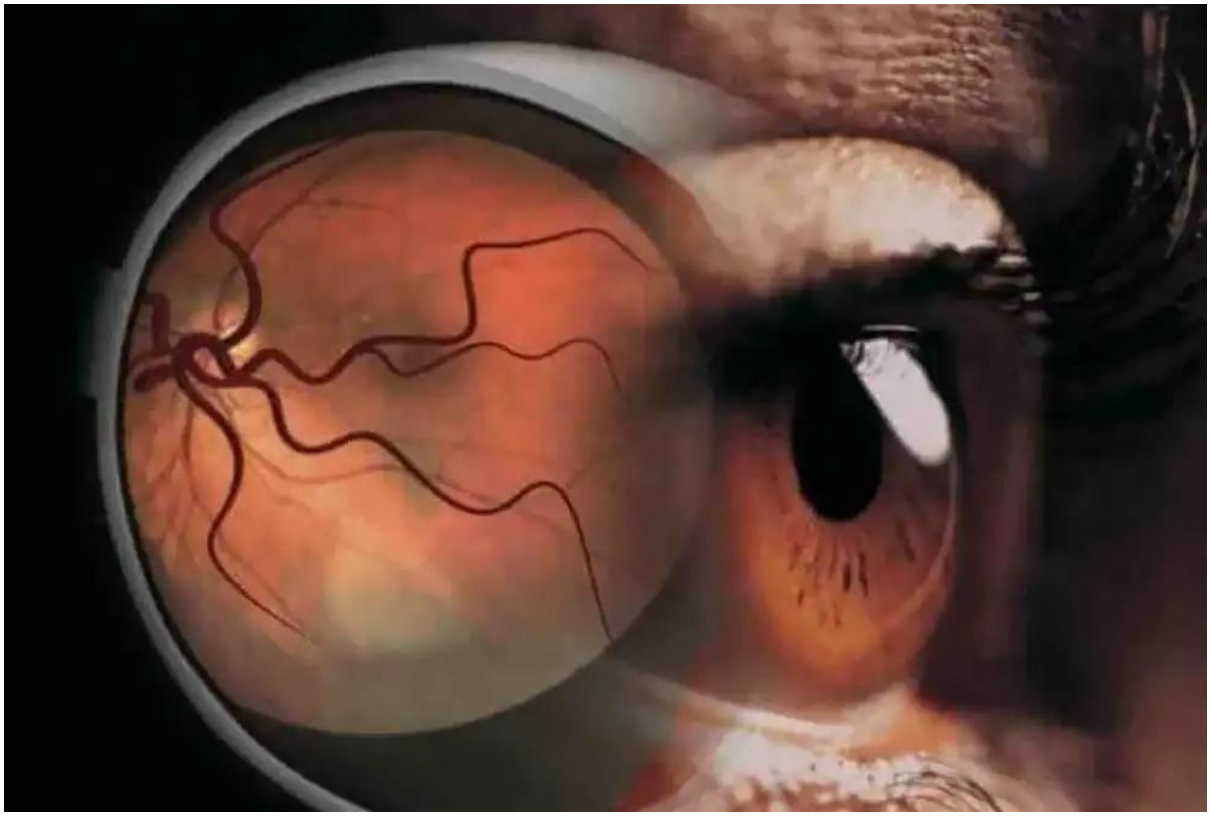
DIABETIC RETINOPATHY

Atlas

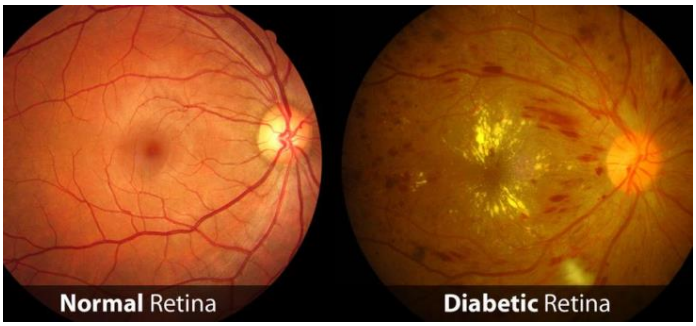


Centre for Eye Care,
Faculty of Medicine,
University of Colombo.

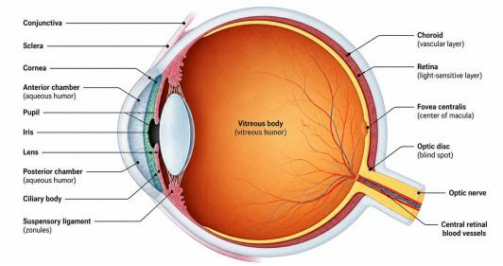
Contents

Definition

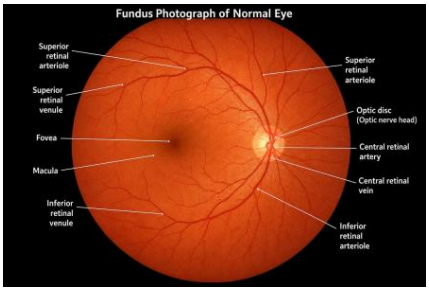
- Diabetic retinopathy is a diabetes induced chronic progressive sight threatening disease of retinal microcirculation (microvascular complication of diabetes) which results in leakage, ischemia, and abnormal vessels formation.
- Is a leading cause of blindness among working – age adults worldwide.



