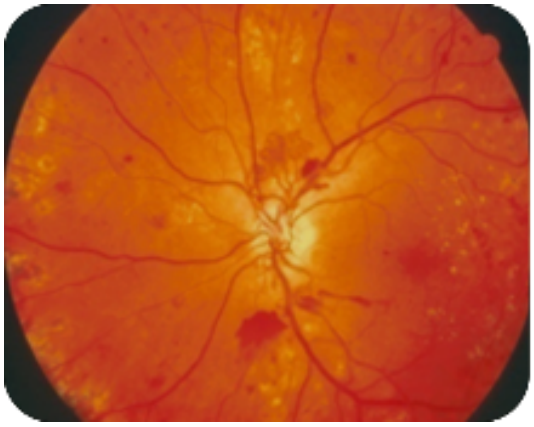
Diabetic retinopathy: Clinical features and classifications

Clinically, diabetic retinopathy (DR) is defined as the presence of typical retinal microvascular signs in an individual with diabetes mellitus. High blood glucose levels cause the endothelial cells lining the blood vessels to absorb more glucose than normal. This leads to excess formation of glycoproteins. The walls of the vessels grow thicker but weaker, leading to bleeding, leakage of water, proteins and lipids, resulting in swelling of the fovea, which is responsible for sharp central vision. Furthermore, blood flow is reduced leading to ischaemia. In response to this, new vessels grow to re-establish blood supply (revascularisation); however, these are fragile and may bleed causing vitreous haemorrhage and retinal detachment. Clinical assessment is thus essential to detect these signs, and in their absence assess the risk of progression to vision-threatening disease.

Non-proliferative diabetic retinopathy [1,2]

Non-proliferative or pre-proliferative diabetic retinopathy (NPDR) is an indication that the eye will soon be affected by vision-threatening disease. Consequently, recognition of NPDR with its retinal signs is highly important.[1]



Background retinopathy

The earliest stage of DR is background retinopathy This is characterized by thickening of the capillary wall, loss of pericytes, increased leukocyte adhesion to the vessel wall and alteration of blood flow. As the disease progresses the retinal vessels become increasingly damaged, leading to progressive endothelial cell loss. This in turn results in blocked retinal capillaries and chronic retinal ischaemic areas.

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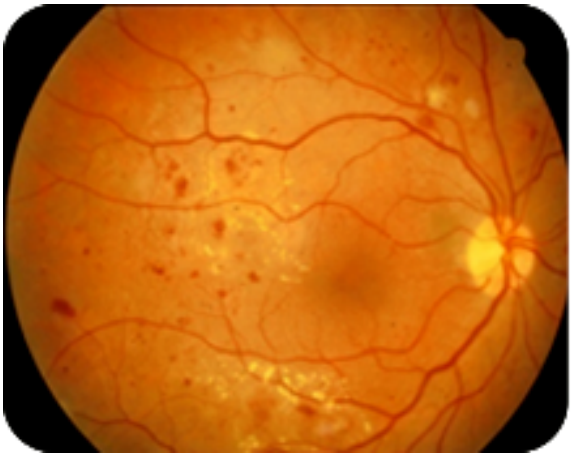
The clinical signs of NPDR include (1) multiple cotton wool spots (accumulations of axoplasmic debris within adjacent bundles of ganglion cell axons); (2) venous beading and/or looping; (3) microaneurysms (deep round and blot haemorrhages); (4) hard exudates (lipid deposits); and (5) intraretinal microvascular abnormalities (dilated pre-existing capillaries).



Pre-proliferative retinopathy

According to the grading system suggested by the American Academy of Ophthalmology (AAO) and based on the Early Treatment of Diabetic Retinopathy Study (ETDRS), mild NPDR is characterised by the presence of microaneurysms only, whereas moderate NPDR includes other microvascular lesions. These two stages are defined as grade R1 according to the UK National Screening Committee (NSC) guidelines. The AAO defines *severe NPDR* as the presence of more than 20 intraretinal haemorrhages in four quadrants or venous beading in two or more quadrants, or intraretinal microvascular abnormalities in one or more quadrant, but with no development of new vessels. This is the equivalent of stage R2 according to the UK system.

The NSC grading system was developed specifically for screening purposes with a view to early detection and treatment of DR. The AAO grading based on ETDRS using seven-field stereoscopic retinal photograph with levels 10 to 85 is appropriate for the US health system where patients with DR are examined by ophthalmologists, but was considered complicated for routine clinical use and not adapted to screening using only two fields in the UK. Additionally, the AAO definitions, in particular of maculopathy, were not adapted to a computerized system.

