DIABETIC RETINOPATHY

The most common microangiopathy in both DM1 & DM2

Diabetic eye disease

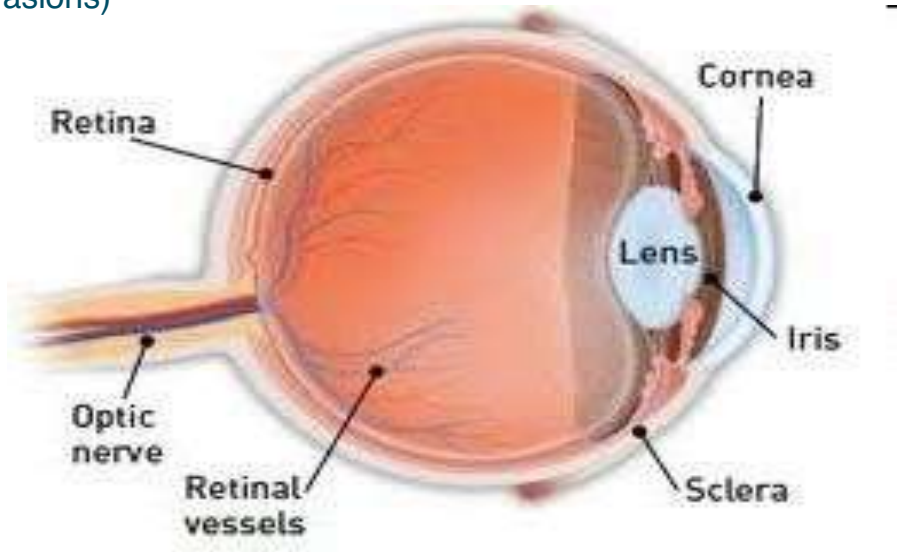
Refers to a group of eye problems that people with diabetes may face as a complication of diabetes.

All can cause variable degrees of vision loss or visual symptoms (pain and Diplopia)

When diabetes causes enough damage to the body's circulation, it can lead to paralysis of the eye muscles.

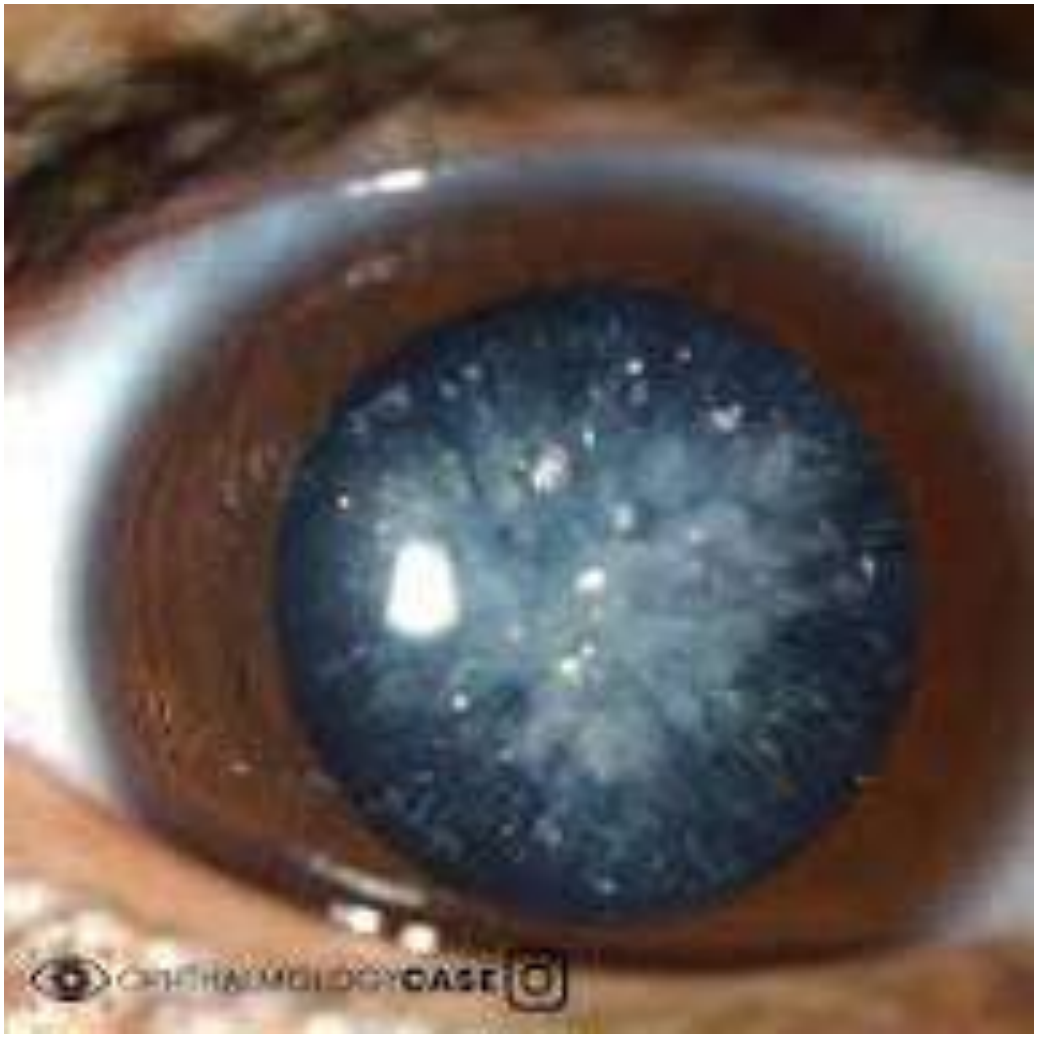
Diabetic eye disease

- Corneal abnormalities (e.g: abrasions)
- Iris and angle Neovascularization.
- Neovascular Glaucoma
- Cataracts… snowflake cataracts in young pts and greater frequency and earlier onset of age related cataract.
- Ocular Neuropathies.
- Diabetic Retinopathy. The most common & serious diabetic eye disease



Diabetic cataract, or “snowflake” cataract,

Specific for DM yet not the most common type of cataract in diabetics (the most common type is senile cataract (in diabetics it has an earlier onset and a greater prevalence))



Diabetic retinopathy :

It is a progressive microangiopathy of the retinal blood vessels caused by chronic hyperglycemia.

Diabetic retinopathy - most common cause of moderate to severe vision loss between ages 25 and 74 years.

The Retina

A structure that lines the inside of the globe

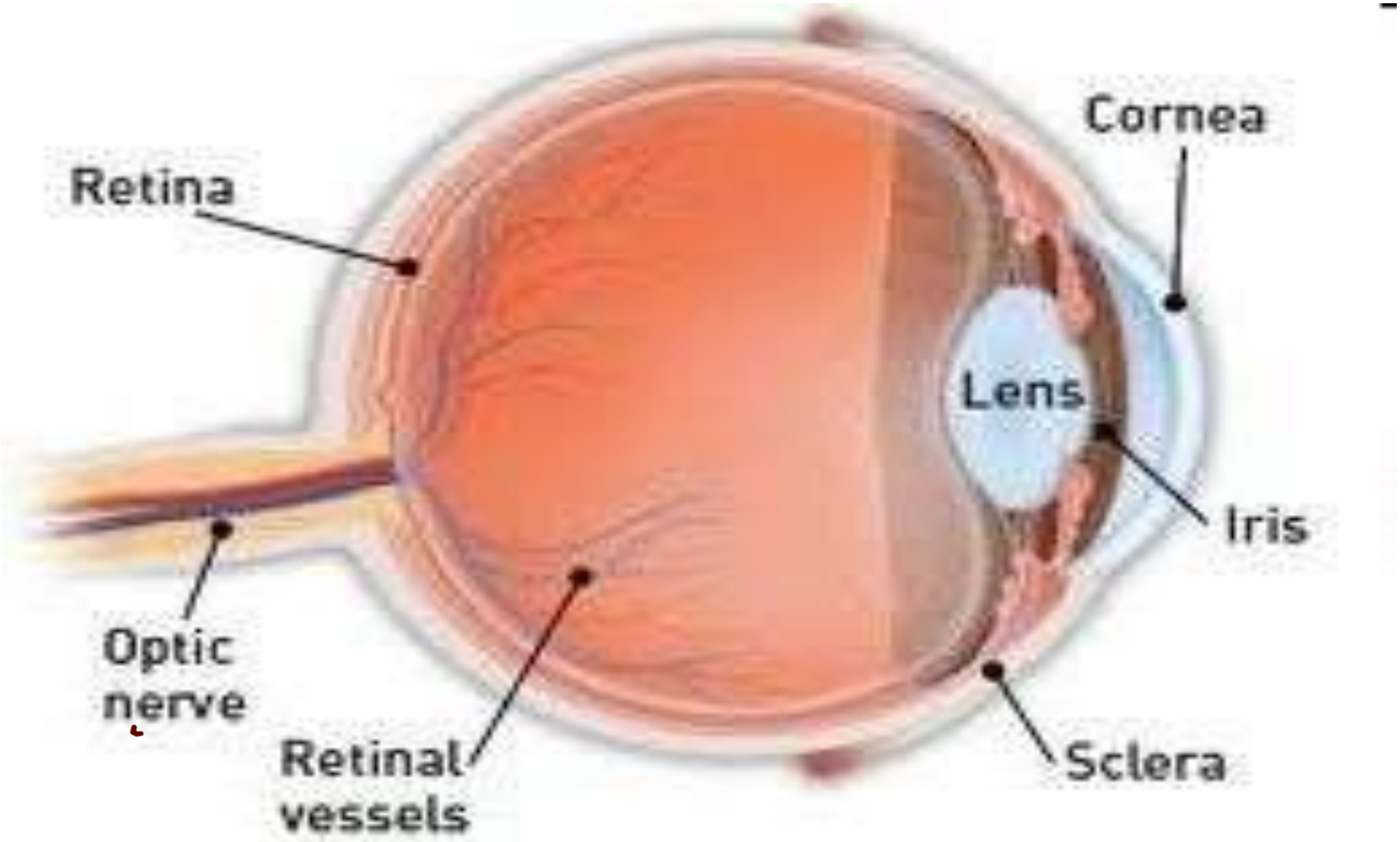
- **Two major layers:**

- Inner neurosensory retina (NSR): transparent, has the photoreceptors (rods and cones),light sensitive
- Outer retinal pigment epithelium (RPE).

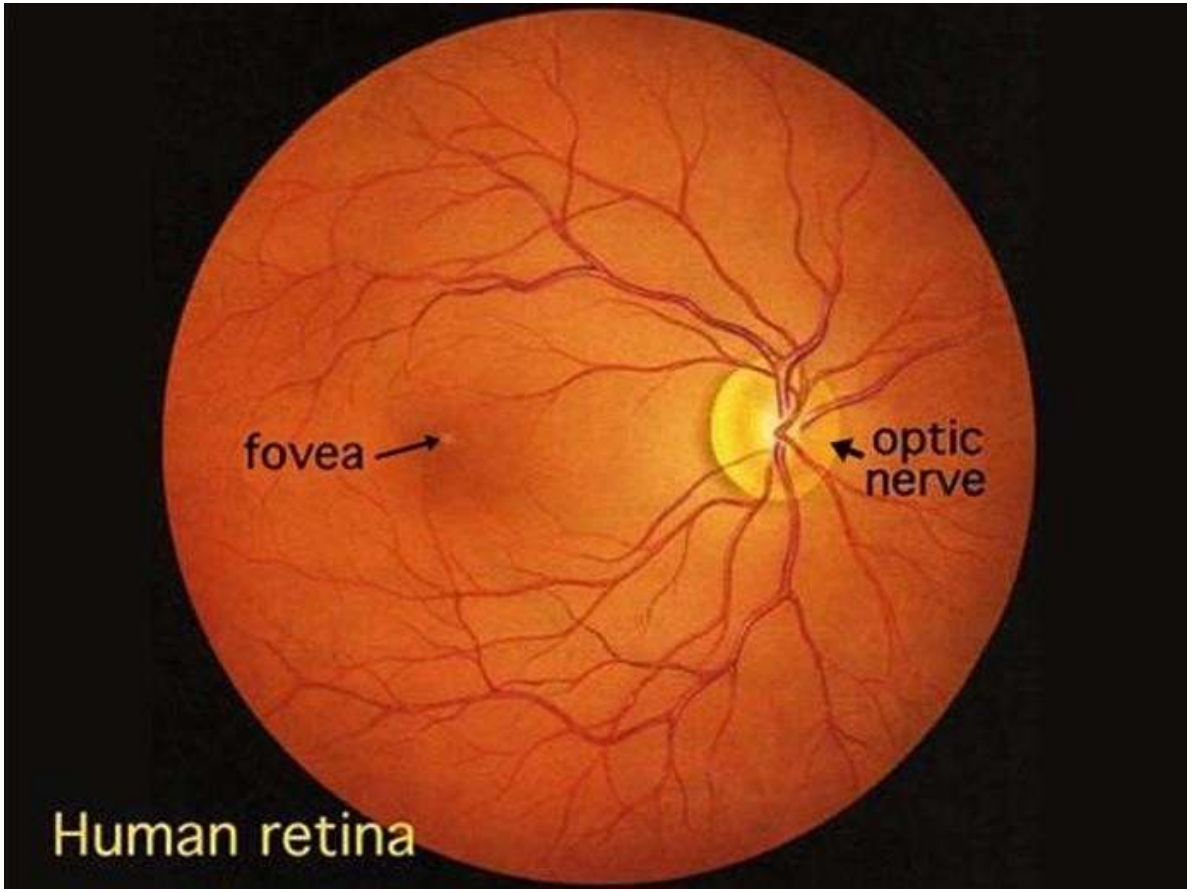
Between these two there's a potential space termed as the subretinal space

- **Retinal blood supply:**

From central retinal artery and choroidal circulation.


