the time of diagnosis and annually thereafter

- The patient should be counseled properly regarding the prognosis of diabetic retinopathy. Early diagnosis, management, and follow-up visits at timely intervals, depending on the stage of presentation of diabetic retinopathy, are mandatory.

- Systemic dysregulation of diabetes can lead to an exponential worsening of diabetic retinopathy.

- Lifestyle modification should be done along with proper systemic medications to halt the progression of diabetic retinopathy

# Hypertensive Retinopathy

Epidemiology:
In the United States, 33% of adults have hypertension and only 52% have controlled blood pressures.

Hypertensive retinopathy ranges from 2-17% in non-diabetic patients but the prevalence varies by demographic groups.

The major risk for arteriosclerotic hypertensive retinopathy is the **duration** of elevated blood pressure.

## Risk Factors:

- high salt diet.
- Obesity.
- Tobacco use.
- Alcohol.
- Family history.
- stress.
- Ethnic background.

# Pathophysiology

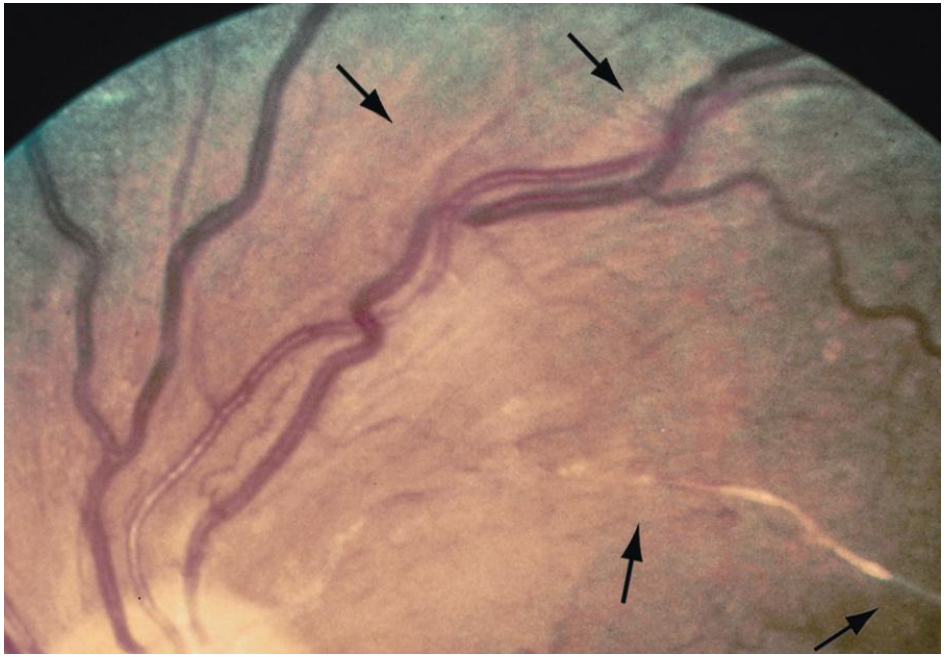
The manifestations of hypertensive retinopathy may be caused by either an **acute rise** in blood pressure or **chronically elevated** blood pressure.

Chronic hypertension typically follows sequential phases of histologic damage **vasoconstrictive**, **sclerotic**, and **exudative**.

<u>vascoconstrictive phase:</u>
vasospasm and vasoconstriction to optimize blood flow. This phase of disease is evident by narrowing of retinal arteries.

<u>sclerotic phase:</u>
elevated blood pressure causes endothelial damage with additional intimal thickening and narrowing of vessels.

This phase results in focal or diffuse arterial wall opacification (copper wiring),
with arteriovenous nicking caused by the pressure of thickened arteries over veins at their crossing points, where they share a common adventitial sheath.