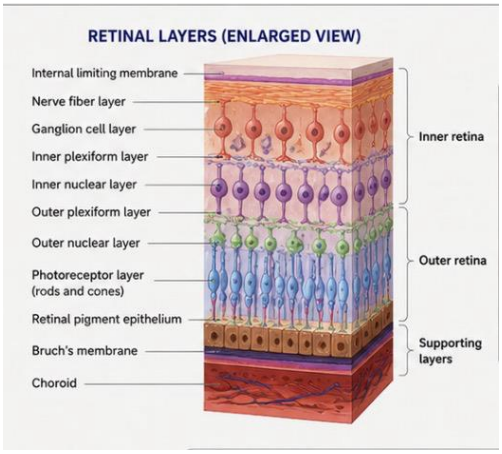
Normal Eye



Cross section of the eye

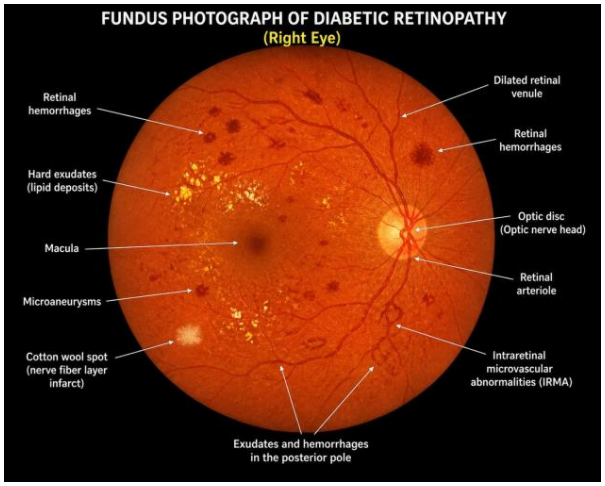


Fundus photograph of the eye

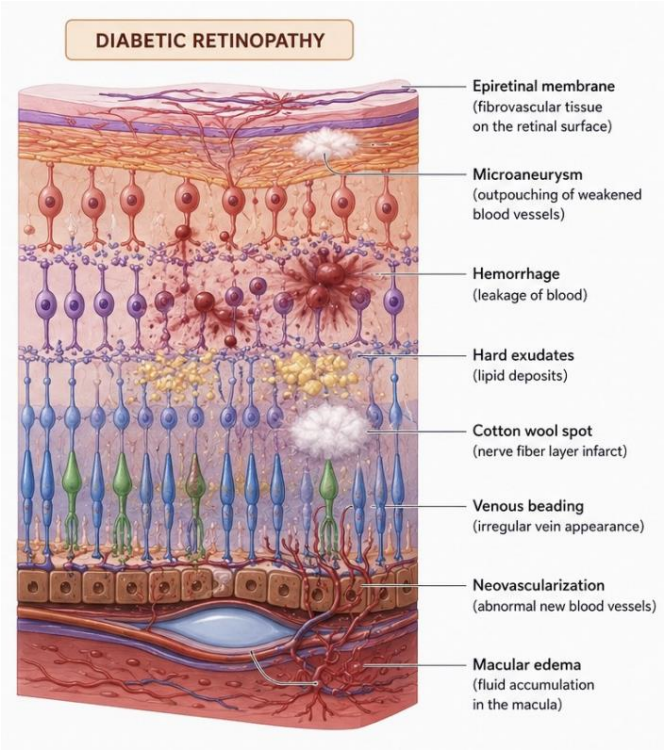


Layers of the retina

Eye with Diabetic Retinopathy



Fundus photograph of an eye with diabetic retinopathy

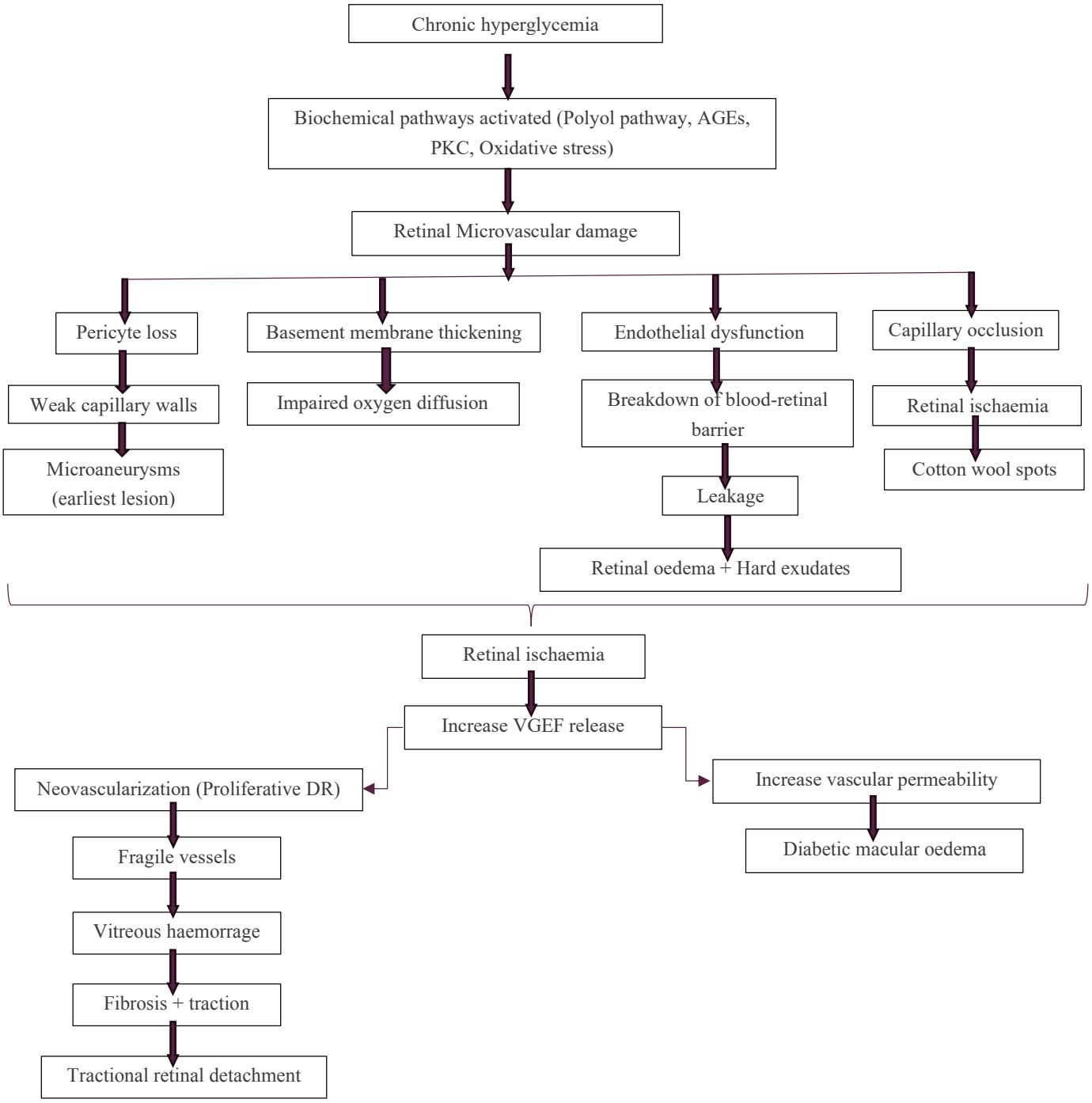


Retinal layers of an eye with diabetic retinopathy

Prevalence

- Around 22-27% of people with diabetes have some degree of diabetic retinopathy.
- Around 6% have vision threatening diabetic retinopathy (VTDR)
- About 4% have clinically significant macular odema (described later)
- More common in Type 1 diabetes than Type 2
- Prevalence differs between regions
    - Highest prevalence rates reported in,
        Africa (35.9%)
        North America and the Caribbean (33.3%)
        Middle East and North Africa (32.9%)
    - Lowest prevalence seen in
        South and Central America (13.4%)
    -In Asia prevalence varies widely ranging from 10% in India to 43% in Indonesia and expected to increase due to rising diabetes burden.

Pathophysiology



Risk factors

- Age and age at diagnosis
- Duration of diabetes mellitus
- Poor controlled diabetes mellitus
- Hypertension
- Hyperlipidemia
- Pregnancy
- Smoking
- Alcohol use
- Obesity
- Anemia
- Ethnicity

Symptoms

In early stages,

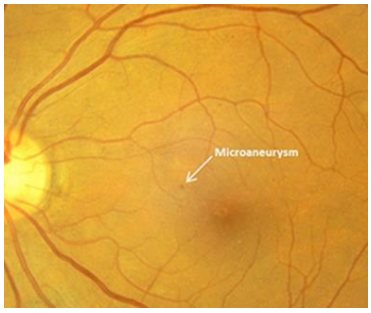
- No symptoms at first or slight changes in vision

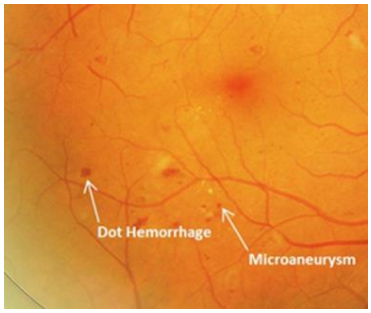
As the condition progresses,

- Blurred vision
- Fluctuating vision (vision that changes sometimes from blurry to clear)
- Dark spots or floaters
- Colours appearing faded or washed out
- Poor night vision
- Blank or dark areas in the field of vision
- Sudden vision loss
- Partial or severe blindness in severe cases

Signs

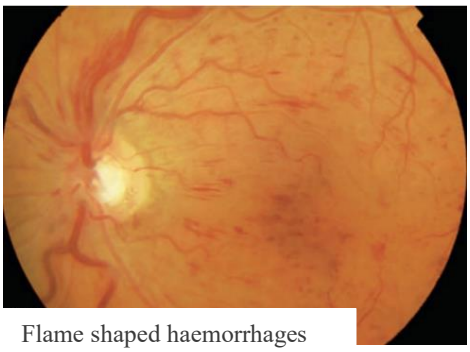
❖ Microaneurysms





- Earliest change in diabetic retinopathy
- Tiny red dots.
- Localized out-pouchings,mainly saccular
- May form either by focal dilatation of the capillary wall or by fusion of two arms of a capillary loop.
- Plasma constituents leak into the retina as a result of breakdown in the blood–retinal barrier or may thrombose.
- Commonly temporal to fovea.

❖ Retinal hemorrhages



Flame shaped haemorrhages

Dot/blot haemorrhages

Deeper dark round haemorrhages

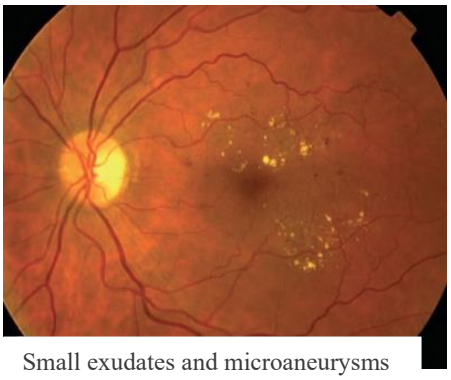
- Bleeding within the retina due to damaged blood vessels.
- Appear as,

✓ Flame shaped hemorrhages -Haemorrhages in retinal nerve fibre layer

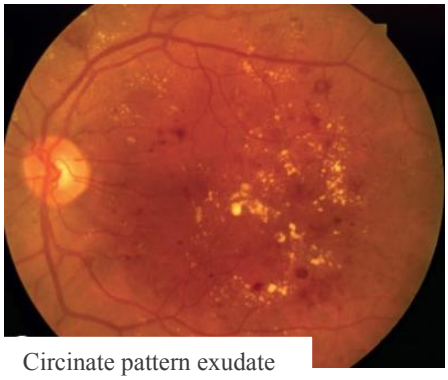
✓ Dot/blot hemorrhages / Intraretinal hemorrhages - Located in the compact middle layers of the retina

✓ Deeper dark round hemorrhages (hemorrhagic retinal infarcts) - Located within the middle retinal layers