Retina
Cornea
Lens
Iris
Optic nerve
Retinal vessels
Sclera

Retinal Anatomy



Normal optic nerve:
1- pinkish
2- cup:disc ratio <= 0.5-0.6
3- well-circumscribed

RISK FACTORS:

Duration of diabetes

Poor control of diabetes

Hypertension

Nephropathy

hyperlipidemia

Smoking

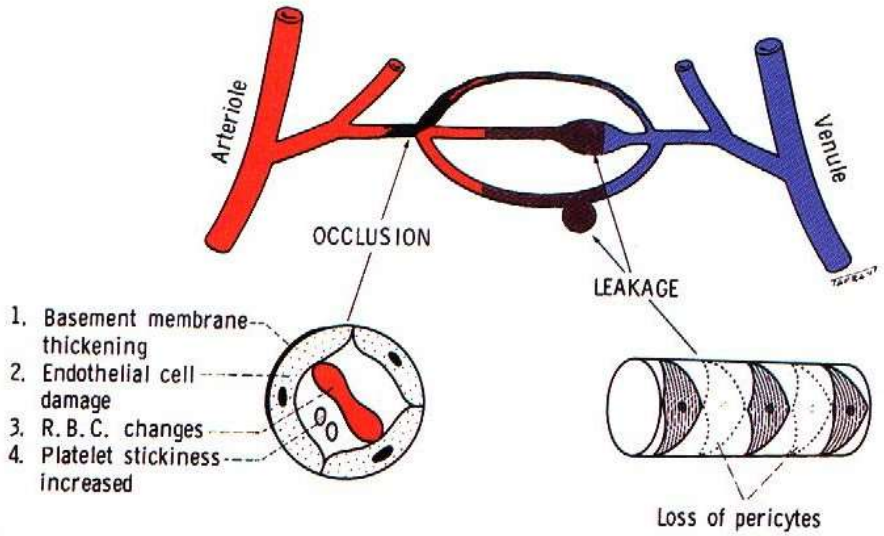
Obesity

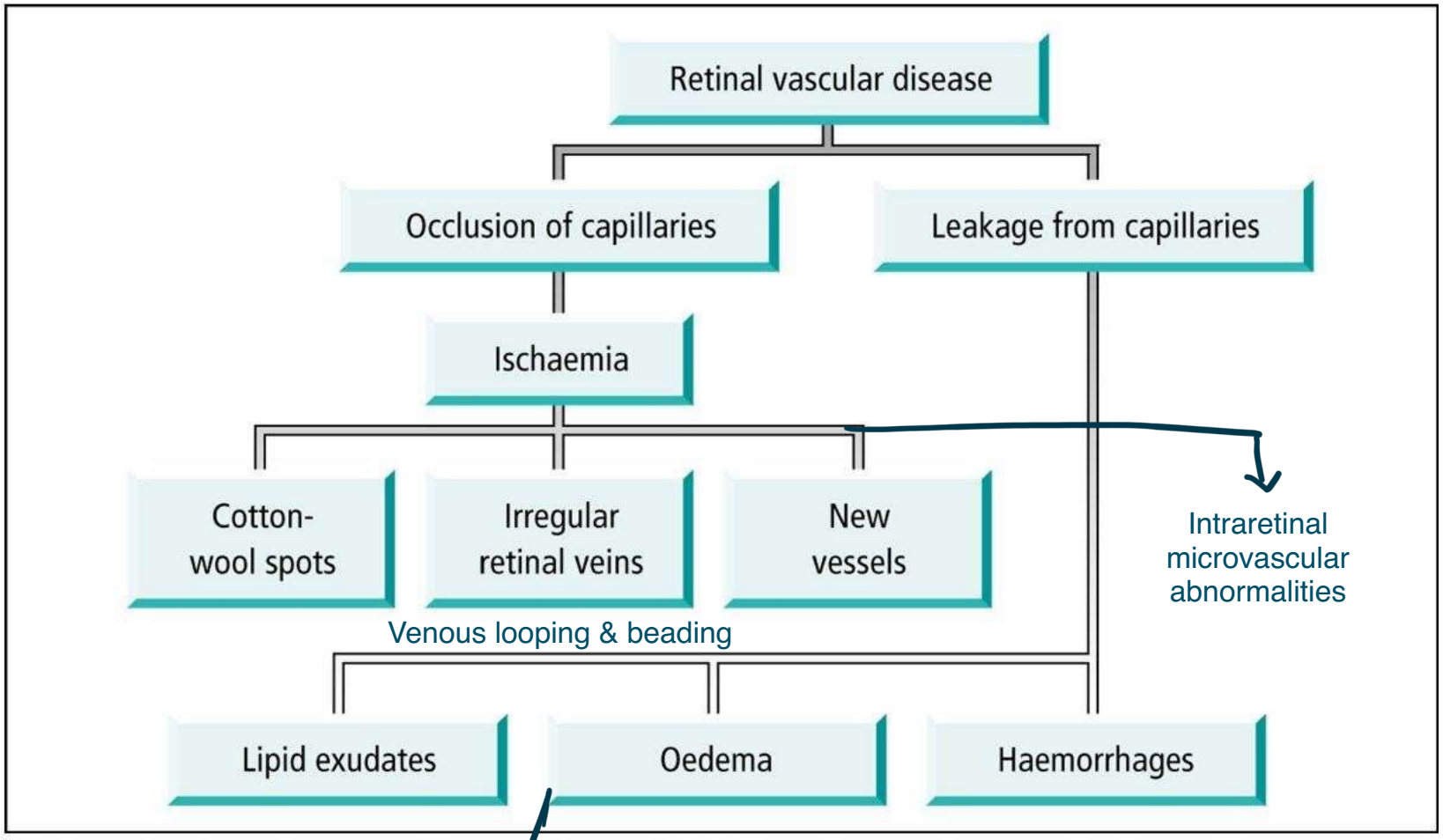
Pregnancy

The most important risk factors

Pathogenesis

Microangiopathy which has features of both microvascular leakage and occlusion.





Ophthalmology Lecture Notes, Eleventh Edition. Bruce James, Anthony Bron.

Figure 12.1 The building blocks of retinal vascular disease. Capillary leakage and occlusion often occur together.

Macular edema is the most common cause of visual impairment and visual loss in diabetic retinopathy

Microvascular leakage

Loss of pericytes results into :

Distention of capillary wall producing *microaneurysms*

Disruption of the inner Blood-retinal barrier p causing plasma constituents to leak into the retina *retinal edema, hard exudates*

Microvascular occlusion

Basement membrane thickening, endothelial cell damage, deformed RBCs, platelet stickiness and aggregation

Due to sustained hyperglycemia

Vascular Endothelial Growth Factor (VEGF) is produced by hypoxic retina

Within the retina (intraretinal microvascular abnormalities) / NPDR

VEGF stimulates the shunt and growth of new vessels

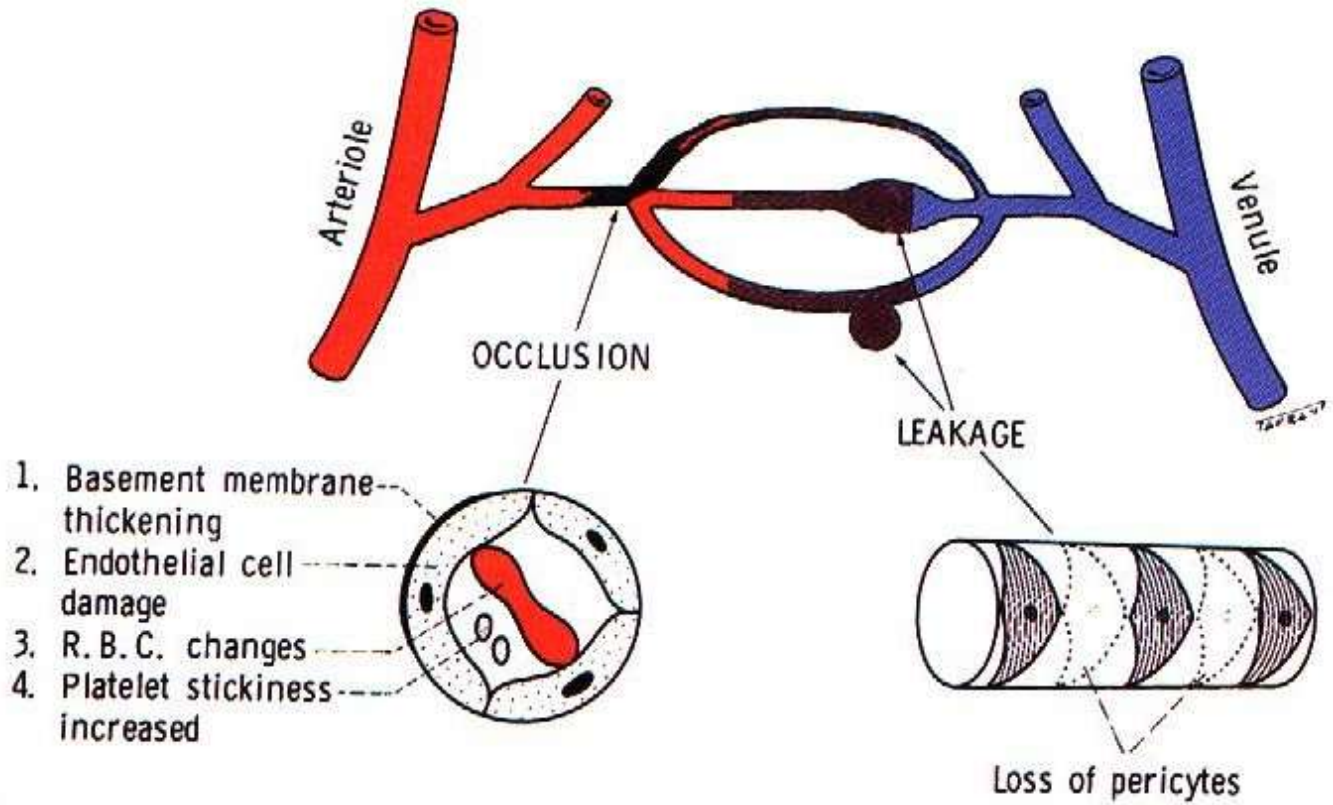
On the surface of the retina / PDR

New vessels is the hallmark of proliferative diabetic retinopathy

These new vessels forms at or near the optic disc (NVDs) , anywhere in the retina (NVEs) or at iris (NVIs)

The new vessels break easily and leak into the vitreous gel producing vitreous hemorrhage.

