Diabetic Retinopathy

Pathogenesis:

Diabetic retinopathy (DR) is a microangiopathy primarily affecting the arterioles, capillaries and post-capillary venules, although large vessels may also be involved.

Epidemiology: Diabetic retinopathy is one of the main causes of acquired blindness in the industrialized countries. Approximately 90% of all diabetic patients have retinopathy after twenty years.

Pathogenesis and individual stages of diabetic retinopathy:

- Diabetes mellitus can lead to changes in almost every ocular tissue.
- These include symptoms of keratoconjunctivitis sicca, xanthelasma, mycotic orbital infections, transitory refractory changes, cataract, glaucoma, neuropathy of the optic nerve, oculomotor palsy.
- However, *90% of all visual impairments* in diabetic patients are caused by diabetic retinopathy.
- The most common international nomenclature used to describe the various changes in diabetic retinopathy (Table 12.**1**) is based on the classification of the Diabetic Retinopathy Study. A distinction is made between nonproliferative stages (1. mild, 2. moderate, 3. severe; Fig. 12.**14**) and proliferative stages (1. non-high-risk 2. high-risk; Fig. 12.**15–**12.**17**)

Table 12.**1** Changes in diabetic retinopathy

Stage of retinopathy	Retinal changes
Nonproliferative diabetic retinopathy	❖ Microaneurysms. ❖ Intraretinal hemorrhages ❖ Lipid deposits in the retina (hard exudates) ❖ Retinal edema ❖ Venous beading ❖ Excessive hemorrhages ❖ Cotton-wool spots (nerve fiber infarctions with soft exudates) ❖ Intraretinal microvascular anomalies
Proliferative diabetic retinopathy	❖ Preretinal neovascularization ❖ Vitreous hemorrhage ❖ Tractional retinal detachment (due to traction of vitreous scarring) ❖ Rubeosis iridis (neovascularization of the iris that can occlude the angle of the anterior chamber; this entails the risk of acute secondary angle closure glaucoma)

Moderate nonproliferative diabetic retinopathy.

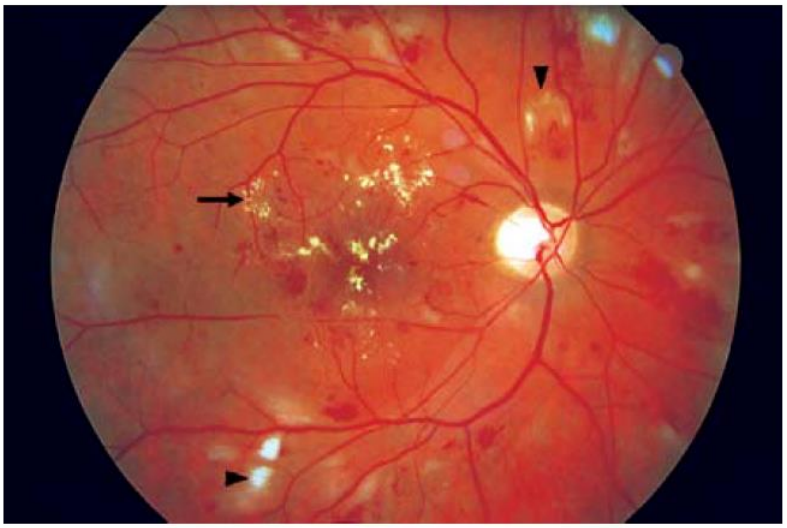


Fig. 12.**14** Microaneurysms, intraretinal hemorrhages, hard exudates (arrow), and cotton-wool spots (arrowheads).

Proliferative diabetic retinopathy.