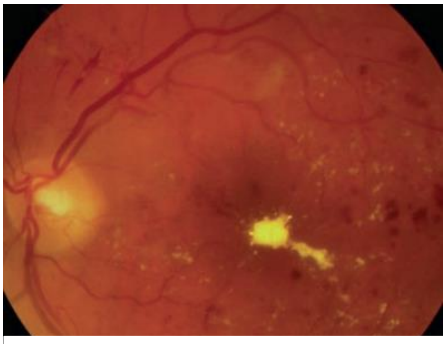
❖ Exudates



Small exudates and microaneurysms



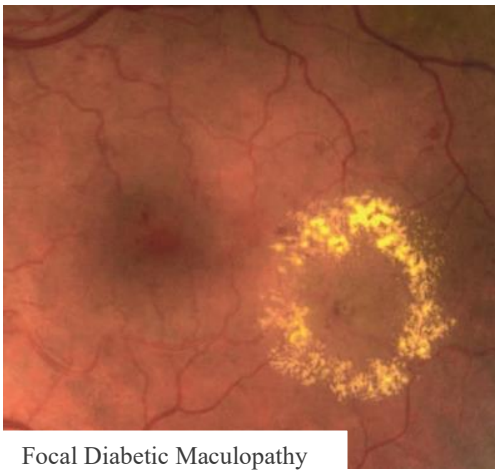
Circinate pattern exudate



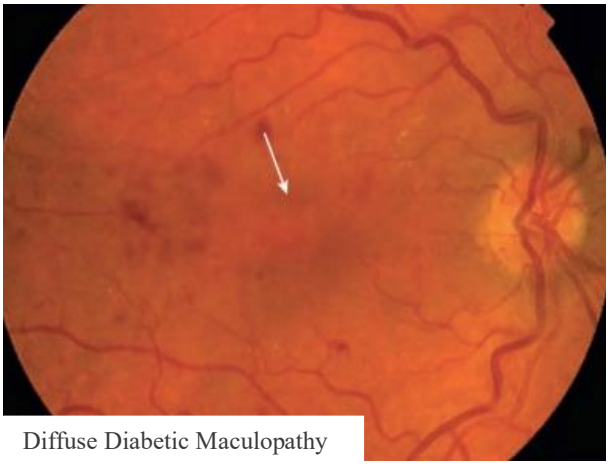
Exudates involving fovea, central crystalline cholesterol deposition

- Waxy yellow lesions with relatively distinct margins
- Arranged in clumps andor rings at the posterior pole.
- Often around the leaking microaneurysms.
- Caused by chronic localized retinal oedema.
- Composed of lipoprotein and lipid-filled macrophages.
- Hyperlipidaemia may increase the likelihood of exudate formation.

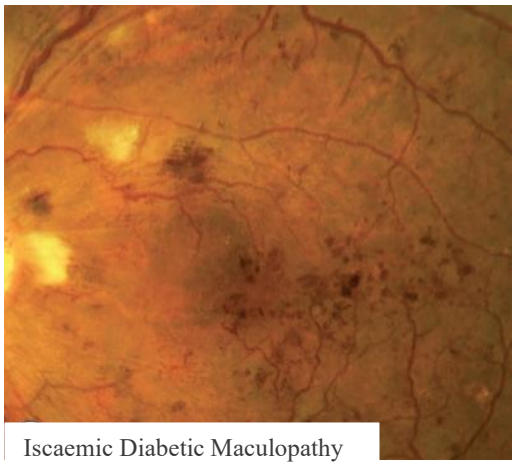
❖ Diabetic macular oedema



Focal Diabetic Maculopathy



Diffuse Diabetic Maculopathy

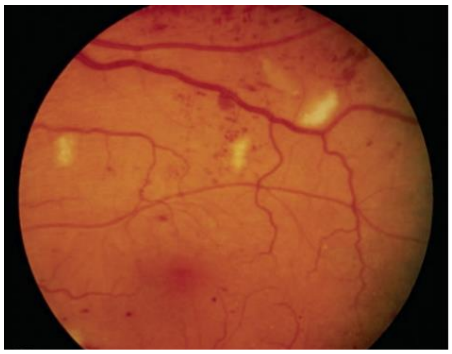


Iscaemic Diabetic Maculopathy

- Retinal oedema is caused by extensive capillary leakage and localized oedema by focal leakage from microaneurysms and dilated capillary segments.
- Diabetic maculopathy (diabetic macular odema) is the most common cause of visual impairment in diabetic patients, particularly Type 2 diabetes.
- Types,

1. Focal maculopathy - localized leakage
2. Diffuse maculopathy - wide spread leakage
3. Ischemic maculopathy- poor perfusion

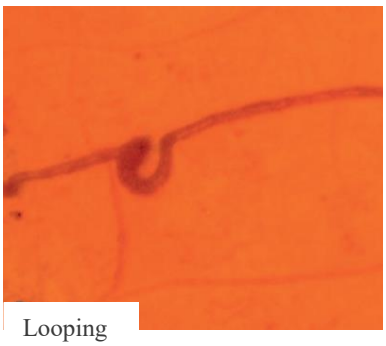
❖ Cotton wool spots



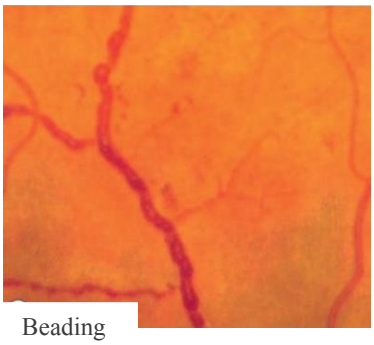
Clinical appearance of cotton wool spots

- Small fluffy whitish superficial lesions that obscure underlying blood vessels.
- Composed of accumulations of neuronal debris within the nerve fibre layer.
- Results from ischaemic disruption of nerve axons.

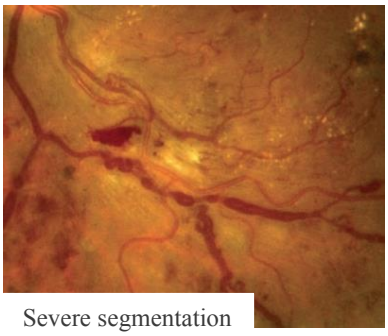
❖ Venous changes



Looping



Beading

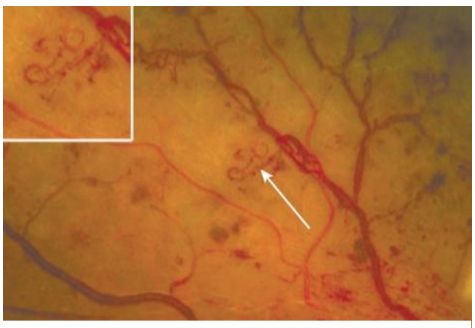


Severe segmentation

- Venous anomalies seen in ischaemia,

1. Generalized dilatation and tortuosity
2. Looping
3. Beading (focal narrowing and dilatation)
4. Sausage-like segmentation

❖ Intraretinal microvascular abnormalities



Pre-proliferative retinopathy with IRMA

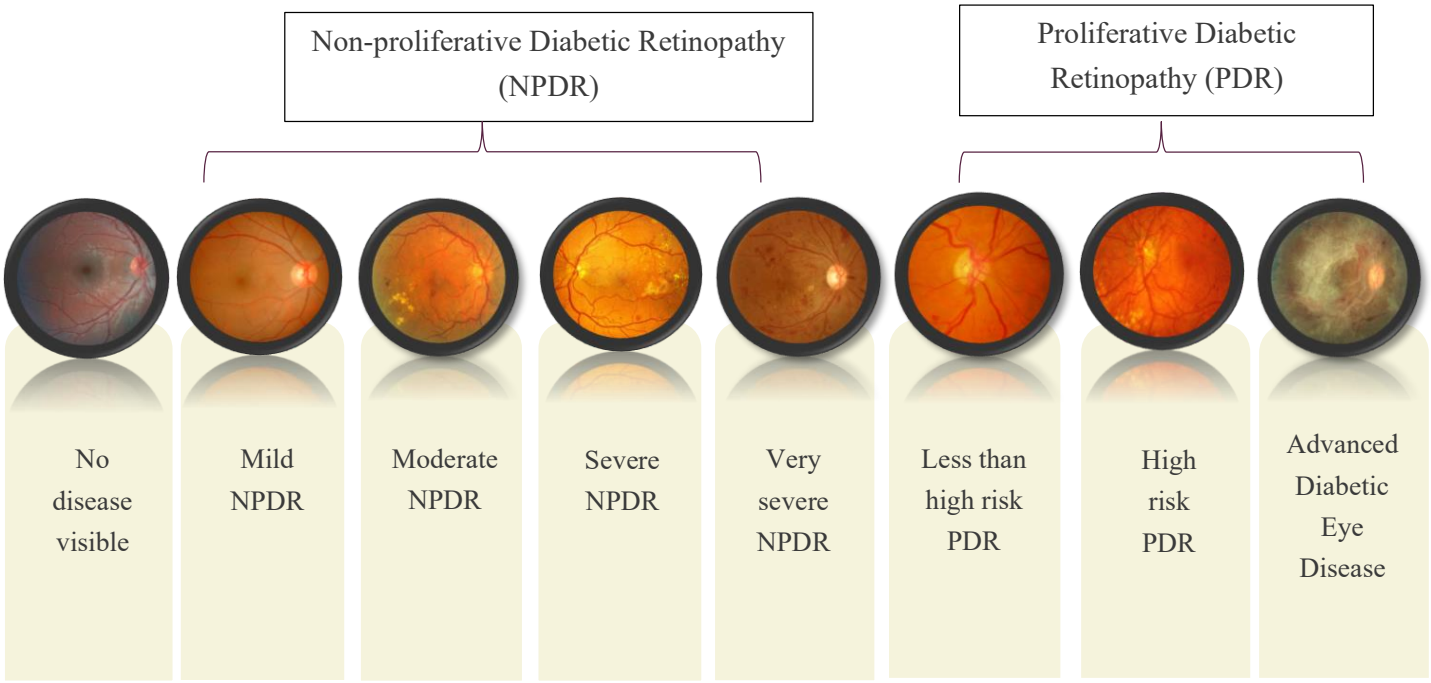
- Arteriolar-venular shunts that run from retinal arterioles to venules, thus bypassing the capillary bed and are therefore often seen adjacent to areas of marked capillary hypoperfusion.