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UK national grading system

Retinopathy (R)

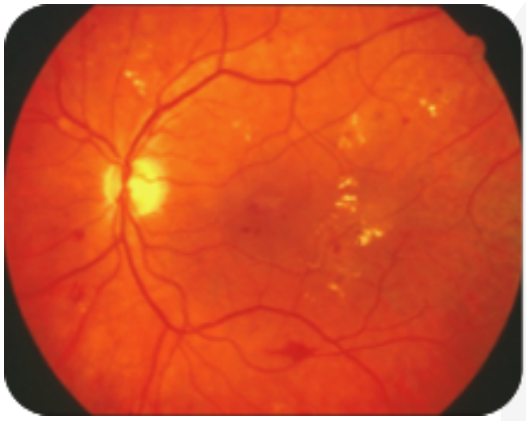
Level	Description	Action
RO	No retinopathy	Annual rescreen
R1	Haemorrhage and/or microaneurysms only	Annual rescreen
R2	Venous abnormality; multiple deep, round haemorrhages	Refer to Hospital Eye Service
R3	Proliferative	Urgent referral

Maculopathy (M)

Level	Description	Action
MO	No maculopathy	Annual rescreen
M1	Exudate within 1 disc diameter (DD) Circinate within 2DD Haemorrhage and/or microaneurysm within 1 DD+VA 6/12 or worse	Refer to Hospital Eye Service

Diabetic retinopathy: Clinical features and classifications

Proliferative diabetic retinopathy (PDR) [1,2]



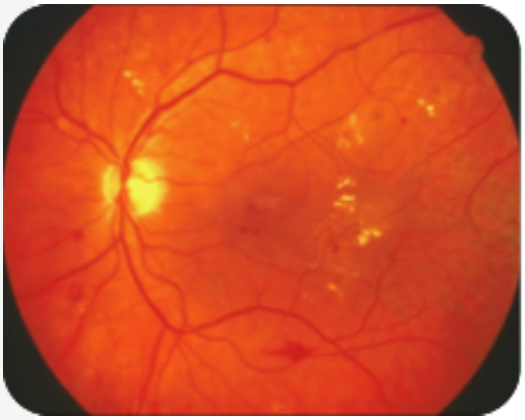
Proliferative DR

In order to counteract ischaemia, new blood vessels grow in the vitreo-retinal interface between the vitreous gel and retina with no support from surrounding structures . As a result they are fragile and can rupture, causing pre-retinal and vitreous haemorrhage. This neovascularisation in the optic disc (NVD) or elsewhere (NVE), i.e. on the surface of the retina or on the iris, indicates a critical change in the progression from NPDR to PDR (UK grade R3). High-risk characteristics are mild NVD with vitreous haemorrhage, moderate-to-severe NVD with or without vitreous haemorrhage; and moderate NVE with vitreous haemorrhage.[3]

Diabetic Macular Oedema (DMO) [1,2]

Diabetic macular oedema (DMO) is an important sign that is assessed separately from the stages of retinopathy because it can run an independent course. The US system defines this as retinal thickening within 500 μm from the centre of the macula; hard exudates within 500 μm from the centre of the macula with adjacent retinal thickening; and retinal thickening of more than one optic disc area within one optic disc diameter from centre of macula.[1]

The UK NSC has recommended that to define maculopathy, the distance of the lesion from the fovea is critical, and considers that any exudates within 1 disc diameter (DD) of the centre of the fovea is significant. This takes the best surrogate markers from a two-dimensional picture to predict a three-dimensional phenomenon.[2]



Macular oedema and proliferative DR

Diabetic retinopathy: Clinical features and classifications

Currently it is recommended that diabetic patients with no DR should be screened once every 1 to 2 years since the risk of progression to vision-threatening retinopathy is low, while patients with mild NPDR (R0–R1) should be screened annually.[1] However, there is good evidence to suggest that patients with no DR at their first screen could probably be screened every two years.[3] Once moderate NPDR (R2) is reached, patients are at a higher risk of developing PDR (12–26% within 1 year and 30–48% within 3 years) and should be screened on a six-monthly basis. Patients with PDR should be referred urgently to the eye clinic and appropriate treatment administered. [1,2]

References

1. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet* 2010;376:124-36.

2. Dodson PM (ed.) *Diabetic Retinopathy: Screening to Treatment.* Oxford: Oxford University Press, 2008.

3. Jones CD, Greenwood RH, Misra A, Bachmann MO. Incidence and progression of diabetic retinopathy during 17 years of a population-based screening program in England. *Diabetes Care* 2012;35:592-6.