With time the fibrous component of new vessels contracts and results into traction retinal detachment


Arteriole
Venule
OCCLUSION
LEAKAGE
1. Basement membrane thickening
2. Endothelial cell damage
3. R.B.C. changes
4. Platelet stickiness increased
Loss of pericytes

Signs of diabetic retinopathy :

Early signs (signs of non proliferative DR) :

- **Microaneurysms**
- Dot and blot hemorrhages → Intraretinal
- Flame-shaped hemorrhages
- Cotton-wool spots
- Hard exudates
- Edema
- Venous changes (Beading, and looping)
- Intraretinal microvascular abnormalities (IRMAs)

Shunts

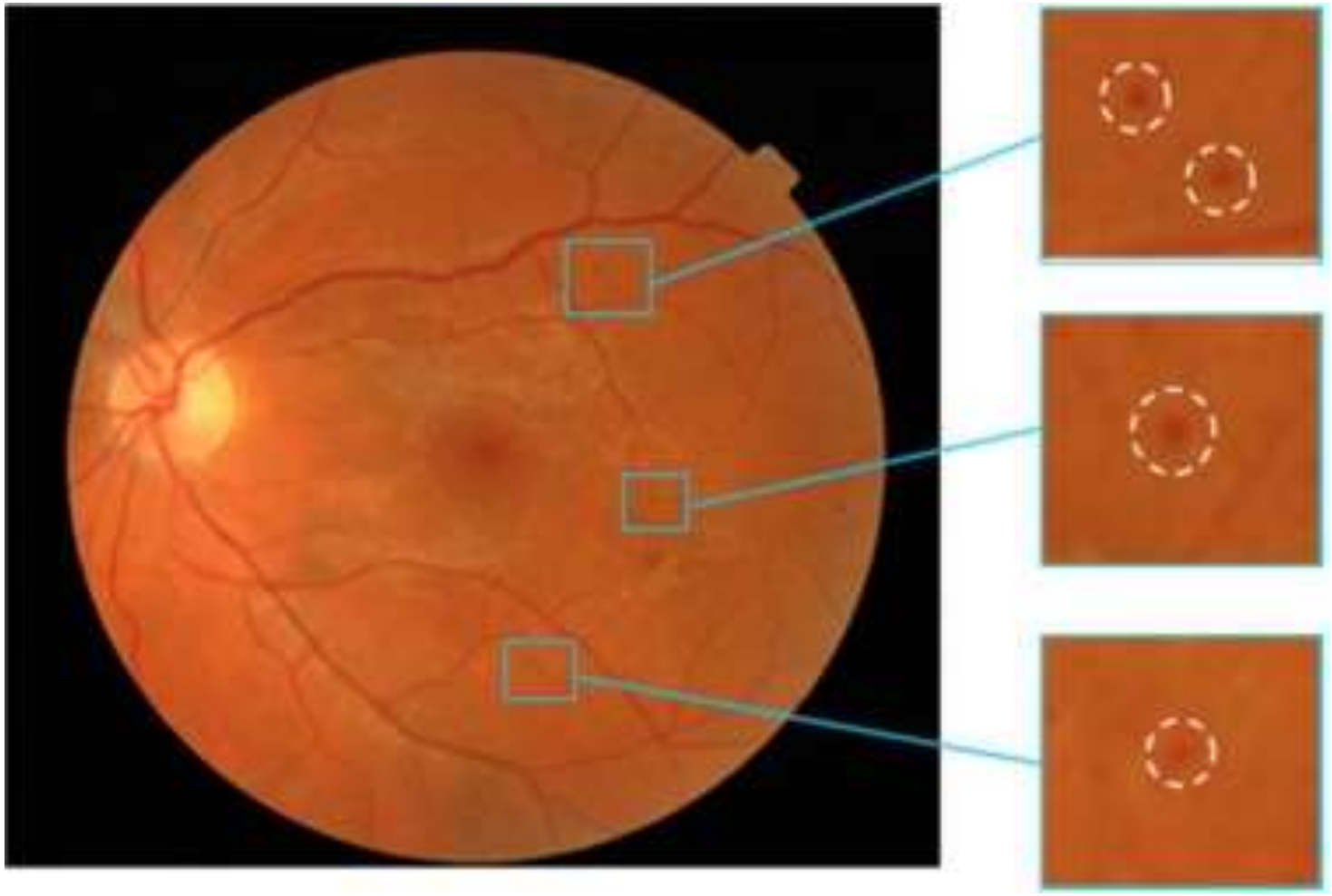
❖ Microaneurysms :

-Earliest clinical sign of diabetic retinopathy.

Usually in the macular area around the fovea

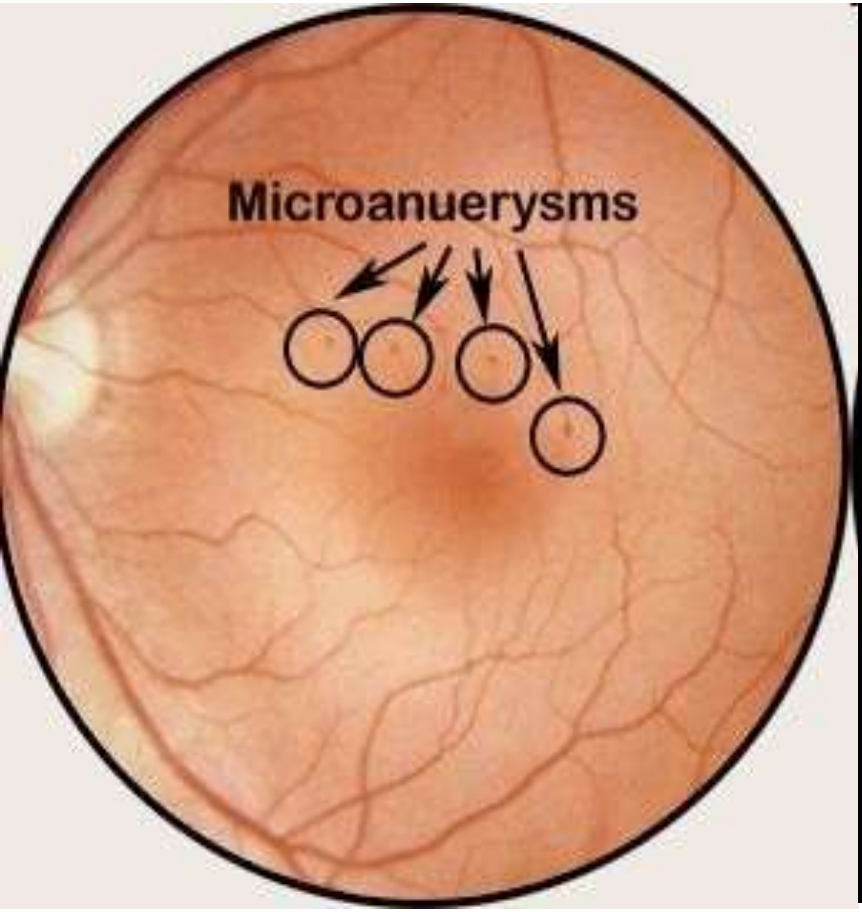
-Appear as small red dots in the superficial retinal layers

-Rupture produces dot, blot and flame shaped hemorrhages



** We can't differentiate between microaneurysms & dot hemorrhages clinically

** We can differentiate between them through Fluorescein angiography (dot hemorrhages >> hypo-fluorescent / microaneurysms >> hyper-fluorescent)


Microanuerysms

❖ Dot and blot hemorrhages

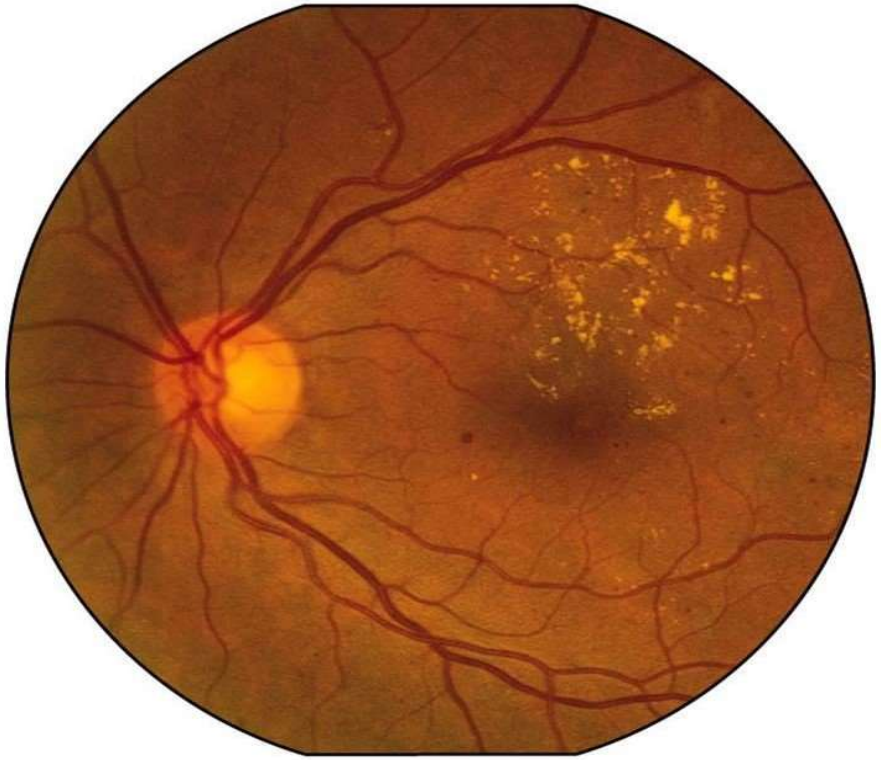
Occur as microaneurysms rupture in the deeper layers of the retina (similar to microaneuryms if they are small, distinguish by fluorescein angio).

❖ - Splinter or flame shaped hemorrhages, superficial.

Flame shaped hemorrhages

❖ Hard exudates

-Caused by the breakdown of the blood-retina barrier, allowing leakage of serum proteins and lipids, from the vessels.

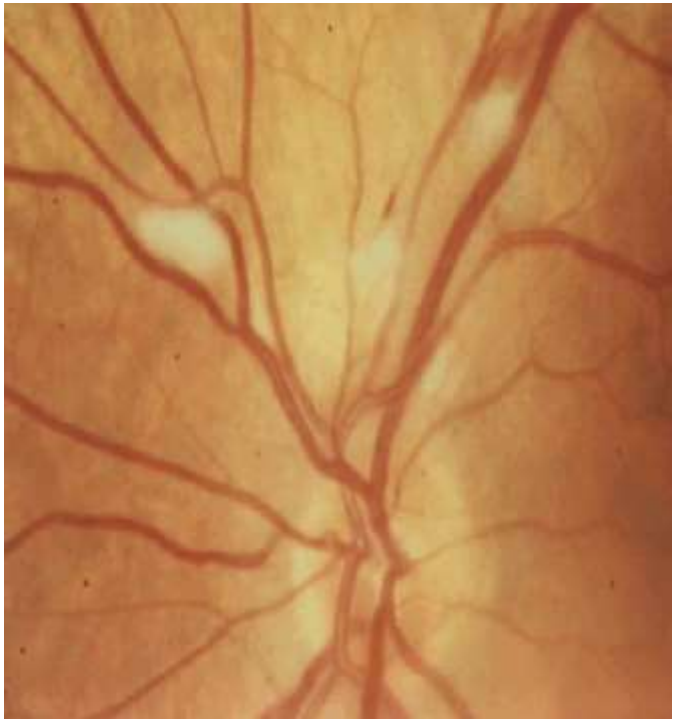


❖Cotton-wool spots

Nerve fiber layer infarction from occlusion of precapillary arterioles

Hypo-fluorescent

Fluorescein angiography - No capillary perfusion



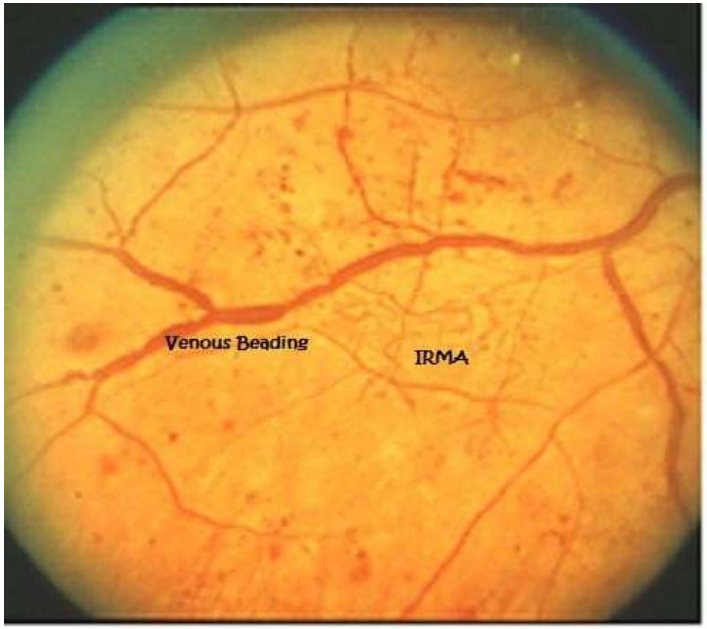
	Hard exudates	Cotton-wool spots
Color	Deep yellow	Pale white
Borders	Well-demarcated	Fluffy/ Ill-defined
Location	Macular area	Close to the optic disc
Associations	Macular thickening/ edema	Splinter shaped hemorrhages