❖ Arterial changes

- Early marker of ischaemic dysfunction - subtle retinal arteriolar dilatation
- Significant ischaemia - signs include peripheral narrowing, ‘silver wiring’ and obliteration, similar to the late appearance following a branch retinal artery occlusion.

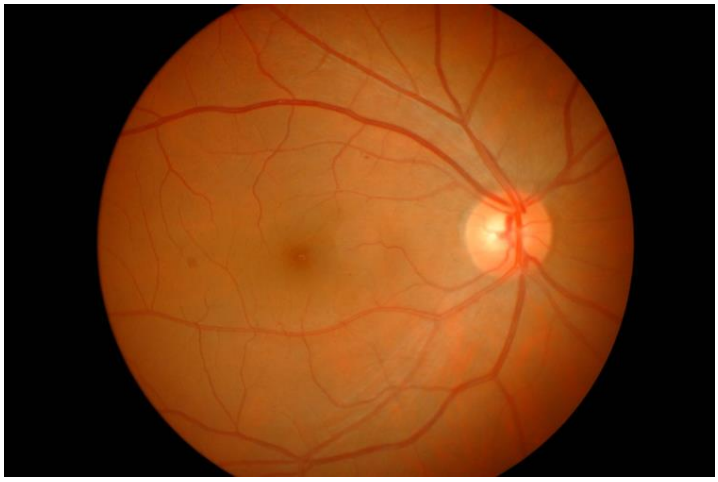
Classification

None	NPDR				PDR		
	Mild	Moderate	Severe	Very severe	Less than high risk characteristics	High risk characteristics	Advanced Diabetic Eye Disease
	BDR (Background)		PPDR (Proliferative)				



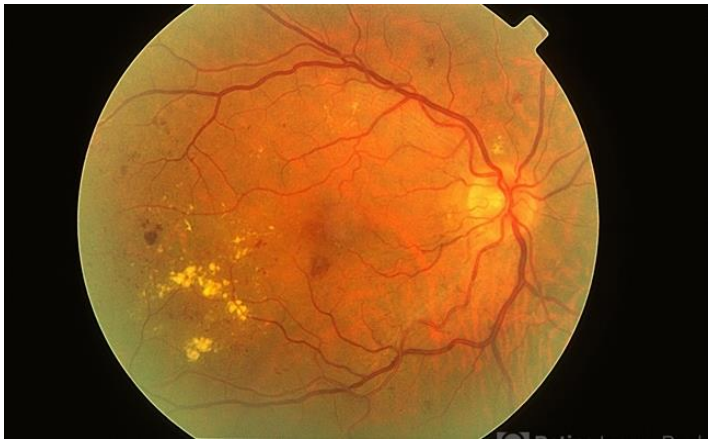
Non-proliferative diabetic retinopathy (NPDR)

➢ Mild NPDR



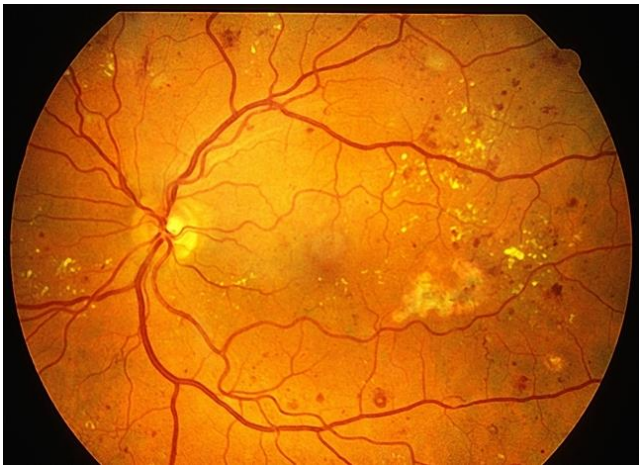
- Any or all of, microaneurysms, retinal haemorrhages, exudates, cotton-wool spots, upto the level of moderate NPDR.
- No intraretinal microvascular abnormalities (IRMA) or significant beading.

➢ Moderate NPDR



- Severe retinal haemorrhages in 1–3 quadrants* or mild intraretinal microvascular anomalies (IRMA).
- Significant venous beading can be present in no more than 1 quadrant*.
- Cotton-wool spots commonly present.

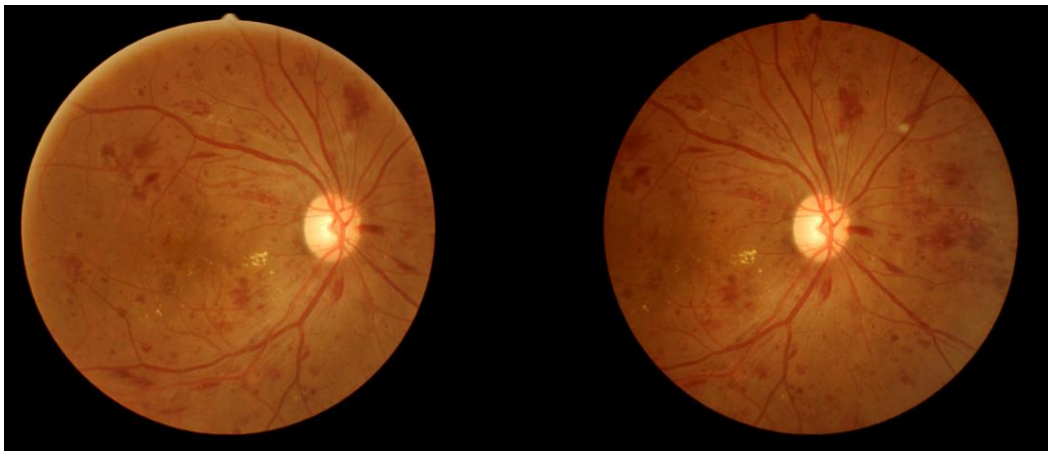
➢ Severe NPDR



The 4-2-1 rule; one or more of,

- Severe haemorrhages in 4 quadrants*
- Significant venous bleeding in 2 or more quadrants*
- Moderate intraretinal microvascular anomalies (IRMA) in 1 or more quadrants*

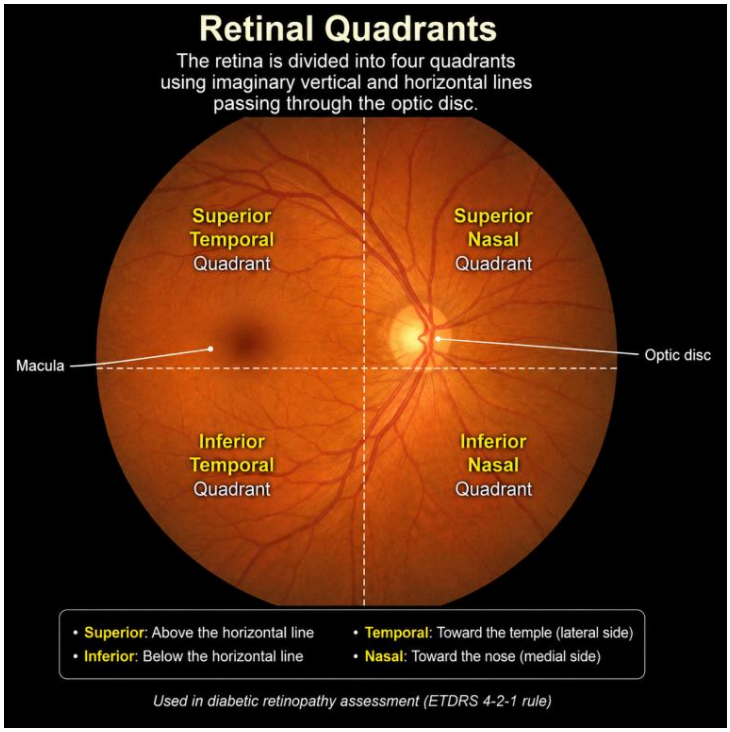
➢ Very severe NPDR



- Two or more of the criteria for severe NPDR

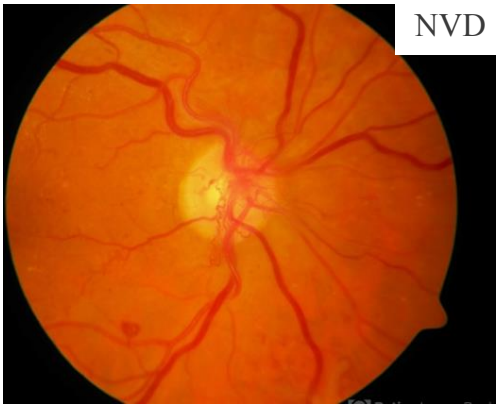
***Retinal Quadrants-**

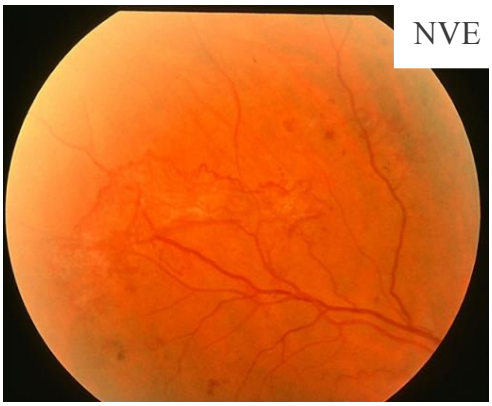
For assessment and classification of diabetic retinopathy, the retina is divided into four quadrants using imaginary vertical and horizontal lines passing through the optic disc.