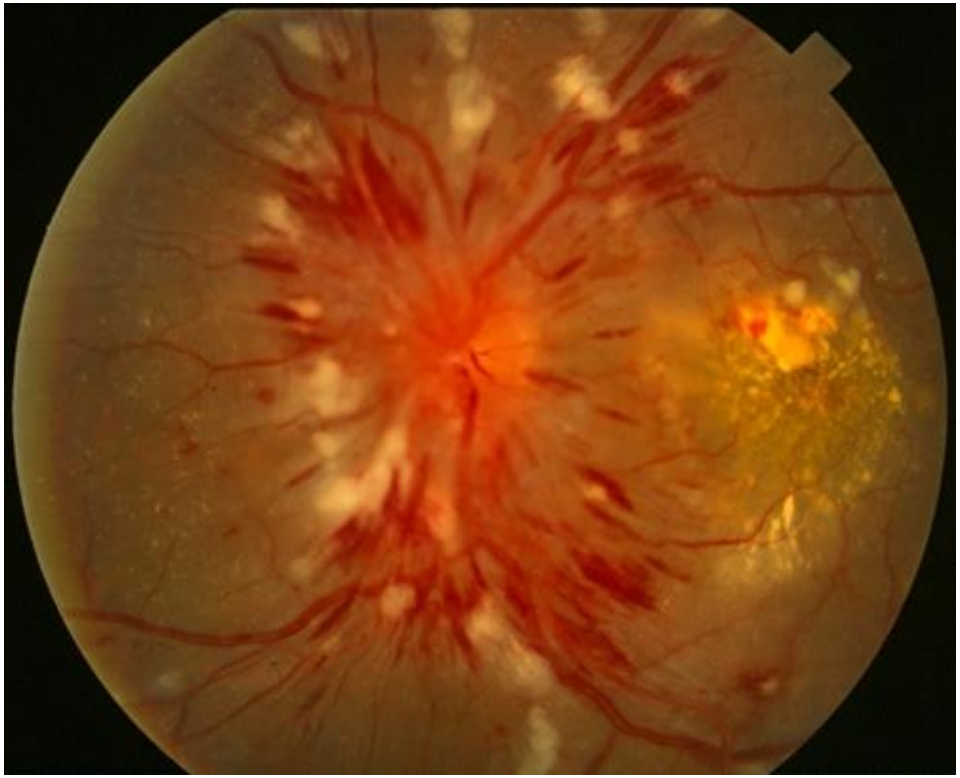
# Pathophysiology

<u>Exudative phase:</u>
persistant un controlled hypertension ---> disruption of the blood-retinal barrier and leakage of plasma material, "exudates" into the retina.

fluid and blood accumulation in multiple layers of the retina.

Additional ischemic findings that occur in this phase include **cotton wool spots** (nerve fiber layer infarcts), retinal vessel endothelial changes **(microaneurysms)**, and **retinal hemorrhages.**

In cases of long-standing hypertension or in severe cases of malignant hypertension, optic nerve head edema (papillitis) and damage can also occur.



# Clinical presentation

**Malignant Hypertension**
- Eye pain.
- Severe headaches.
- Reduced visual acuity.

**Chronic Hypertension**
- Decreased vision.

**Patients may present with one of the following compliactions:**
- Retinal artery occlusion
- Retinal vein occlusion
- Macro aneurysm of retinal arteriole
- Anterior ischemic optic neuropathy
- Retinal arteriolar emboli
- Epiretinal membrane formation
- Cystoid macular edema