❖Intraretinal microvascular abnormalities

A sign of severe NPDR

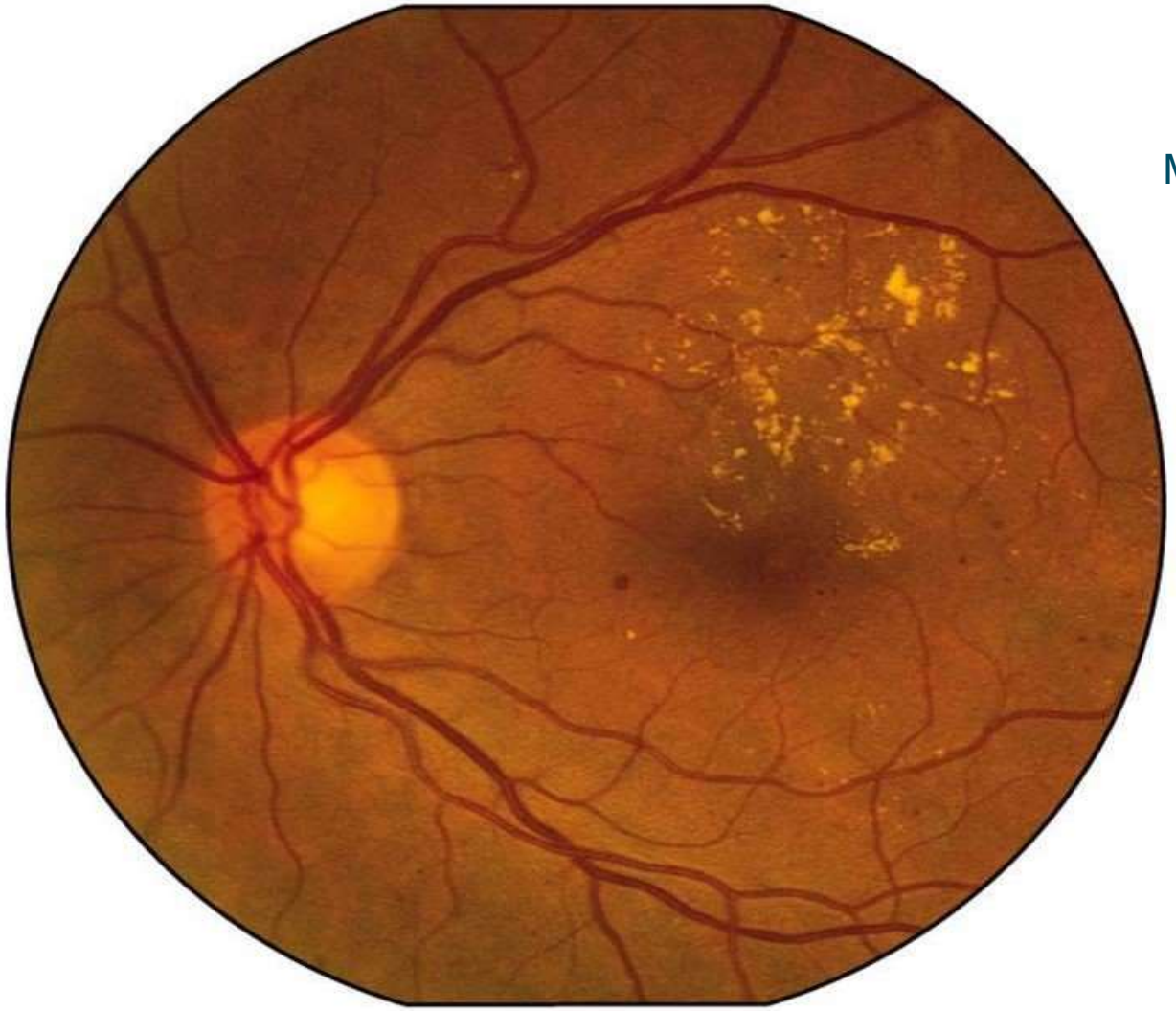
abnormal branching,
sinuous shunt vessels
that typically develop
adjacent to areas of capillary
non perfusion

It is a sign of sever NPDR



Diabetic Macular Edema

Diabetic maculopathy: edema or hard exudates within the macular area



Most likely:
Moderate DME

International Clinical Diabetic Macular Edema (DME) Disease Severity Scale:

- **DME absent:**
  No retinal thickening or hard exudates (HE)present in the posterior pole.
- **DME present:**
  Some retinal thickening or hard exudates (HE) present in the posterior pole.

Not utilized in clinical practice

- If DME present, it can be categorized as follows:

- Mild DME:

Some retinal thickening or HE present in the posterior pole but distant from the center of macula.

- Moderate DME:

Retinal thickening or HE approaching the center of the macula but not involving its center.

- Severe DME:

Retinal thickening or HE involving the center of the macula.

Clinically significant macular edema

This is the one used in clinical practice

the Early Treatment Diabetic Retinopathy Study classification protocol as the presence of :

>> if none: clinically insignificant macular edema (no treatment)
>> if any: clinically significant macular edema (indication for treatment)

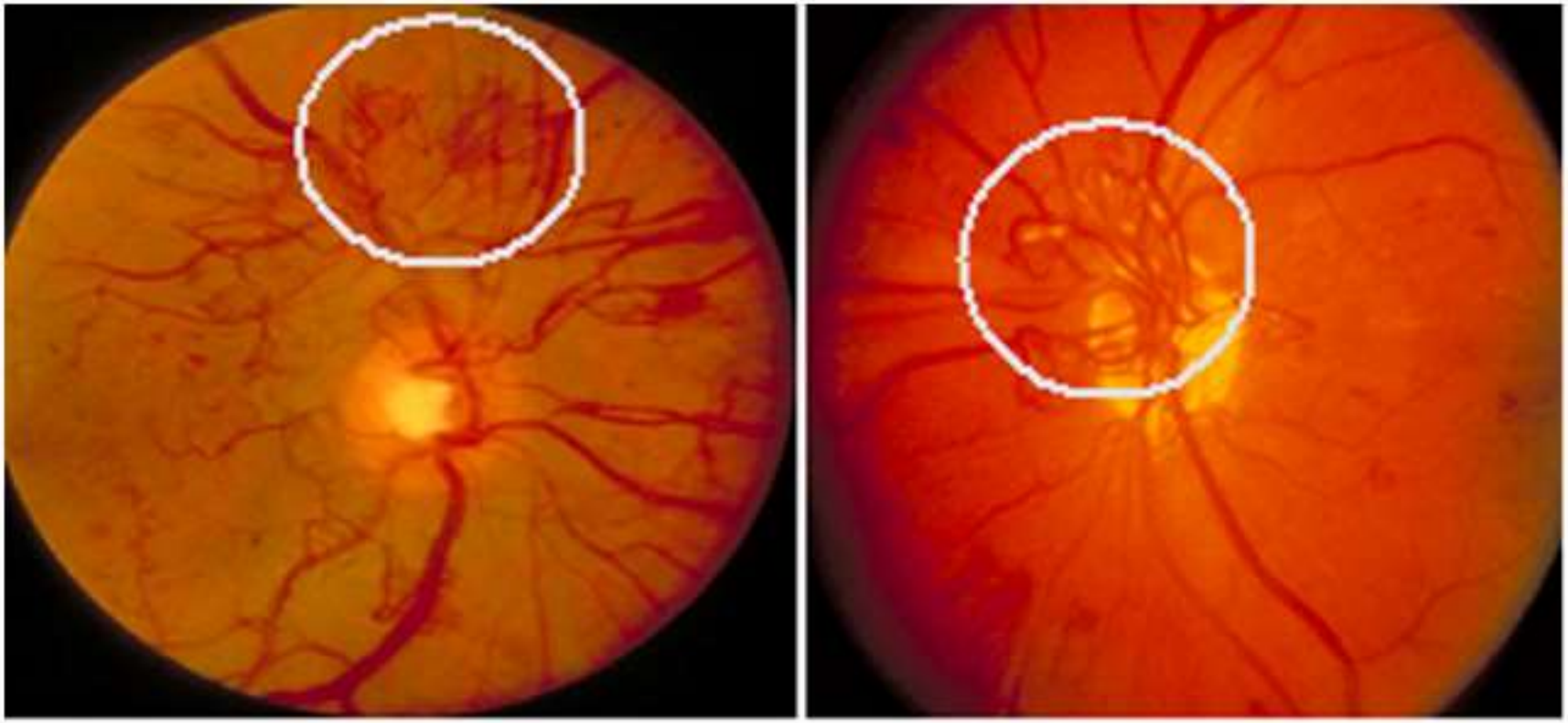
- Retina thickening at or within 500 um from the center of the macula
- Retinal hard exudate at or within 500 um of the center of the macula if associated with edema.
- Zone of thickening one disc diameter, at least part of which is within one disc from the center of the macula.

Signs of diabetic retinopathy :

Late signs (signs of proliferative DR) :

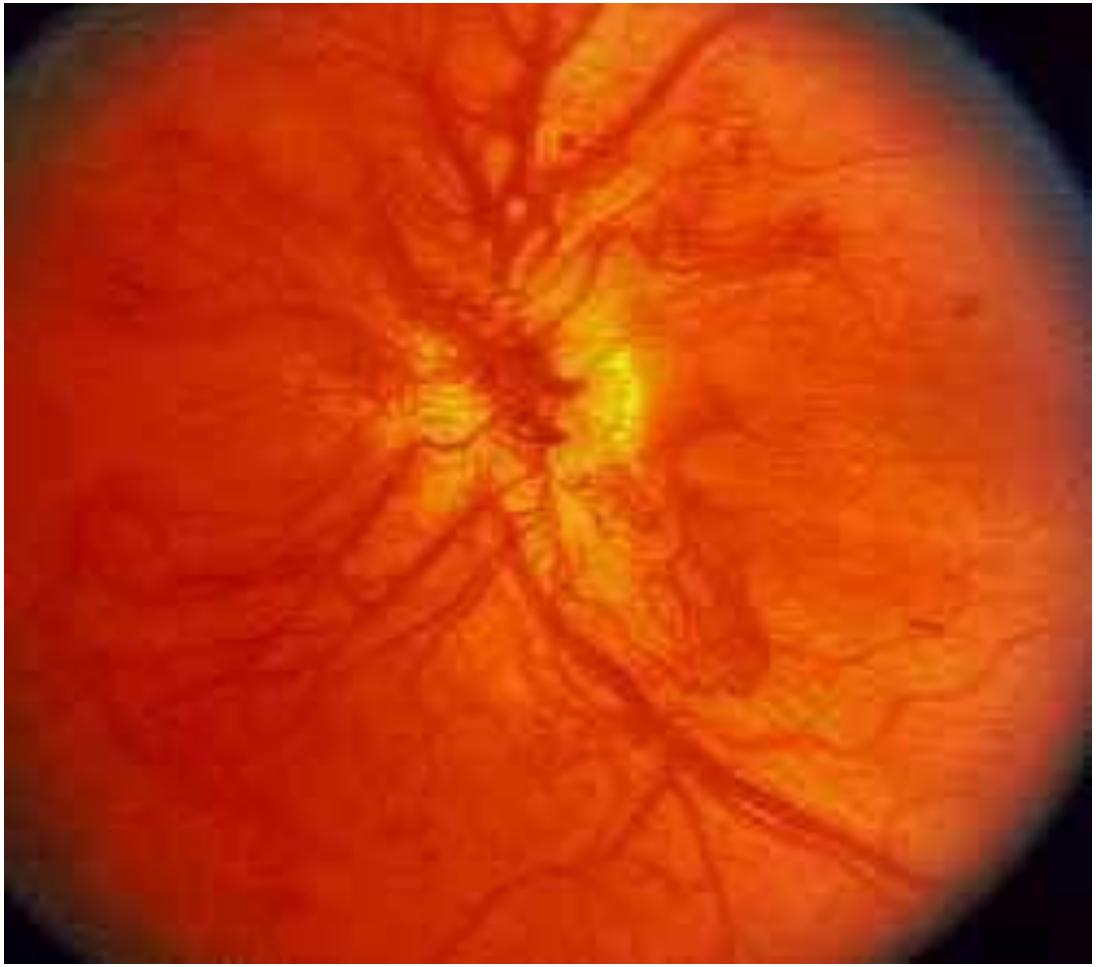
- **Neovasclaization (NVDs,NVEs and NVIs)**
- Vitreous hemorrhages
- Per retinal hemorrhages
- Traction retinal detachment
- Neovacular glaucoma

  Starts as open-angle glaucoma (a fibrovascular sheath forms at the TM and increases the resistance of aqueous outflow) then with time the fibrovascular sheath contracts and causes closure of the drainage angle (closed-angle glaucoma)