Proliferative Diabetic Retinopathy (PDR)

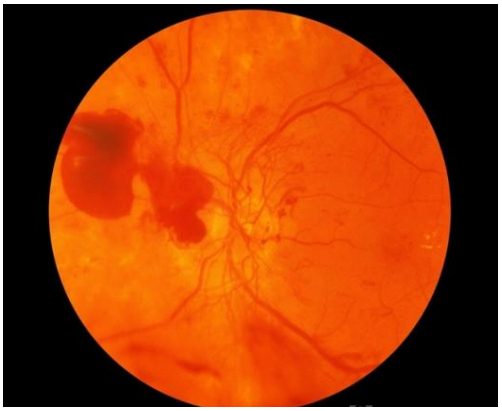
- **Less than high risk PDR**

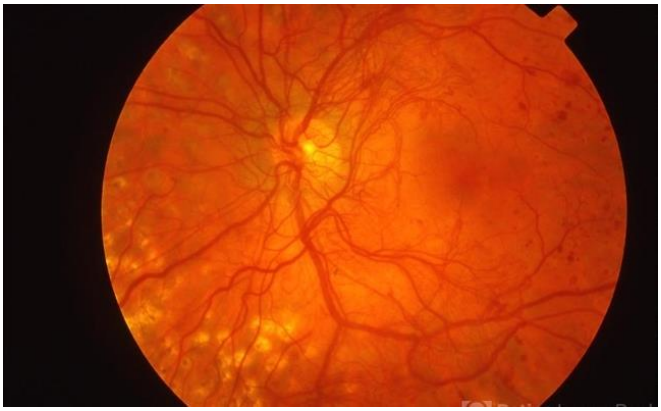




- New vessels on disc (NVD) or new vessels elsewhere (NVE) but extent insufficient to meet the high-risk criteria.

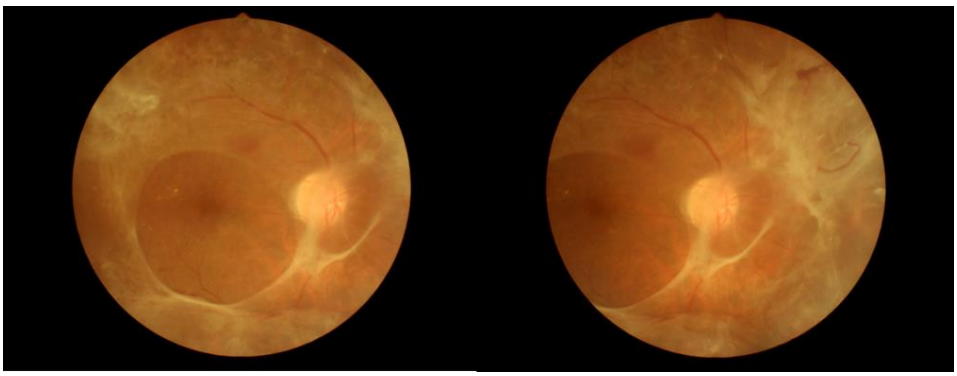
- **High risk PDR**





- New vessels on disc (NVD) greater than Early Treatment Diabetic Retinopathy Study (ETDRS) standard photograph 10A (about 1/3-disc area)
- Any NVD with vitreous haemorrhage
- New vessels elsewhere (NVE) greater than 1/2-disc area with vitreous haemorrhage

- **Advanced Diabetic Eye Disease (ADED)**

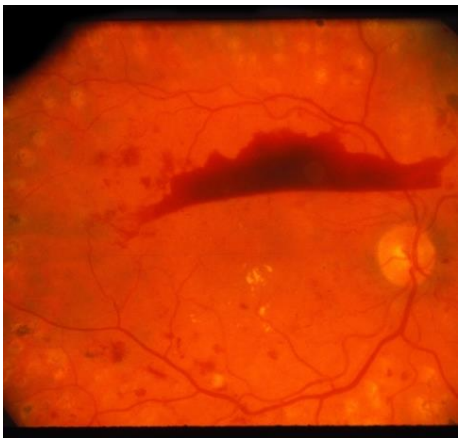


Advanced diabetic eye disease (ADED) is the severe end stage of proliferative diabetic retinopathy (PDR)that occurs in patients, in whom treatment has been inadequate or unsuccessful. But sometimes, advanced disease is evident at presentation. It develops due to extensive retinal ischaemia and fibrovascular proliferation. This is characterized by persistent vitreous haemorrhage, tractional retinal detachment and neovascular complications that may result in severe visual loss.

Pathogenesis

Retinal ischaemia stimulates the release of vascular endothelial growth factor (VEGF), resulting in neovascularization the inner surface of the retina and into the vitreous. New vessels on or near the optic disc (neovascularization of the disc [NVD]) and new vessels elsewhere (NVE) in the retina are prone to bleed, resulting in vitreous hemorrhage. The new vessels grow along the posterior hyaloid face together with fibrous tissue. These new vessels may undergo fibrosis and contraction. Contraction of this fibrovascular tissue produces vitreoretinal traction, retinal tears and retinal detachments.

✓ Vitreous haemorrhage



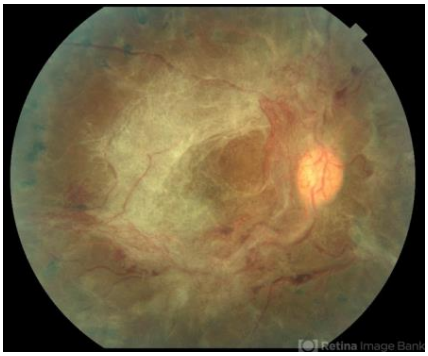
- Occurs when blood leaks into the vitreous cavity usually due to rupture of newly formed abnormal blood vessels which are extremely fragile.
- Common clinical features:
  - Sudden painless visual loss
  - Floaters, cobwebs
  - Hazy or redish vision
- Severity of symptoms depends on amount of bleeding; while mild haemorrhages may cause only a few floaters, dense haemorrhage may cause profound vision loss.
- Repeated haemorrhage can undergo organization and fibrosis and formation of fibrovascular membranes.

✓ Fibrovascular proliferation

- Refers to the growth of abnormal new vessels (neovascularization) together with fibrous tissue (fibrovascular membranes) in the retinal surface or extending into the vitreous cavity.
- Overtime contraction of these causes:
  - Vitreoretinal traction
  - Retinal distortion
  - Retinal detachment

    Ultimately severe visual impairment

✓ Tractional retinal detachment (TRD)



- Occurs due to contraction of fibrovascular membranes and pull the neurosensory retina away from the retinal pigment epithelium.
- Features:
  - Concave retinal detachment
  - Retina appears immobile
  - Usually involves the posterior pole
- Patient may experience gradual painless visual loss, distortion of vision, visual field defects and visual prognosis is poor when macula becomes detached.

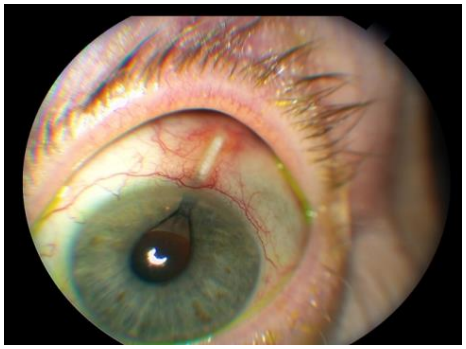
✓ Combined Tractional and Rhegmatogenous retinal detachment

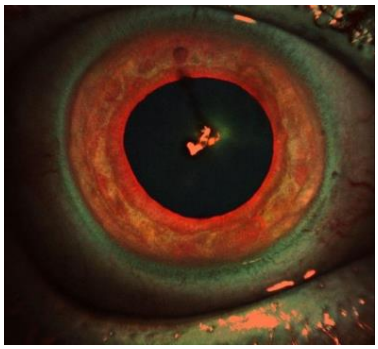
- Called as above when tractional retinal detachment is complicated by formation of retinal tear or break.
- Severe traction may produce retinal breaks, allowing fluid to pass beneath the retina and causing combined retinal detachment.
- This type progresses rapidly and has a poorer prognosis.
- Patients often present with marked visual deterioration, flashes, floaters, or extensive visual field loss.