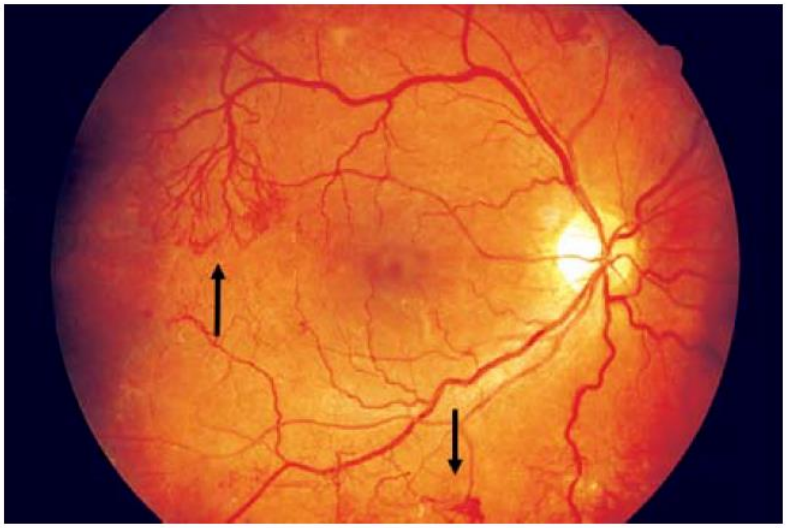
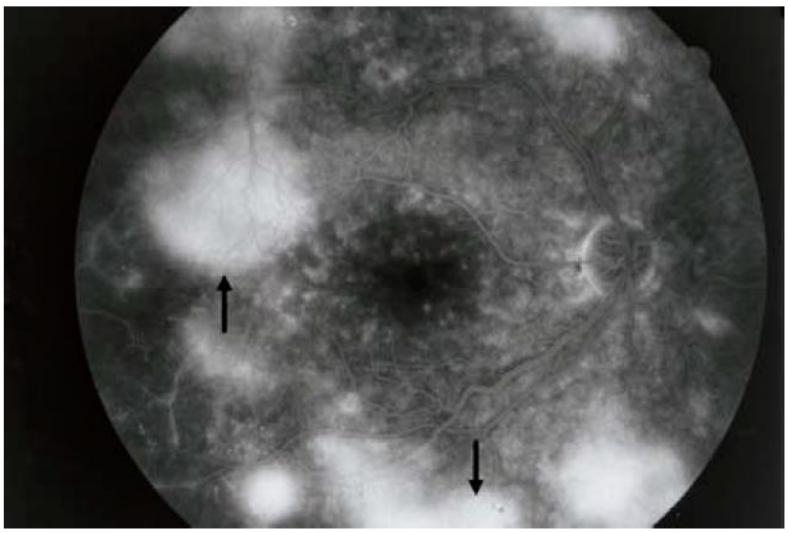


Fig. 12.**15** **a** Preretinal neovascularization (arrows) is a typical sign.



b Corresponding angiographic image. Fluorescein dye leakage is seen in the neovascularized area (arrows).

Risk factors

1. Duration of DM.
2. Poor metabolic control.
3. Pregnancy.
4. Hypertension.
5. Hyperlipideamia.
6. Nephropathy.
7. Obesity.
8. Smoking.

Symptoms:

- Diabetic retinopathy remains asymptomatic for a long time.
- Only in the late stages with macular involvement or vitreous hemorrhage will the patient notice visual impairment or suddenly go blind.

Diagnostic considerations:

- Diabetic retinopathy and its various stages (see Table 12.**1**) are diagnosed by stereoscopic examination of the fundus with the pupil dilated.
- Ophthalmoscopy and evaluation of stereoscopic fundus photographs represent the gold standard.
- Fluorescein angiography is used to determine if laser treatment is indicated.
- The presence of rubeosis iridis is confirmed or excluded in slit-lamp examination with a mobile pupil, i.e., without the use of amydriatic, and by gonioscopy of the angle of the anterior chamber.

High-risk proliferative diabetic retinopathy.