(a) New vessels elsewhere (NVE) (b) New vessels on disc (NVD)

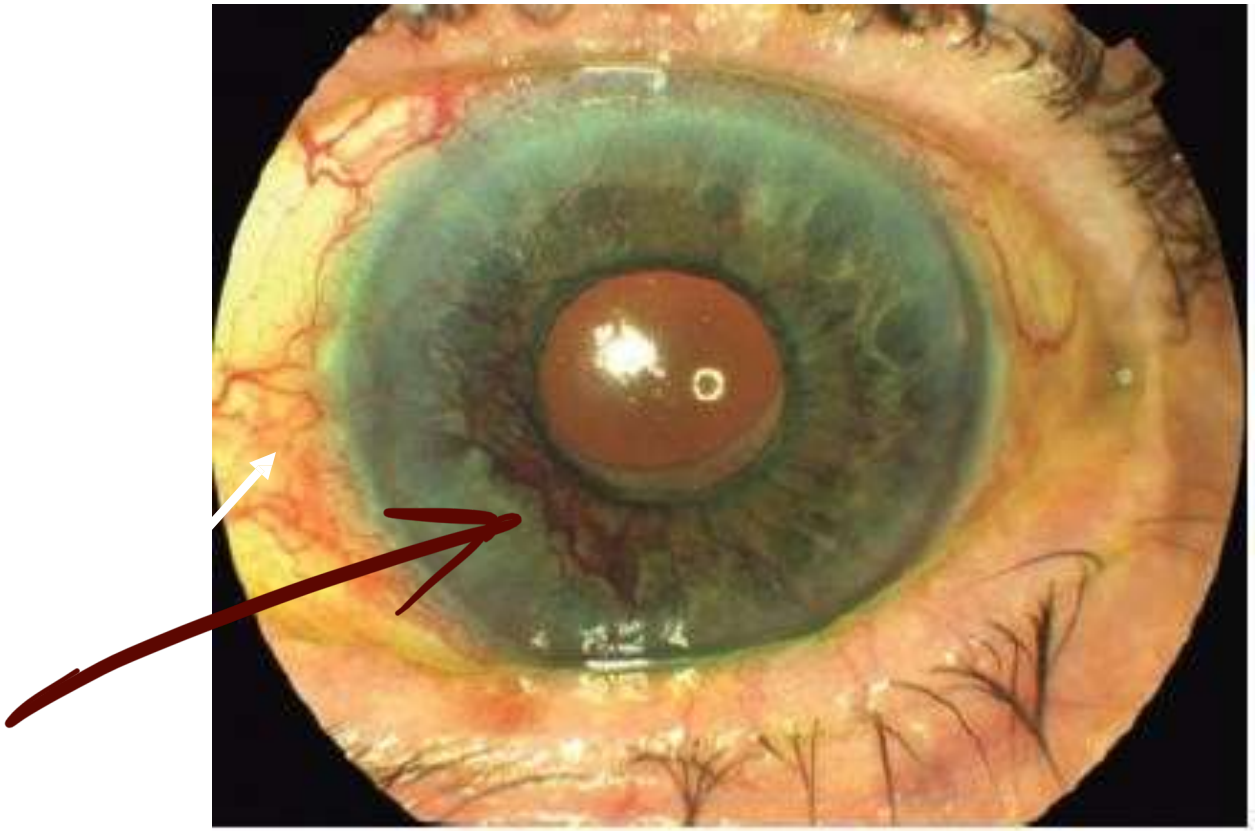
NVDs



Rubeosis Iridis

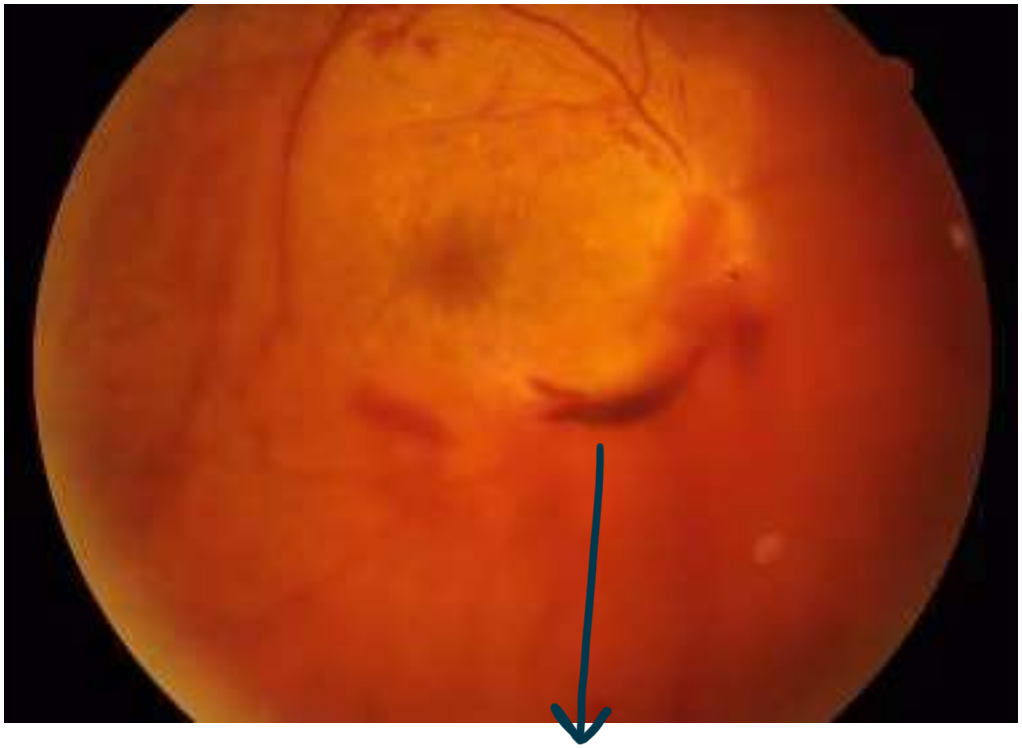
Initially appears on the margins of the pupil

Neovascularization of the iris.



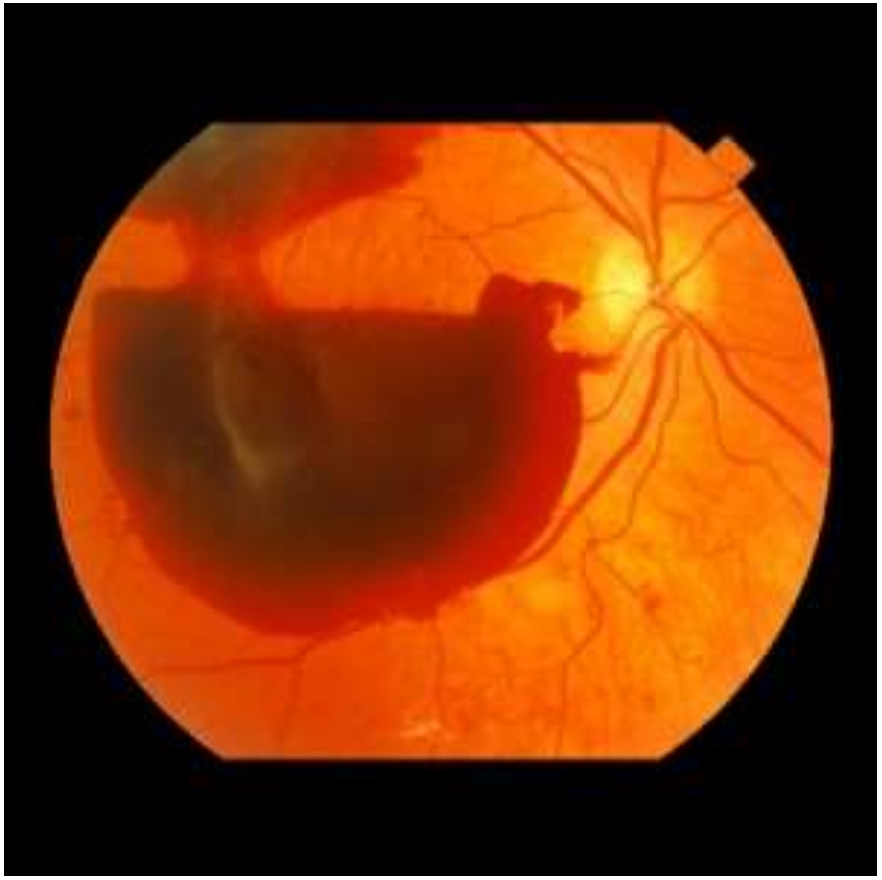
❖ Vitreous hemorrhages

Absence of vascular markings on the retinal surface >> severe
Some of the vascular markings are visible >> moderate
Fine details of the vascular markings are visible >> mild



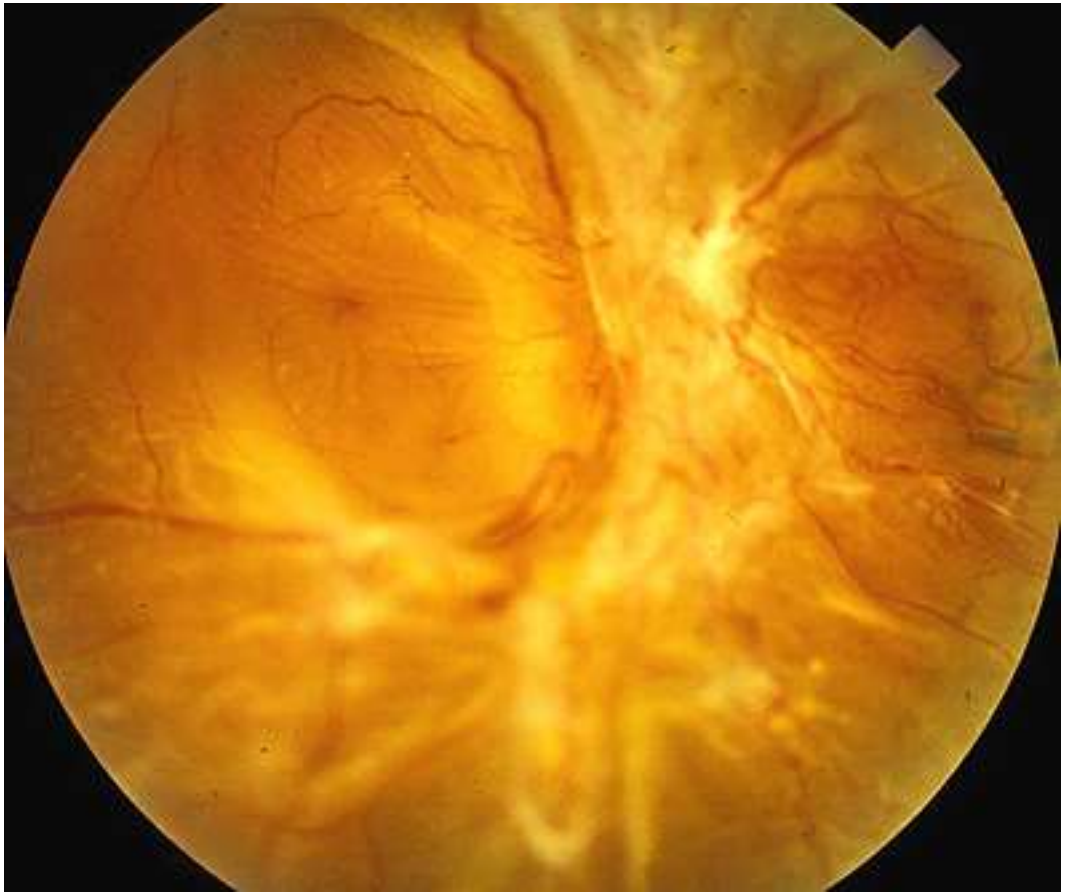
Boat-shaped hemorrhage

Pre-retinal or sub-hyloid Hemorrhage

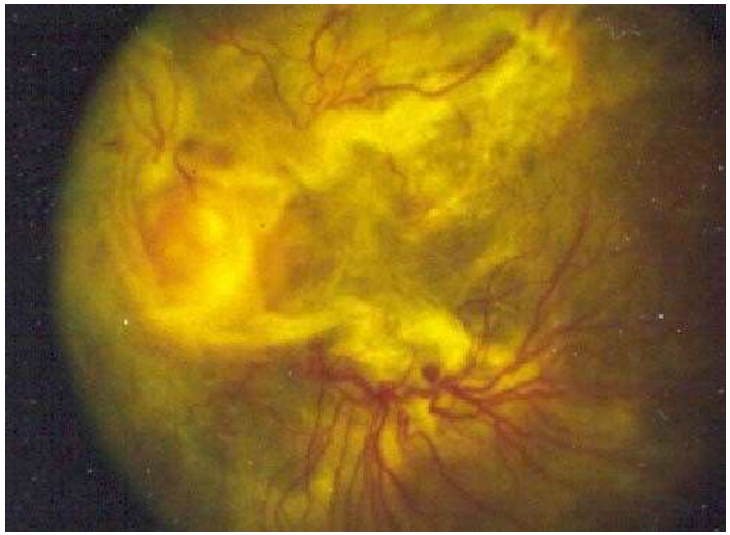


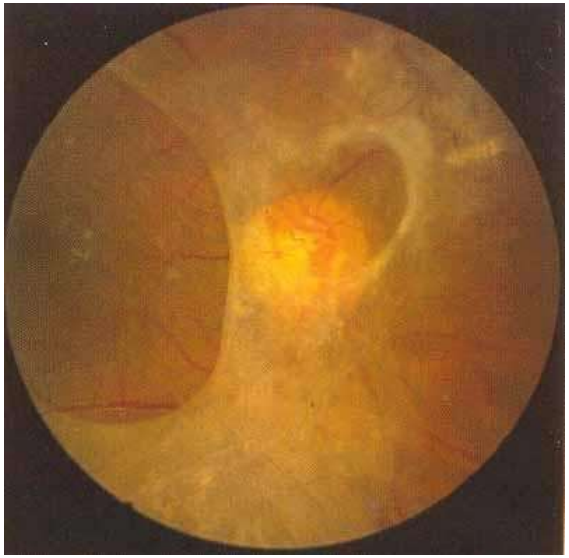
The sub-hyloid space is a space between the posterior limiting layer of the vitreous and the retina