✓ Rubeosis Iridis

- The development of new blood vessels (neovascularization) on the anterior surface of the iris, usually begins at the pupillary margin due to severe retinal ischemia.
- Initially those abnormal vessels are fine and difficult to detect but gradually spread across the iris surface into the anterior chamber angle, these vessels are fragile and may bleed easily.

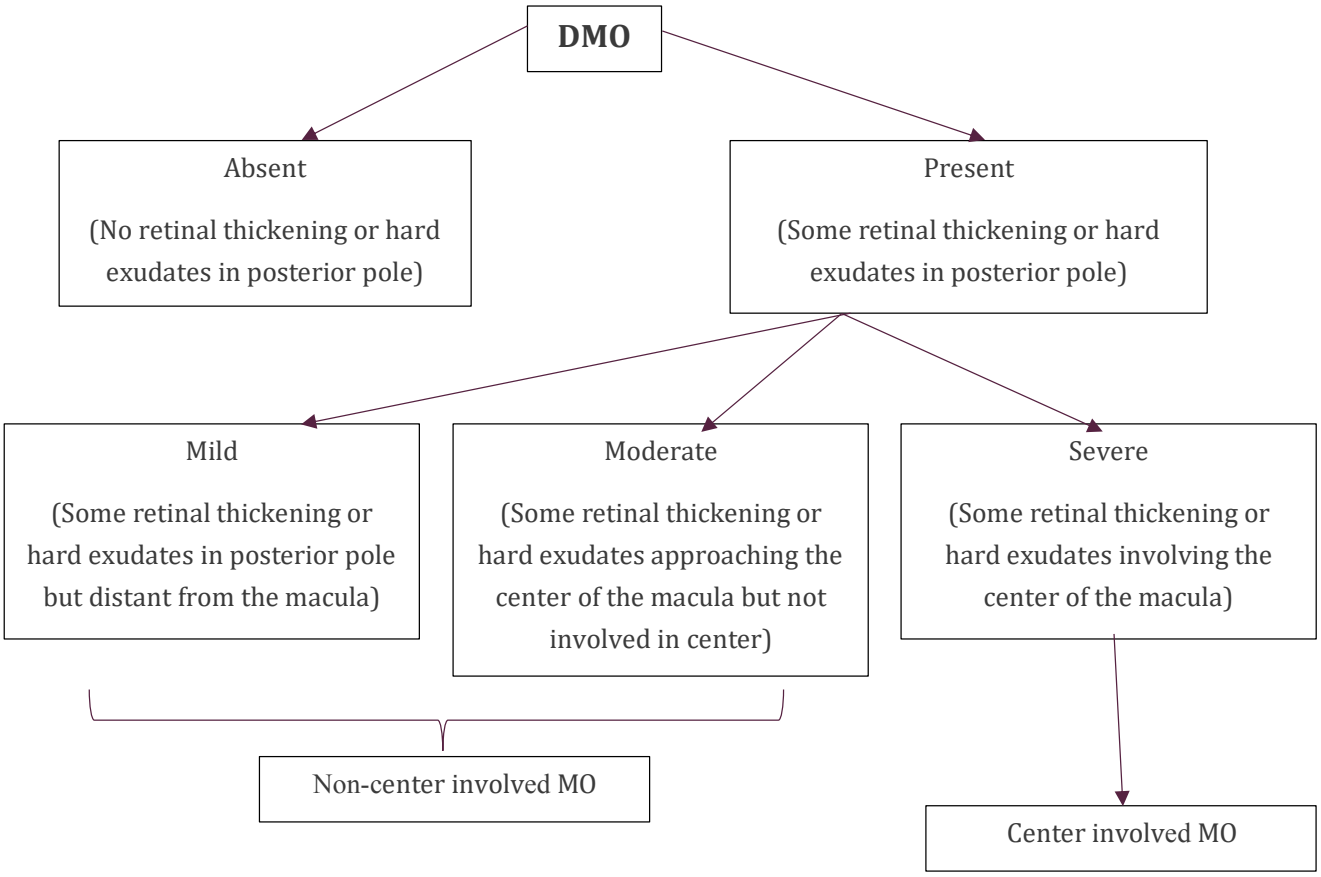
✓ Neovascular glaucoma

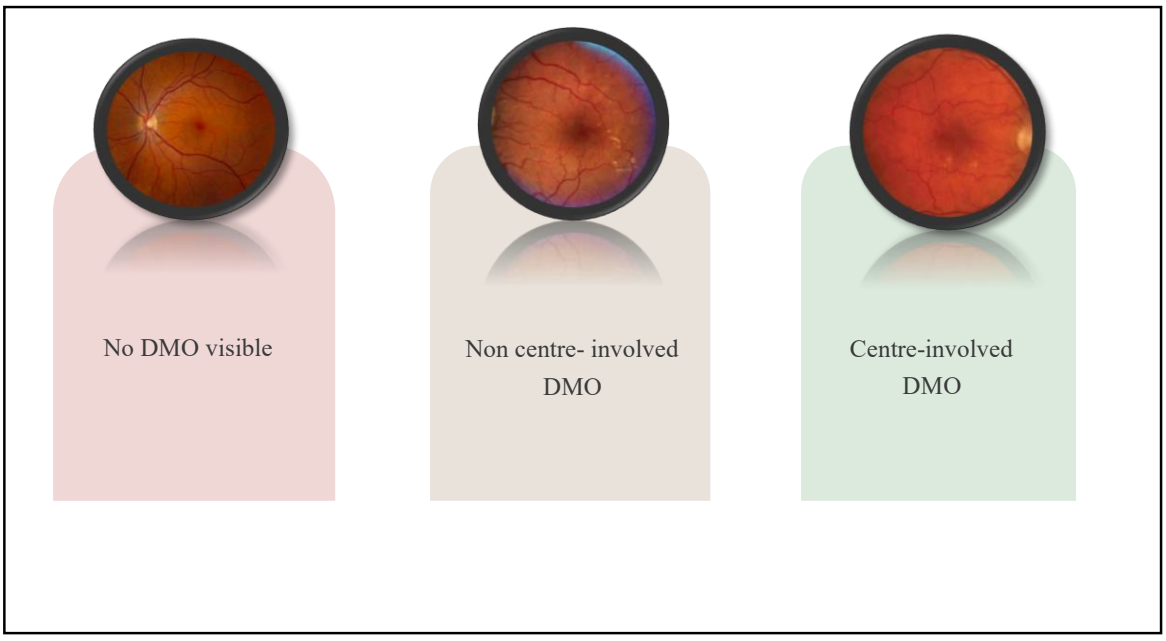


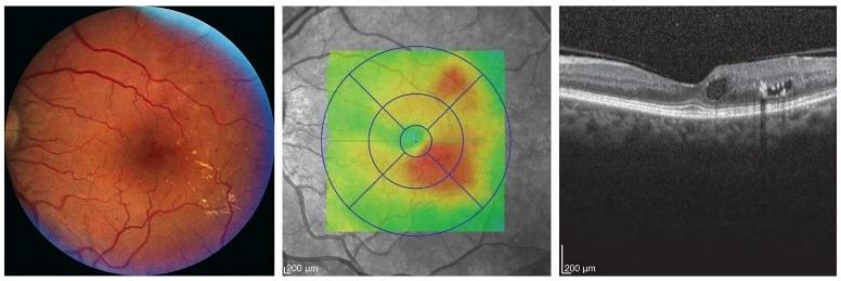


- Is a secondary glaucoma
- Formation of fibrovascular tissue over the iris and anterior chamber angle leads to obstructs aqueous outflow and causes markedly elevated intraocular pressure.
- Clinical features:
    - Painful red eye
    - Corneal oedema
    - Severe visual loss
    - Headache
    - Photophobia
- Neovascular glaucoma is one of the most serious complications of advanced diabetic eye disease (ADED)

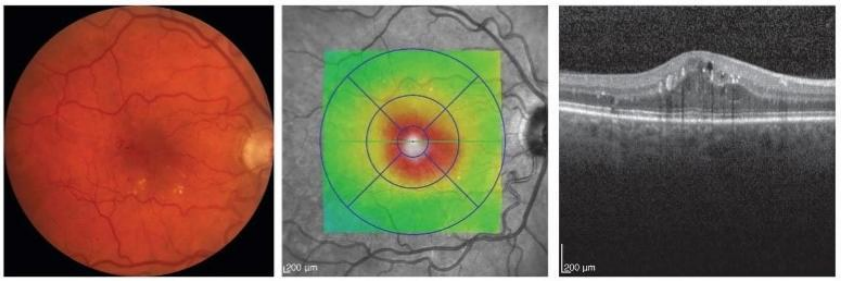
Diabetic Macular Oedema (DMO) Classification





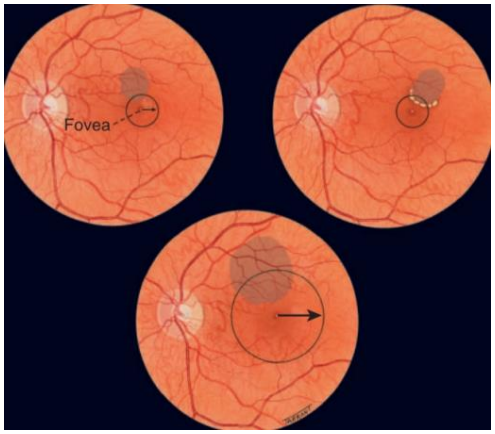


Non-centre-involved DMO



Centre-involved DMO

Clinically significant macular oedema (CSMO)



Clinically significant macular oedema (CSMO) is detected on clinical examination as defined in the Early Treatment Diabetic Retinopathy Study (ETDRS).