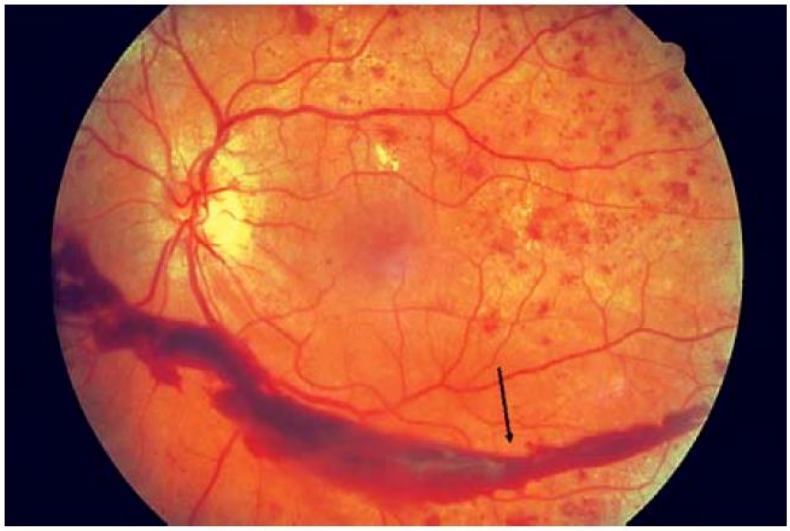


Fig. 12.**16** The clearly visible vitreous hemorrhage seen here (arrow) is a typical sign of this stage of diabetic retinopathy. The patient will only notice deterioration of vision in this later stage.

Differential diagnosis:

- A differential diagnosis must exclude other vascular retinal diseases, primarily hypertonic changes of the fundus (this is done by excluding the underlying disorder).

The **main pathology** in DR is: either ***microvascular occlusion.***
Or ***microvascular leakage.***

Microvascular occlusion occurs due to:

1- Thickening of the blood vessels basement membrane.
2- Damage and proliferation of the endothelial cells.
3- Increased RBC formation.
4- Increased platelet stickiness and aggregation.

The consequences of microvascular occlusion:

The occlusion of blood vessels leads to retinal ischemia and hypoxia. Hypoxic retinal tissue elaborate vasoformative substances "Growth factors" in an attempt to revascularize hypoxic retinal tissue by new blood vessels formation "**Neovascularization**", formed at optic disc "**NVD** (=**N**eo**V**ascularization of the **D**isc)", or elsewhere in the retina "**NVE** (=**N**eo**V**ascularization **E**lsewhere in retina)", and occasionally on the iris "**Rubeosis Iridis**".

Microvascular leakage occurs due to:

1- Breakdown of the inner BRB leads to leakage of plasma constituents into the retina.
2- Physical weakening of the capillary walls results in localized saccular outpouchings of the vessel wall termed "**Microaneurysms**" which may leak.

The consequences of *leakage* and *increased vascular permeability* include the development of intraretinal haemorrahges and oedema.

Clinically DR may be:

1- Background DR.
2- Pre-proliferative DR.
3- Proliferative DR.
4- Advanced diabetic eye disease (ADED).
5- Maculopathy, which associates **(1)**, **(2)**,**(3)** and even **(4)**.

1- Background DR:

Fundoscopy shows: **a- Microaneurysms** (saccular dilatations)**.**
b- Exudation (leakage of lipoprotein)**.**
c- Retinal oedema (due to leakage of fluid)**.**
d- Intaretinal Haemorrhages: Dot-blot haemorrhage or flame-shaped haemorrhage at level of nerve fiber layer**.** Sometimes it is difficult to differentiate intraretinal haemorrhages from microaneurysm, however, can be differentiated by fluorescein angiography, as aneurysms will leak dye.

Management:

It requires **NO** treatment, but should be reviewed every **6** months. In addition, patients need to control of diabetes and associating factors as hypertension, anemia and renal failure.

2- Pre-proliferative DR:

Fundoscopy shows, in addition to all features of background DR, the following:

a- Cotton wool spots which represent focal infarction of retinal nerve fiber layer due to occlusion of pre-capillary arterioles. Interruptions of axoplasmic transport with subsequent build-up of transported material within the axis (axoplasmic stasis) are responsible for the white appearance of the lesions.

b- Intra Retinal Microvascular Abnormalities (IRMA), which represent shunts that run from retinal arterioles to venules, bypassing the capillary bed.