Tractional retinal detachment



Tractional retinal detachment





ADDITIONAL

(1) Rhegmatogenous retinal detachment:
The most common type of retinal detachment. It can happen if you have a small tear or break in your retina.
When your retina has a tear or break, the gel-like fluid in the center of your eye (called vitreous) can get behind your retina. The vitreous then pushes your retina away from the back of your eye, causing it to detach.
Possible cause: severe myopia (> -4.00 to -5.00)

(2) Tractional retinal detachment:
Happens if scar tissue on your retina pulls your retina away from the back of your eye.
Possible cause: vitreous hemorrhage

Classification of the American Academy of Ophthalmologists

Dilated Ophthalmoscopy Findings	Proposed Disease Severity Level
No abnormalities bcoz we can't rule out changes on the cellular level	No apparent DR Management: control RFs
Microaneurysms only	Mild NPDR
More than "mild" but less than "severe"	Moderate NPDR
Any of the following: 20 or more microaneurysims in 4 quadrants Definite venous beading in 2 or more quadrants Prominent IRMA in 1 or more quadrants and no neovascularization	Severe NPDR
1 or more of the following: Definite neovascularization Preretinal or vitreous hemorrhage	PDR

Table 7. International Clinical Diabetic Retinopathy Disease Severity Scale.

** When evaluating the severity we take diabetic maculopathy into consideration
If clinically insignificant > no treatment / control RFs
If clinically significant > indication for treatment/ 3-4 anti-VEGF injections (1 month apart) then: if resolved >> follow up / if still present >> either more anti-VEGF injections or we go for steroid injections

** Generally speaking:
If the early changes are present in 1 quadrant >> mild NPDR
If the early changes are present in 2-3 quadrants >> moderate NPDR
If the early changes are present in 4 quadrants >> severe NPDR
HOWEVER if the changes are present in 4 quadrants but don't follow the 4-2-1 rule then MODERATE

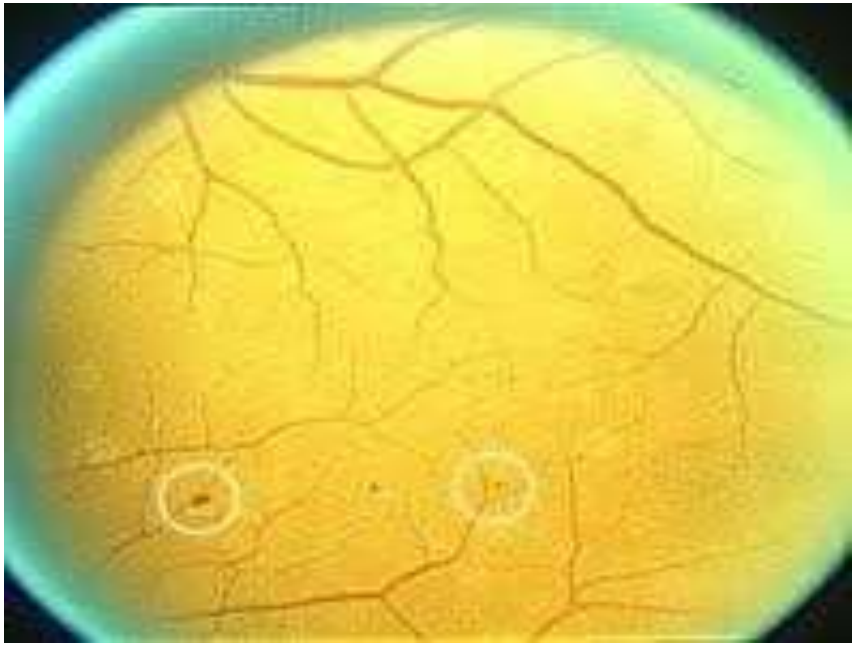
** Management: NPDR >> control RFs
If mild >> follow up: 9-12 months
If moderate >> follow up: 6-9 months
If severe >> follow up: 3-4 months
(follow up duration depends on the metabolic control & the presence + severity of other RFs)

PDR >> PRP (involves the entire retina except: the macula/ the optic disc/ major retinal vessels)
>>> decreases oxygen demand > decreases VEGF > regression of the new vessels

For example: a patient with PDR & clinically significant ME … How to manage? PRP & anti-VEGF injections

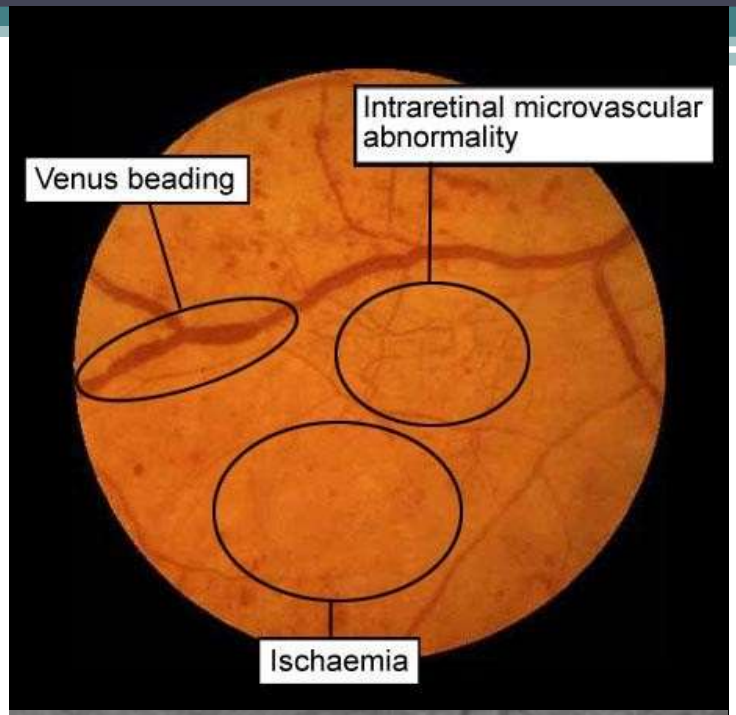
Mild NPDR

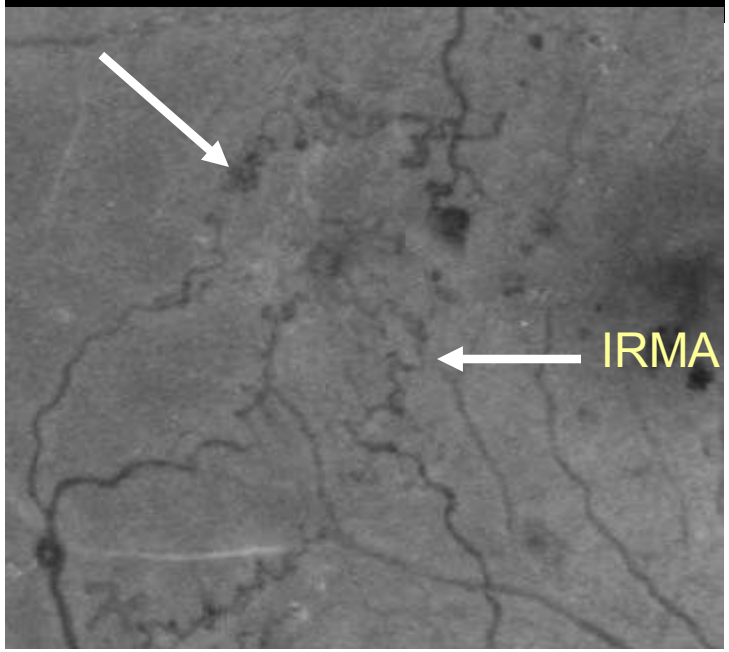
- Microaneurisms only
- Earliest clinically detectable lesion