- Retinal thickening within 500 µm of the centre of the macula.
- Exudates within 500 µm of the centre of the macula, if associated with retinal thickening. The thickening itself may be outside the 500 µm.
- Retinal thickening one-disc area (1500 µm) or larger, any part of which is within one disc diameter of the centre of the macula.

Assessment of a patient with diabetic retinopathy

When we assess a patient with diabetic retinopathy we need to take their histories carefully, do a detailed ocular examination and do the appropriate investigations.

Our goal is to identify how severe the retinopathy is, to detect diabetic macular oedema, to identify complications that can threaten the vision and decide the need for treatment and follow up.

1. History taking

- A detailed history is an essential part of assessing a patient with diabetic retinopathy.
- Should include followings-

1)Duration of diabetes:

Longer a patient has had diabetes the risk of diabetic retinopathy increases. Long-standing diabetes is strongly associated with severe retinopathy and proliferative diabetic retinopathy (PDR)

Important,

- What type of diabetes the patient has (Type 1 or Type 2)
- Year of diagnosis

2)Glycemic control

Poor blood sugar control accelerates retinal vascular damage.

Important,

- Recent HbA1c and fasting blood sugar (FBS) level
- Compliance with diabetic medications

3)Medical history

Diabetic retinopathy can get worse if patient has systemic hypertension, renal disease, dyslipidemia, and cardiovascular disease.

So, ask about above diseases and

- Pregnancy
- Neuropathy
- Cystic Fibrosis
- Obesity

4) Ocular symptoms:

Patients may be asymptomatic in early disease.

Common symptoms,

- Blurring of vision
- Floaters or dark spots
- Reduced or fluctuating vision
- Sudden painless loss of vision
- Difficult reading
- Poor night vision
- Impaired colour vision

5)Previous ocular history:

Ask about

- Trauma
- Other eye diseases
- Ocular injections
- Surgery including retinal laser surgery

6) Current medications

2. Ocular examination

- **Visual acuity assessment:**
  - Measured using Snellen chart.
  - Importance,
    - Baseline assessment of vision
    - Monitoring disease progression
    - Evaluating treatment response

- **Slit lamp biomicroscopy**
  - Most useful examination in diabetic retinopathy.
  - Used to evaluate both anterior and posterior segments of the eye under high magnification and illumination.
  - Often use a special non-contact fundus lens such as 90-diopter (90D) lens together commonly use in diabetic retinopathy assessment, which help to visualize signs of diabetic retinopathy such as microaneurysms, retinal haemorrhages, hard exudates, neovascularization.

Slit lamp biomicroscopy

90D lens

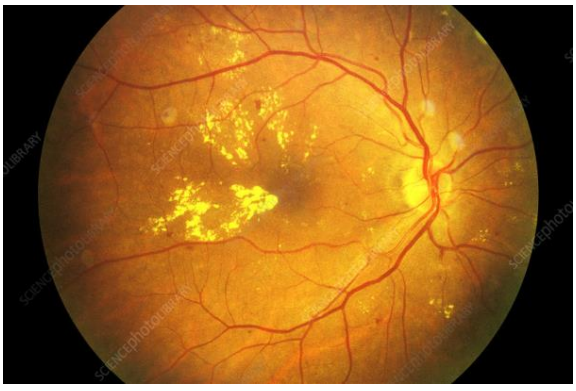
➢ **Intraocular pressure (IOP) measurement**:

- This helps to detects glaucoma.
- Importance,
  - Raised IOP may occur due to neovascular glaucoma in advanced PDR.
- Commonly measured using tonometry.
- The gold standard method is Goldmann applanation tonometry, which is usually performed with a slit lamp biomicroscope.

3.Investigations

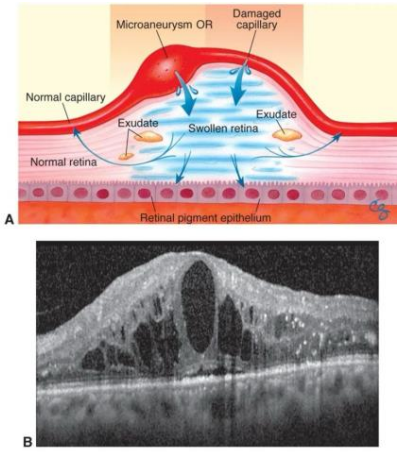
❖ **Fundus photography:**

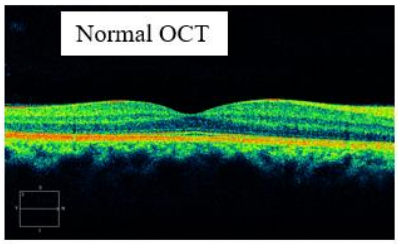
- Non-invasive imaging technique.
- Provides photographic documentation of retinal findings.
- Commonly used in the assessment and monitoring of diabetic retinopathy because this helps to identify characteristic findings of diabetic retinopathy.
- Uses,
  - Documentation of retinopathy
  - Monitoring progression
  - Comparing treatment response
  - Screening programmes

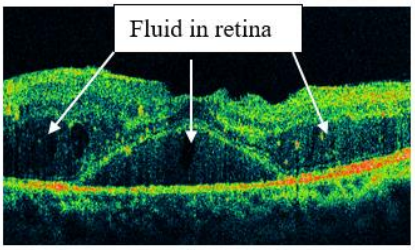


❖ **Optical Coherence Tomography (OCT)**:

- Non-invasive imaging technique that takes high-resolution cross-sectional images of the retina.
- Uses,
  - Detect diabetic macular odema
  - Measure retinal thickening
  - Identify vitreomacular traction
  - Monitor response to treatment
- OCT findings in diabetic macular odema,
  - Retinal thickening
  - Intraretinal thickening
  - Subretinal fluid
  - Vitreomacular traction





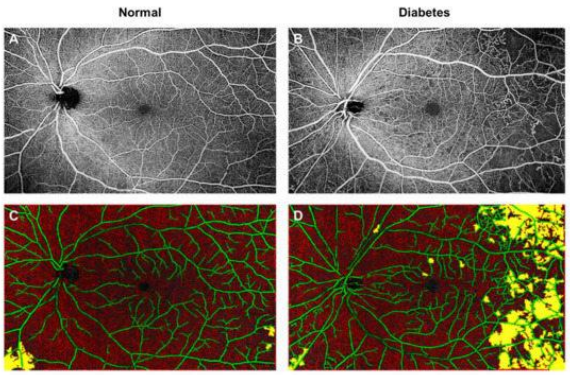


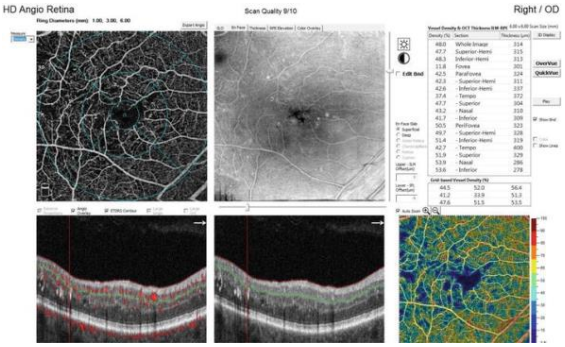
❖ **Fluorescein Angiography**:

- Using intravenous fluorescein dye, it evaluates retinal circulation.
- Procedure,
    - Fluorescein dye is injected intravenously, after sequential retinal photographs are taken.
- Limitations
    - Invasive procedure
    - Nausea and allergic reactions (there's a risk)
- Currently not using this.