Management:

Should be watched closely every **3** months because of the risk of PDR (Proliferative Diabetic Retinopathy) is high. Laser photocoagulation is usually not needed ***unless***:

a- Regular follow-up is not possible.

b- Vision in the fellow eye has been already lost due to PDR.

Also, patient need to control the blood sugar and associating factors.

3- Proliferative DR (PDR):

Affects 5-10% of the diabetic population, **type 1 diabetics** are at particular risk. By fundoscopy, neovascularization is the hallmark of PDR, either at disc (NVD) or elsewhere (NVE). Pre-retinal haemorrhage or intravitreal haemorrhage due to sudden rupture (either spontaneous or associating valsalva manoeuvre) of the walls of these abnormally fragile blood vessels (NVD or NVE) and the patient complains of sudden drop of vision. Finally, there will be organization of blood into fibrous tissue causing tractional RD that may end with ADED.

Management:

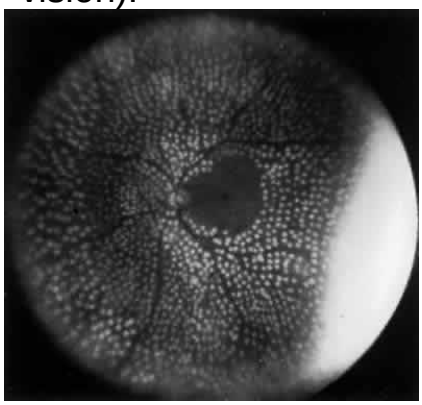
Pan-Retinal Photocoagulation (PRP), it is a destructive procedure, where normal retinal tissue around the temporal arcades (temporal blood vessels) is photocoagulated and destructed in order to decrease retinal ischaemia by decreasing O_2 demand. Then the neovascularization resolves spontaneously (no hypoxia → no growth factors). Now a day, new drugs are used in addition with PRP e.g. Ranibizumab (Lucentis) which are acting as **anti-vascular endothelial growth factor (anti VEGF)** to regress these neovascularizton. These drugs injected directly inside the vitreous under local anesthesia through the area of pars plana.

If pre-retinal or intravitreal hemorrhage occur, it is impossible to do PRP and only anti VEGF can be given until this blood resolve spontaneously or remove by vitrectomy.

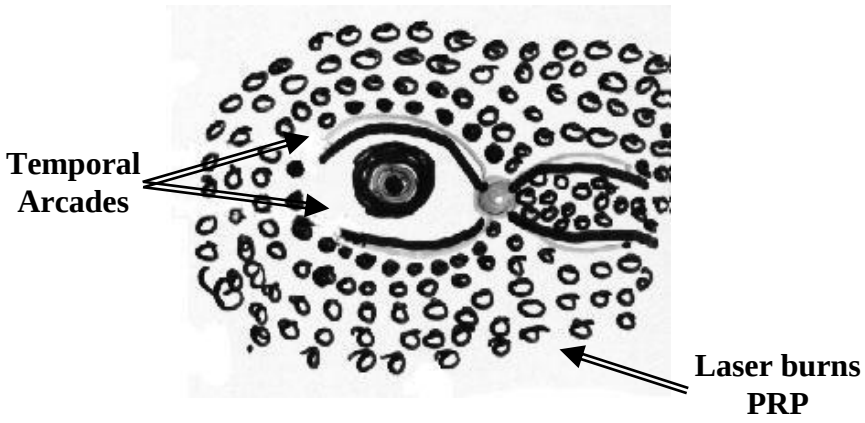
Side effects of PRP:

a- Constriction of visual field (loss of peripheral visual field).

b- Nyctalopia (night vision).



Panretinal Photocoagulation



4- Maculopathy (macular DR):

Is might be associated with: **a-** Background DR.
b- Pre-proliferative DR.
c- Proliferative DR.