# Classification

***Keith-Wagner- Barker classification***

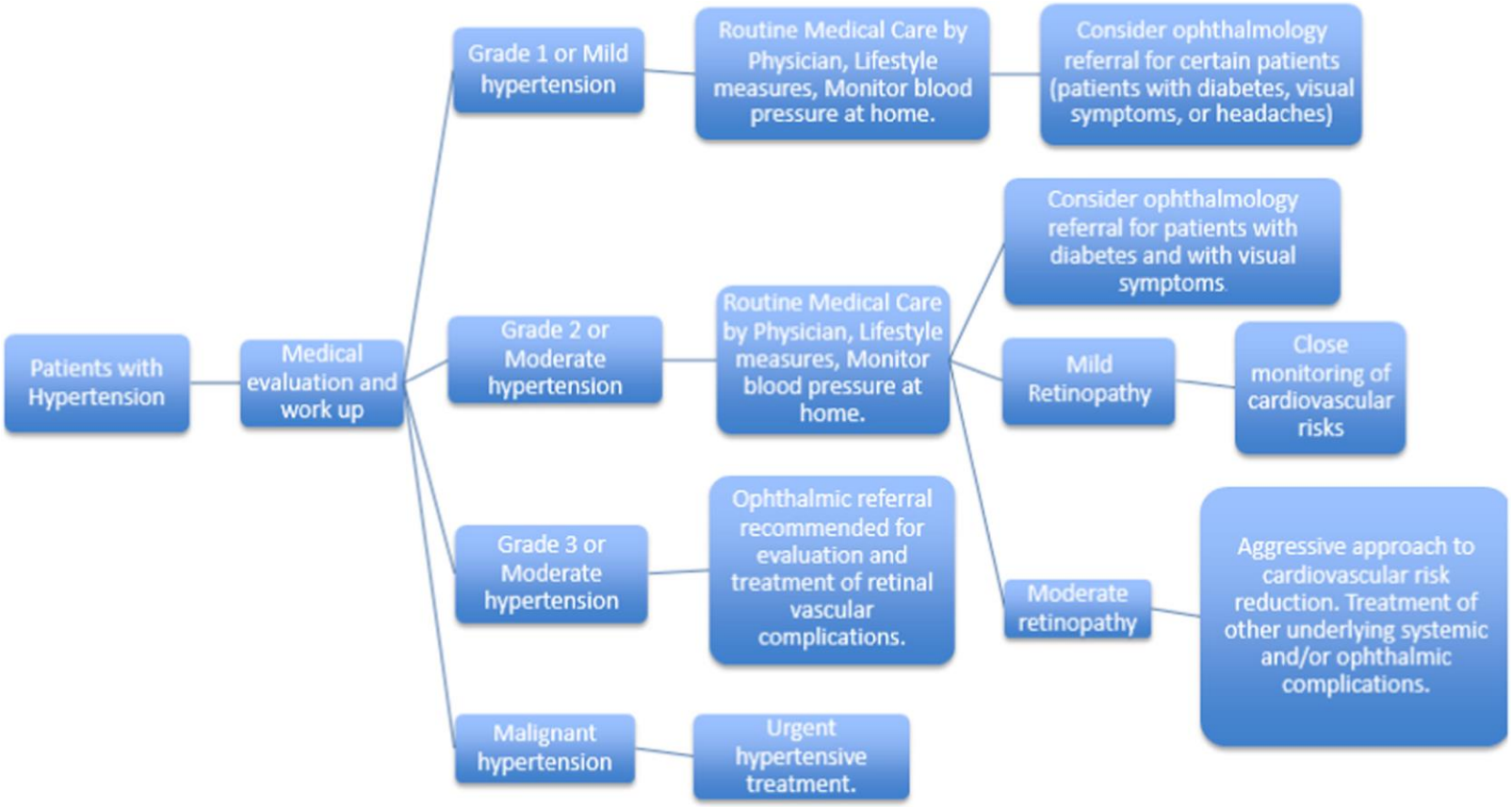
- Group 1: Slight constriction of retinal arterioles
- Group 2: Group 1 + focal narrowing of retinal arterioles + AV nicking
- Group 3: Group 2 + flame-shaped haemorrhages + cotton-wool spots + hard exudates
- Group 4: Group 3 + optic disc swelling

***Scheie Classification***

- Stage 0: No visible abnormalities
- Stage 1: Diffuse arteriolar narrowing
- Stage 2: Stage 1 + focal arteriolar constriction
- Stage 3: Stage 2 + retinal hemorrhage
- Stage 4: Stage 3 + hard exudates + retinal edema+ optic disc swelling

# Management

The treatment of hypertensive retinopathy is primarily focused on **reducing systemic blood** pressure.



# Management

**General treatment**
moderate to severe hypertensive retinopathy -> reduce the mean arterial pressure by 10-15% in the first hour. Of note, blood pressure should be lowered in a controlled manner and by no more than 25% compared to baseline by the end of the first day of treatment to prevent further ischemic damage to target end organs.

Initial treatment often requires parenteral antihypertensive agents and then transitioned to oral agents.

Goal-oriented hypertension treatment aims to lower systolic blood pressure to < 130 mmHG and diastolic pressure to < 80 mm Hg over the next 2-3 months.[17]

**Medical follow up**
Follow up is dependent upon the degree of hypertension and resistance to medications.

Close contact is essential between the **ophthalmologist** and **the primary care physician** for consistent follow up individually tailored to each patient.

# Thank you for your attention