❖ **Optical Coherence Tomography Angiography (OCTA):**

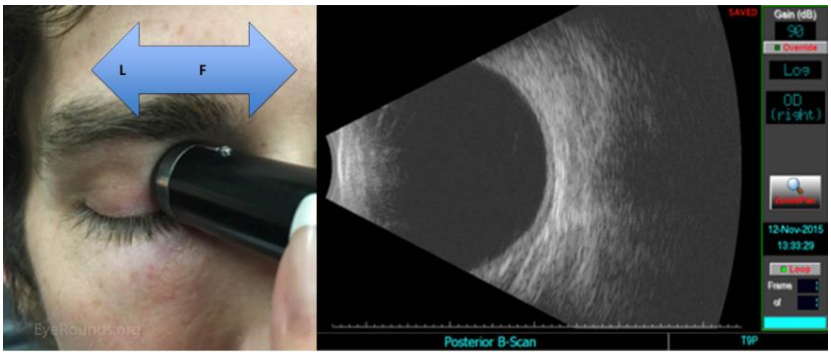
- Non-invasive technique.
- Used to visualize retinal blood vessels without dye injections.
- Uses,
    - Evaluate retinal microvasculature
    - Detect capillary non-perfusion
    - Asses foveal avascular zone
    - Detect early vascular abnormalities

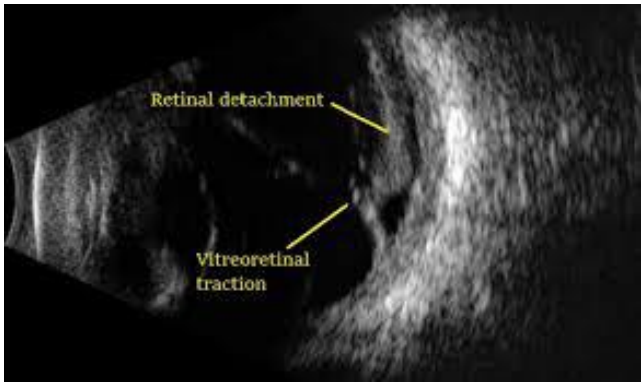




❖ **B-Scan Ultrasonography**:

- Used when retinal visualization is obscurred.
- Indications,
    - Dense vitreous haemorrhage
    - Suspected retinal detachment
- Uses,
    - Detect Tractional retinal detachment (TRD)
    - Assess vitreous haemorrhage
    - Evaluate posterior segment pathology





Management

1. General measures

- ❖ Patient education:
  - Importance of regular eye screening and follow-up.
  - Adherence to treatment schedules.
  - Lifestyle modification including exercise and weight control.
- ❖ Optimize diabetic control:
  - Maintain good long-term blood glucose level and regular check-up
- ❖ Control associated risk factors:
  - Hypertension
  - Hyperlipidemia
  - Anaemia
  - Renal impairment
- ❖ Smoking cessation:
  - Stopping is recommended to improve overall vascular health.

✓ So, the key to prevent diabetic retinopathy is patient education & long-term control of blood sugar level.

2. Laser Photocoagulation

✓ Laser treatment has been a major treatment modality for diabetic retinopathy for many years.

✓ There are several types of laser treatment;

A. Panretinal Photocoagulation

Also called as scatter laser photocoagulation, is mainly used for proliferative diabetic retinopathy (PDR).

- ❖ Indications:
  - PDR
  - High risk PDR
  - Severe NPDR in selected cases
- ❖ Advantages:
  - Reduces risk of severe visual loss
  - Causes regression of neovascularization

❖ Disadvantages:

- Peripheral visual field loss
- Reduced night vision
- Possible worsening of macular edema
- Multiple sessions may be required

B. Focal/Grid Laser Photocoagulation

This treatment is mainly used for Diabetic macular oedema, esepecially non-center involved diabetic macular oedema

❖ Mechanism:

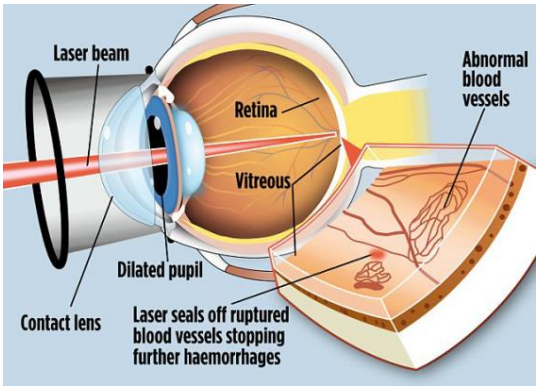
- Laser is applied to leaking microaneurysms and areas of diffuse leakage to reduce retinal oedema.

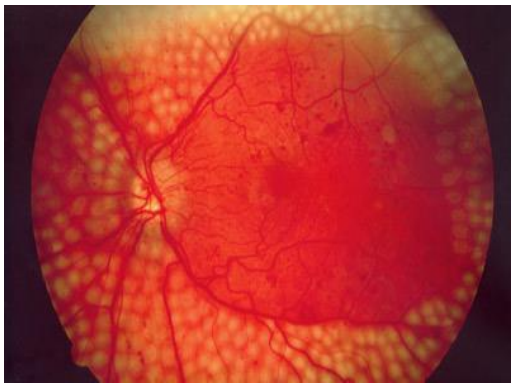
❖ Indications:

- Non-center involved diabetic macular oedema
- Selected cases of center-involved DMO combined with anti-VEGF therapy

❖ Advantages:

- Stabilizes vision
- Reduces retinal edema





3. Intravitreal Anti-VEGF therapy

Anti-vascular endothelial growth factor (anti-VEGF) therapy is currently the first line treatment for Centre- involved DMO (CI-DMO).
Also effective for PDR.

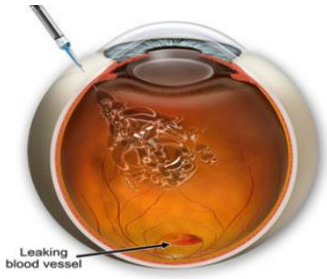
- ❖ Common anti-VEGF agents:
  - Ranibizumab
  - Aflibercep
  - Bevacizumab

- ❖ Mechanism:
  - Inhibits vascular endothelial growth factor. By doing so, it reduces vascular permeability and neovascularization.

- ❖ Indications:
  - Centre involved Diabetic Macular Oedema
  - PDR
  - Persistent macular edema

- ❖ Advantages:
  - Improves visual acuity
  - Reduces macular edema
  - Causes regression of neovascularization
  - Less peripheral visual field loss compared with PRP

- ❖ Limitations:
  - Requires repeated injections
  - Expensive
  - Need close follow-up



4. Intravitreal Corticorsteroid therapy

Mainly used in persistent or refractory diabetic macular odema.

- ❖ Common agents:
  - Triamcinolone acetonide
  - Dexamethasone implant
  - Flucinolone acetonide implant

- ❖ Mechanism:
  - Steroids reduce inflammation, vascular leakage and oedema.

- ❖ Indications:
  - Persistent DMO despite anti-VEGF therapy
  - Patients unable to attend frequent follow-up visits

- ❖ Advantages:
  - Long duration of action
  - Effective reduction of edema

- ❖ Disadvantages:
  - Cataract formation
  - Steroid induced glaucom
  - Raised intraocular pressure

5. Vitrectomy surgery

Three port Pars Plana Vitrectomy (TPPV) is indicated in advanced diabetic eye disease.

❖ Mechanism:

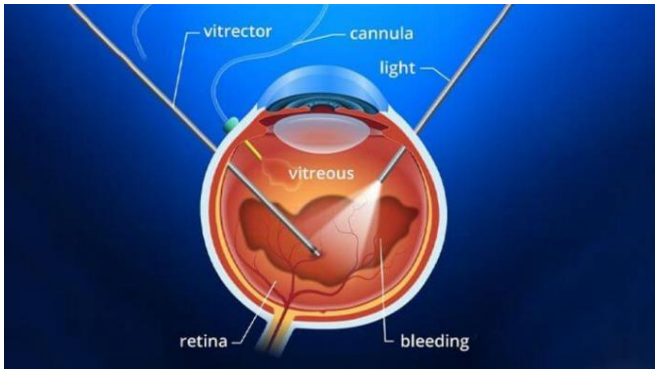
- The vitreous gel removed to clear haemorrhage and relieved vitreoretinal traction.

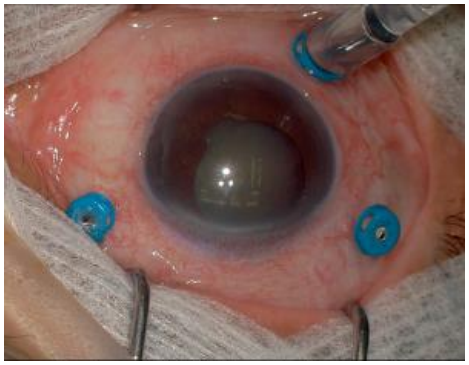
❖ Indications:

- Non-clearing vitreous hemorrhage
- Tractional retinal detachment involving the macula
- Combined tractional and rhegmatogenous retinal detachment
- Severe fibrovascular proliferation
- Vitreomacular traction with diabetic macular odema

❖ Advantages:

- Clears vitreous haemorrhages
- Relieves traction
- Improves retinal anatomy
- May improve vision





6. Combination therapy

In many patients, combined treatment methods are used

- ❖ Examples:
  - Anti-VEGF + PRP
  - Anti VEGF + Focal laser
  - Anti VEGF + Intravitreal steroid
- ❖ Benefits:
  - Better control of neovascularization
  - Reduced recurrence
  - Improved macular edema control

References

- Kanski's Clinical Ophthalmology
- American Academy of Ophthalmology
- ABC of Ophthalmology
- Retina Image bank - https://share.google/q6n35ccUYiNzdz7yO
- https://share.google/PJJOzDcxQVc4l7ebn
- https://eyewiki.org/Main_Page
- https://share.google/IDJYVMXu6FxypPRke
- https://share.google/qfk8Hcg21EMjvjeaC