It is the involvement of the fovea by oedema and exudates (leakage) or ischaemia (occlusion). Diabetic maculopathy is the most common cause of visual impairment in diabetic patients particularly those with **type 2 diabetes**.

Management:

Fluorescein angiography by injection of IV fluorescein with fundal photograph and OCT should be done to differentiate between leakage type (edematous or exudative maculopathy) and ischaemic type (ischaemic maculopathy) and to find the site of leakage in first type.

For exudative and edematous maculopathy, the treatment is direct (focal laser photocoagulation) to occlude the site of leakage. Also, intravitreal triamcinolone and anti VEGF having a role in treatment of maculopathy especially if it is sever and diffuse, with or without focal laser treatment.

For ischaemic maculopathy, no treatment available. If laser photocoagulation is done for such cases, it induce more ischaemia and more deterioration of visual acuity (laser is contraindicated in ischaemic maculopathy).

5- Advanced diabetic eye disease (ADED):

Serious vision-threatening complication of diabetic retinopathy occurs in patients who have not had laser therapy or in whom laser photocoagulation has been unsuccessful or inadequate.

Fundoscopy shows:

a- Hemorrhage. (Pre-retinal or intravitreal).

b- Tractional RD: due to fibrovascular membranes formation or fibrous tissue formation due to organization of pre-retinal or intravitreal hemorrhage.

Management:

Vitrectomy **+**Anti VEGF**+** Endolaser (PRP).

*** Endolaser:** done in the theatre by applying the laser through a fiberoptic probe in the eye, instead of using slit-lamp biomicroscope.

Prophylaxis:

- Failure to perform regular ophthalmologic screening exposes patients to the risk of blindness.
- Therefore, all type II diabetics should undergo ophthalmologic examination upon diagnosis of the disorder, and type I diabetics should undergo ophthalmologic examination within five years of the diagnosis.
- Thereafter, diabetic patients should undergo ophthalmologic examination once a year, or more often if diabetic retinopathy is present.
- Pregnant patients should be examined once every trimester.

Clinical course and prognosis:

- Optimum control of blood glucose can prevent or delay retinopathy.
- However, diabetic retinopathy can occur despite optimum therapy.
- Rubeosis iridis (neovascularization in the iris) in proliferative diabetic retinopathy lead to loss of the eye as rubeosis iridis is a relentless and irreversible process.
- The risk of blindness due to diabetic retinopathy can be reduced by optimum control of blood glucose, regular ophthalmologic examination, and timely therapy, but it cannot be completely eliminated.

Muqdad fuad

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

إِنَّمَا إِلَهُكُمُ اللَّهُ الَّذِي لَا إِلَهَ إِلَّا هُوَ وَسِعَ كُلَّ شَيْءٍ عِلْمًا (٩٨) كَذَلِكَ نَقُصُّ عَلَيْكَ مِنْ أَنْبَاءِ مَا قَدْ سَبَقَ وَقَدْ آتَيْنَاكَ مِنْ لَدُنَّا ذِكْرًا (٩٩) مَنْ أَعْرَضَ عَنْهُ فَإِنَّهُ يَحْمِلُ يَوْمَ الْقِيَامَةِ وِزْرًا (١٠٠) خَالِدِينَ فِيهِ وَسَاءَ لَهُمْ يَوْمَ الْقِيَامَةِ حِمْلًا (١٠١) يَوْمَ يُنْفَخُ فِي الصُّورِ وَنَحْشُرُ الْمُجْرِمِينَ يَوْمَئِذٍ زُرْقًا (١٠٢) يَتَخَافَتُونَ بَيْنَهُمْ إِنْ لَبِثْتُمْ إِلَّا عَشْرًا (١٠٣) نَحْنُ أَعْلَمُ بِمَا يَقُولُونَ إِذْ يَقُولُ أَمْثَلُهُمْ طَرِيقَةً إِنْ لَبِثْتُمْ إِلَّا يَوْمًا (١٠٤)

صدق الله العظيم