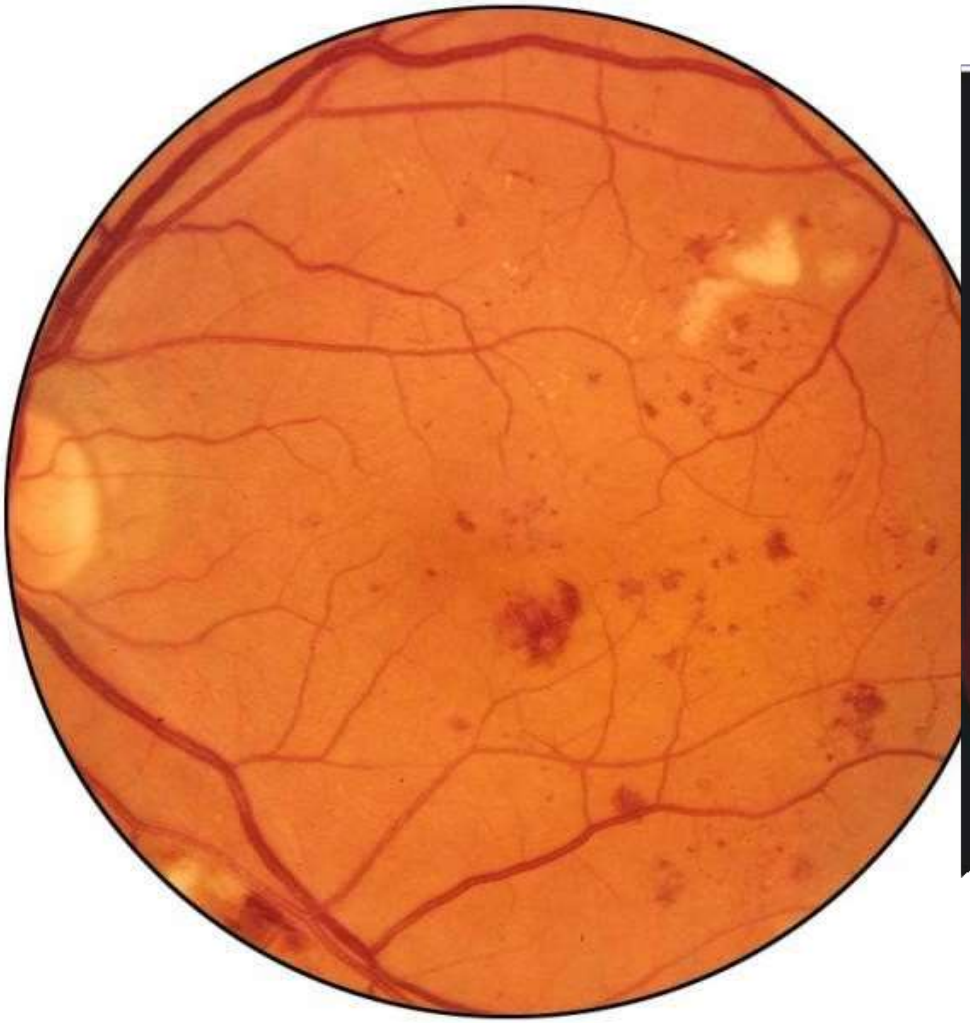


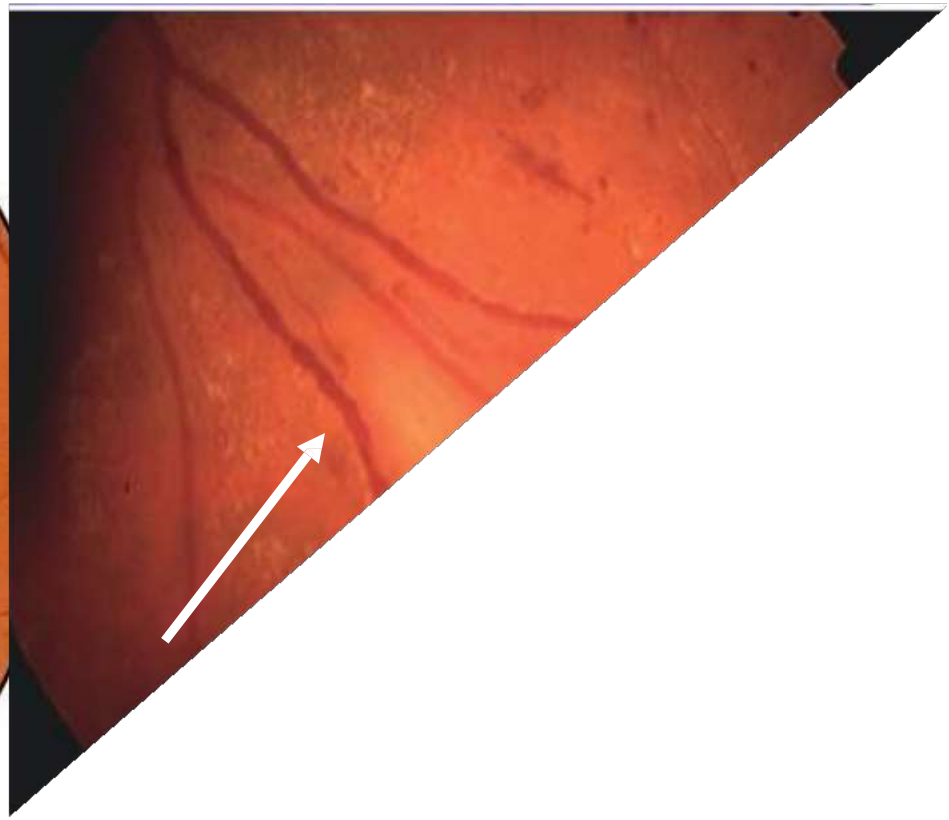
Moderate NPDR

- Microaneurysms and/or dot and blot hemorrhages in more than 1 quadrant.
- Soft exudates (Cotton wool spots).
- Venous beading in one quadrant.

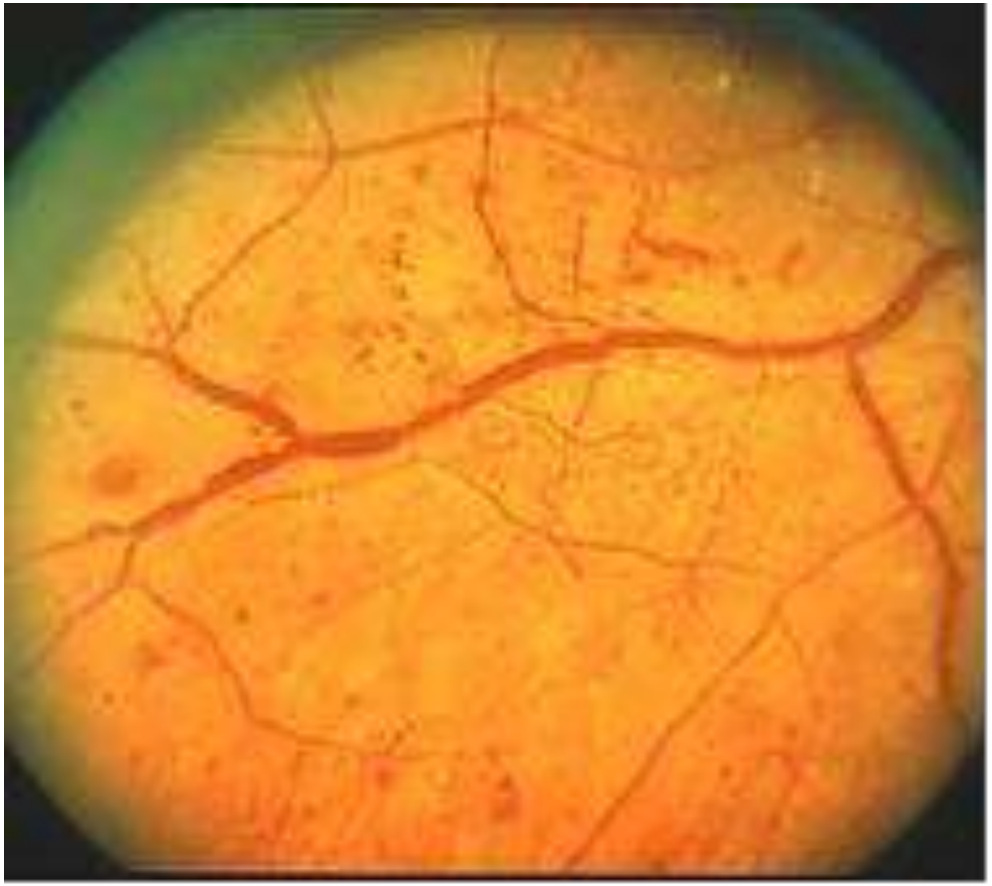






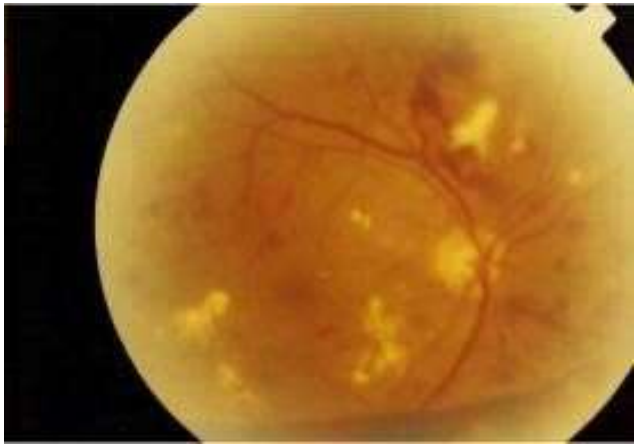


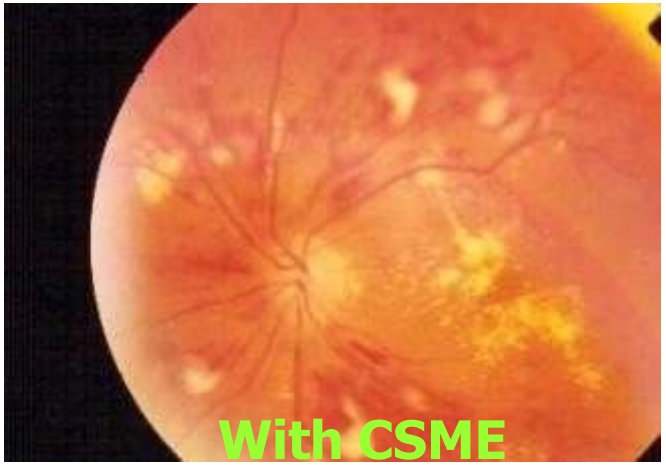
Mild vs Moderate NPDR

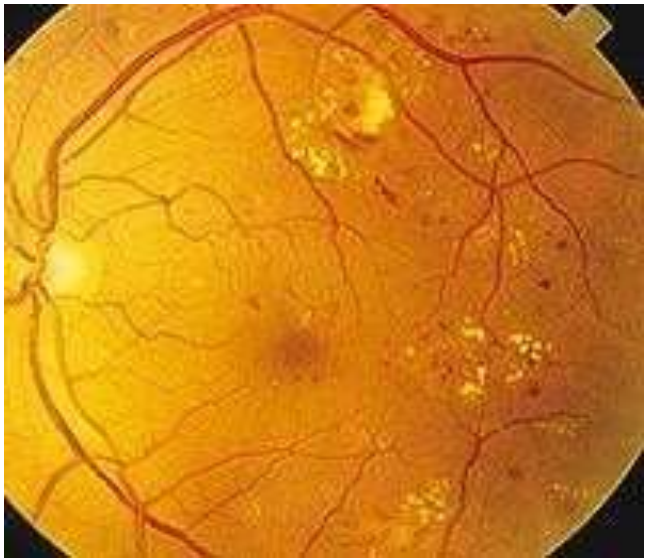


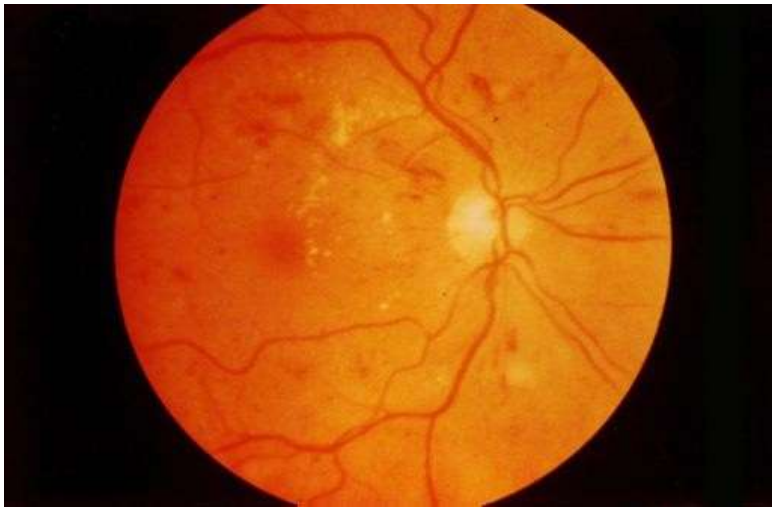
Severe NPDR

Micro anueysms in 4 quadrants, venous changes in 2 quadrants or IRMA in one quadrant





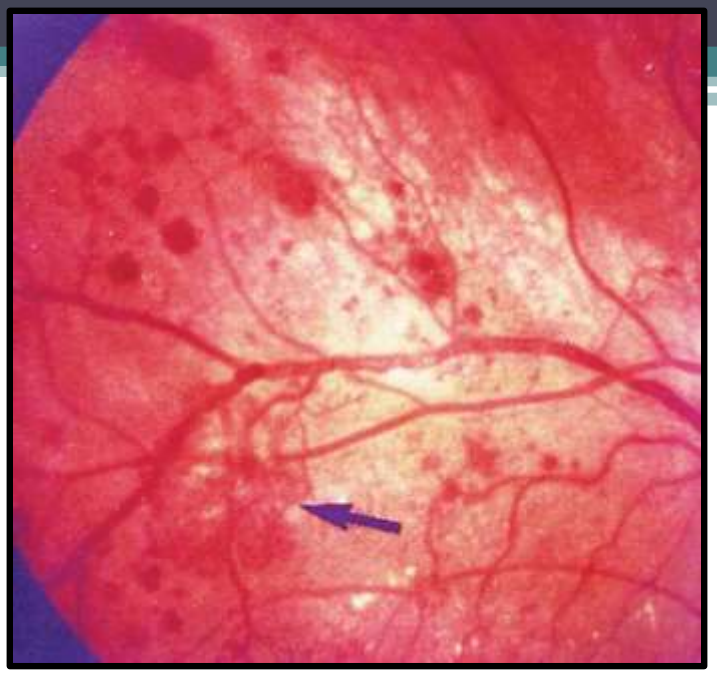




Proliferative DR

Characterized by Proliferation of new vessels from retinal veins

- New vessels on the optic disc
- New vessels elsewhere on the retina



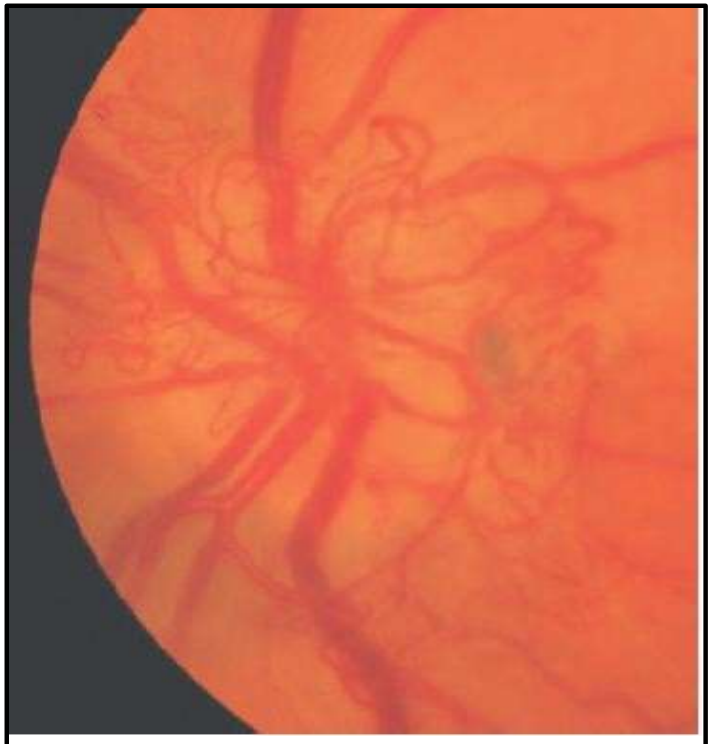


TABLE. RECOMMENDED FOLLOW-UP SCHEDULE FOR DIABETIC PATIENTS

Severity of Retinopathy	Examination Criteria	Follow-up (month)
Normal	No retinopathy	12
Mild NPDR	Microaneurysms only	9
Moderate NPDR	More than microaneurysms but less than severe	6
Severe NPDR	Any of the following (4-2-1 rule)	
• Intraretinal hemorrhages in all four quadrants		4
• Venous beading in two or more quadrants		4
• IRMA in one or more quadrants		4
Proliferative DR	Neovascularization of disc or elsewhere	Refer to retina specialist
Macular edema	Macular thickening and/or cystic edema	Refer to retina specialist

Abbreviations: NPDR, nonproliferative diabetic retinopathy; IRMA, intraretinal microvascular abnormalities; DR, diabetic retinopathy.

Treatment

- Mild & Moderate NPDR

  - No specific treatment for retinopathy
  - Good diabetic control to delay progression
  - Control of associated Hypertension, Anemia and Renal failure

- Severe NPDR

  - Close follow up by Ophthalmologist

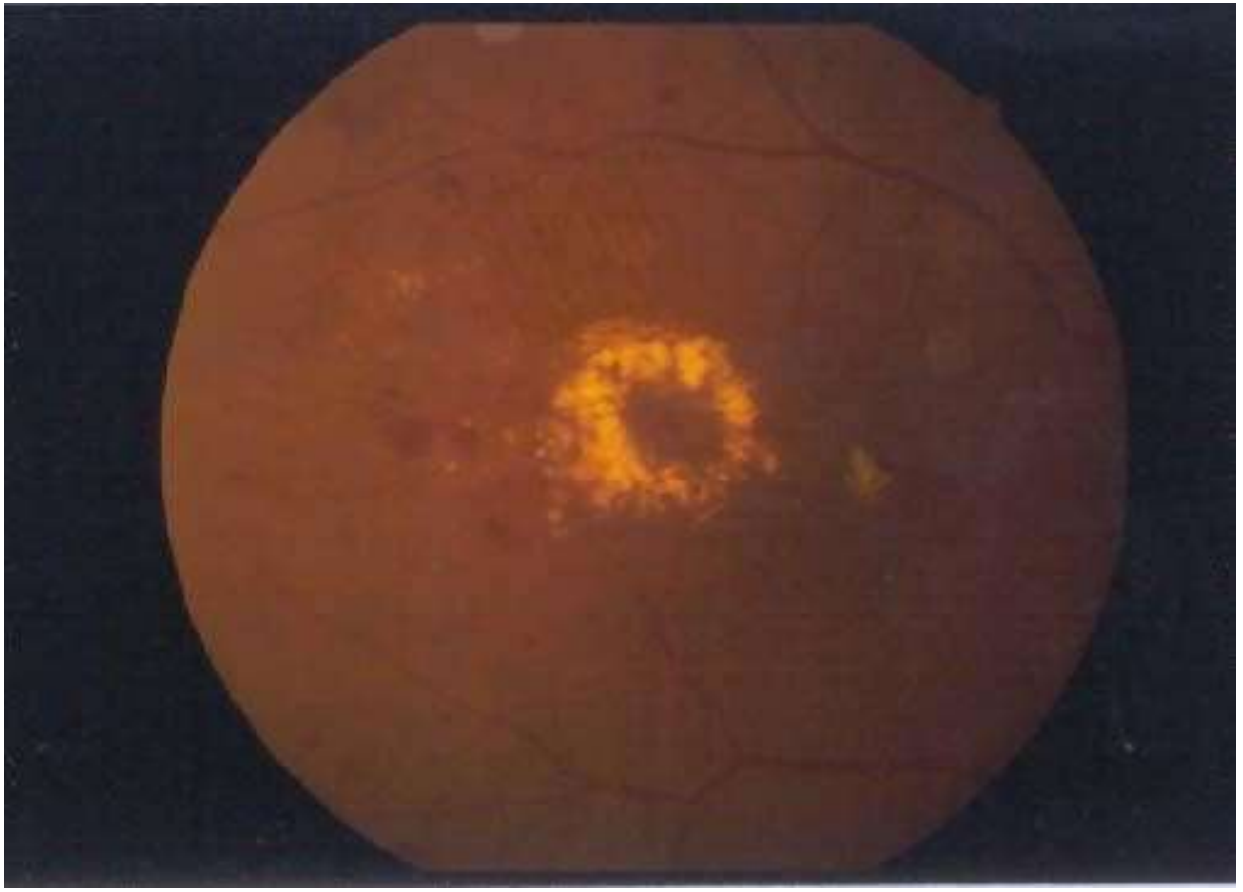
❖Clinically Significant Macular Edema

- Intra-vitreal anti-VEGF.

- Laser photocoagulation to minimize risk of visual loss.

We aim the laser at the points of leakage, the exudate is often seen as to be in a circular or circinate pattern, with the focus of leakage or microaneurysm in the middle. If the treatment is effective, the retinal edema and exudate will resorb, although this may take some months.

Circinate retinopathy – Hard exudates in a ring around leaking aneurysms

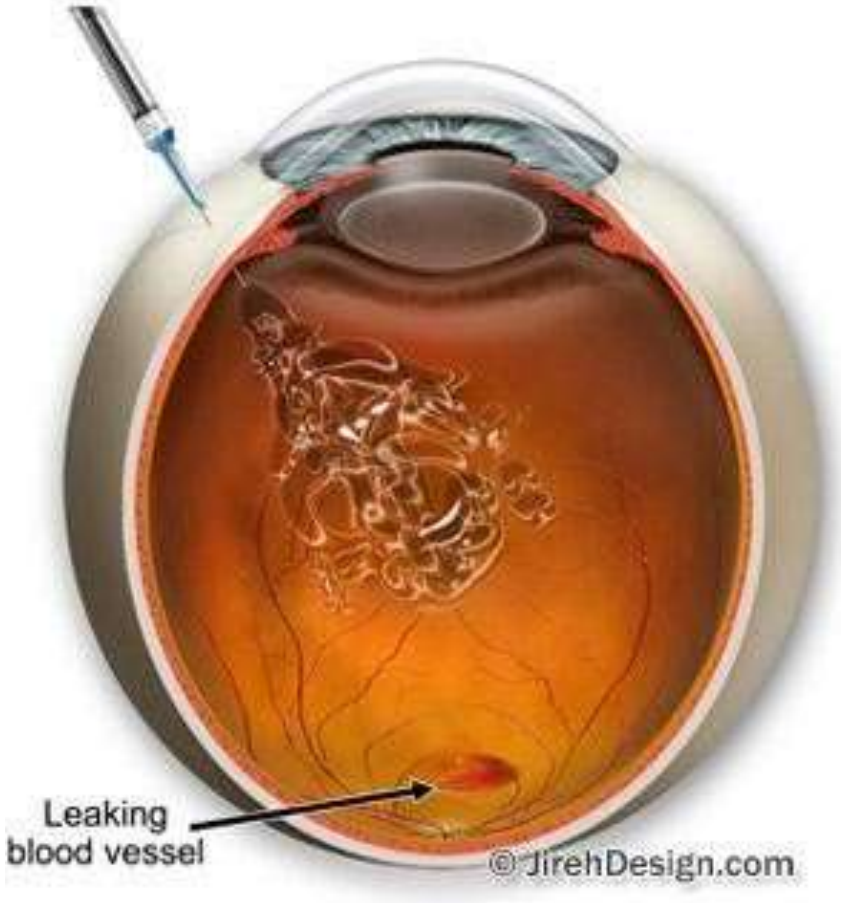


❖Proliferative DR

—Retinal laser photocoagulation as per the judgment of ophthalmologist (in high risk eyes) , it improves retinal circulation and decreases production of vasoprolifrative factors (by ablating areas of ischemic retina).

Our aim here is scattered laser burns to the entire retina (pan-retinal laser pr PRP), leaving an untreated area around the optic disc and around the central region of the macula, to preserve vision.

—Anti-VEGF , shrinks neovasculazation and decrease leakage, given as intravitreal injection, like avastin.


Leaking
blood vessel
© JirehDesign.com

Diabetic retinopathy typically presents no symptoms during the early stages.

The condition is often at an advanced stage when symptoms become noticeable. On occasion, the only detectable symptom is a sudden and complete loss of vision.

DR usually affects both eyes.

The only way people with diabetes can prevent DR is to attend every eye examination scheduled by their doctor.

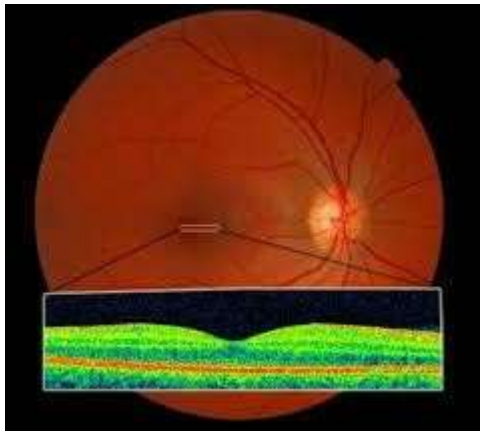
Symptoms of diabetic retinopathy may include:

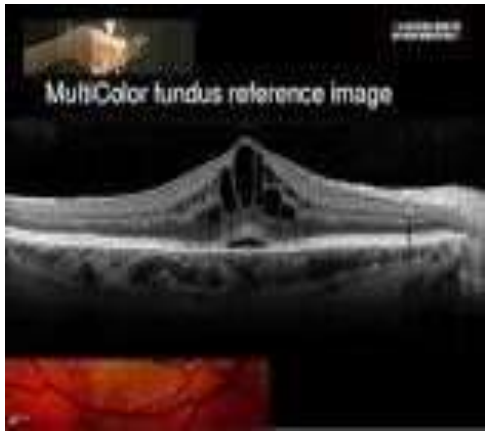
-Blurred vision
-The impairment of color vision
-Floaters, or transparent and colorless spots and dark strings that float in the patient's field of vision
-Patches or streaks that block the person's vision
-Poor night vision
-Sudden and total loss of vision

Investgations

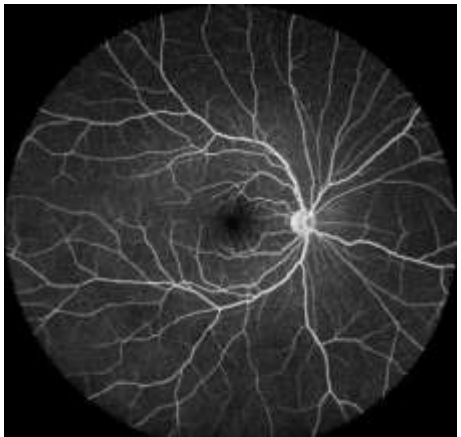
HbA1c, blood sugar

OCT, to determine the thickness, presence of swelling, to diagnose macular edema or CSME





Fluoroscein angiography



Complications of Diabetic Retinopathy

- Vitreous hemorrhage
- Tractional retinal detachment
- Rubeosis Iridis
- Glaucoma
- Blindness

Neovascular Glaucoma

- Complication of rubeosis iridis
- New vessels cause angle closure
- Mechanical obstruction to aqueous outflow
- Intra ocular pressure rises
- Pupil gets distorted as iris gets pulled.
- Eye becomes painful and red
- Loss of vision

Blindness

- Non-clearing vitreous hemorrhage
- Neovascular glaucoma
- Tractional retinal detachment
- Macular ischemia

Prevention of Complications

1- By early institution of appropriate treatment
2-Early detection of DR in its asymptomatic treatable condition
3.Routine fundus examination of all diabetics (at least yearly)
4. Appropriate referral to ophthalmologist