CPD Module 7

Diabetic retinopathy: Fundamentals for primary care

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Diabetic retinopathy is a leading cause of visual impairment in the Western world. Its pathophysiology involves a complex interrelated sequence of events giving rise to clinical signs that can predict the risk of visual loss. Risk factors for the development and progression of diabetic retinopathy are clear and guidelines for their management have been made. With good management of the underlying diabetes, regular screening and optimal treatment it is possible to reduce the risk of visual impairment for people with diabetes.

Learning objectives

After reading this article, the participant should be able to:

1. Describe the basic pathophysiology, epidemiology and classification of diabetic retinopathy (DR).
2. Explain the purpose and practice of systematic screening for DR.
3. Discuss the relevance of various risk factors for the development of DR.
4. Outline the investigations and treatment modalities available for people with sight-threatening DR.

Key words
- Diabetic retinopathy
- Maculopathy
- Microvascular complications
- Screening

Author details can be found at the end of the article.

Diabetic retinopathy remains one of the leading causes of visual impairment, particularly in people of working age, in the industrialised world. In 2009 the World Health Organization (WHO) estimated that there were 314 million visually impaired people in the world, of whom 45 million were blind. Globally, about 85% of all visual impairment and 75% of blindness could be prevented or cured (WHO, 2009).

In 1989 the WHO and the International Diabetes Federation (WHO and IDF, 1989) developed "The St. Vincent Declaration" as a benchmark for the planning of future delivery of diabetes care. Specific targets were included for the prevention of costly complications, including "a reduction of new cases of blindness by 1/3 in the 5 years after 1990".

In November 2005 a European conference took place in Liverpool that reviewed progress since the publication of the St. Vincent target and developed a new declaration, "The Liverpool Declaration" (Screening for Diabetic Retinopathy in Europe, 2006). The Liverpool Declaration stated that European countries should reduce the risk of visual impairment due to diabetic retinopathy by 2010 by:

- Systematic programmes of screening reaching at least 80% of the population with diabetes.
- Using trained professionals and personnel.
- Universal access to laser therapy.

The impact of the complexity of living with diabetes on the individual is vitally important and yet often overlooked by healthcare professionals who, for the best of reasons, tend to concentrate on the objective measures of control. People with diabetes with visual impairment may find it difficult to exercise or may be afraid of the effect that aerobic exercise may have on their eye condition. They cannot follow an appropriate diet if they are not able to get to the shops, to read the labels on food items or see well enough to cook. And if they cannot see they may not be able to draw up

Supported by a grant from MSD Diabetes. These modules were conceived and are delivered by the Primary Care Diabetes Society in association with *Diabetes & Primary Care*. MSD had no input into the modules and is not responsible for their content.

their insulin or self-monitor their blood glucose levels. Loss of independence and reliance on others causes some individuals to avoid activities that they had previously enjoyed.

It is essential for practitioners to understand the underlying pathophysiology of diabetic retinopathy and how it relates to vision and potential treatments. It is also key to consider the effect this can have on people's lives, their fears and their expectations. *Box 1* outlines the fundamental pathophysiology along with a short glossary of terms, and *Figure 1* gives a schematic diagram of the eye.

Classification

Diabetic retinopathy is the collective term for the characteristic features seen in the retina. For the purposes of classification the changes are subdivided into maculopathy (diabetes-related damage to the macula) and retinopathy (diabetes-related damage to the retina).

The macula is the area of retina temporal to the optic disc and contained within the major vascular arcades. At the centre of the macula is the fovea, which consists of cones and provides us with clear vision at distance and for reading and colour vision. Clinically significant macular oedema (CSMO; Early Treatment Diabetic Retinopathy Study [ETDRS] Research Group, 1991a) causes a reduction in vision. The peripheral retina is made up of rods, which allow discrimination of black, white and shades of grey, and provides us with the ability to see in the dark and to see around us (our field of vision) (see *Box 1*).

Many classification systems have been devised over the years. The recognised ultimate system was developed for use in seminal research studies, primarily conducted in the US, from which our knowledge of diabetic eye changes has derived. Based on 7-field stereo photography, the Modified Airlie House Classification was instrumental for the documentation of retinal signs in the ETDRS (ETDRS Research Group, 1991b). This is still used today in research and intervention studies all over the world. It is, however, extremely complicated and not suited to routine clinical use. As the "gold standard",

Box 1. Pathophysiology of diabetic retinopathy (*continued overleaf*).

Retinal blood circulation is unique in a number of ways. In the healthy retina, capillary endothelial cells line the lumen and communicate directly with the pericytes and associated smooth muscle cells across the basement membrane. Endothelial cells actively regulate blood flow by elaboration of vasodilators and vasoconstrictors, and also generate pro- and anticoagulant factors. Pericytes respond to endothelial vasoactive agents to change lumen size. The pericyte secretes both transforming growth factor-β (TGF-β) and vascular endothelial growth factor (VEGF). TGF-β acts on the endothelial cell to inhibit cell proliferation.

Glucose toxicity leads to cell damage and death. Retinal tissues normally have a high metabolic turnover and a high oxygen requirement. Hyperglycaemia increases the oxidative load, leading to a cascade of complex, compensatory and interrelated mechanisms, including the non-enzymatic glycation of proteins (Maillard reaction), conversion of glucose to sorbitol by aldose reductase in the polyol pathway, reduced antioxidant reserve leading to free-radical activity, changes in blood cells (red cells, white cells and platelets) and the release of a myriad of growth factors.

The first pathological changes are basement membrane thickening and pericyte cell loss. Thickening of the basement membrane leads to loss of communication between the endothelial cell and the pericyte. Pericyte cell loss results in vessel dilatation, loss of autoregulation and, consequently, changes in blood flow. Endothelial cell damage (and the effect of VEGF) leads to loss of the tight junctions that maintain the integrity of the blood–retinal barrier.

The cause of early retinopathy, and of maculopathy, is leakage from capillaries. The earliest detectable clinical sign is the microaneurysm (a focal dilatation of retinal capillaries). Microaneurysms leak. Additionally, increased capillary permeability allows osmotically active molecules (including lipids, which are clinically referred to as "exudates") to enter the retina. In the macular region this leakage leads to the development of clinically significant macular oedema (CSMO), a major cause of reduced vision. Damage to the retinal pigment epithelium (RPE) may also contribute to the development of CSMO by failing to remove the tissue fluid accumulating in the retina from the leaking capillaries (Weinberger et al, 1995). Newer investigative techniques (particularly optical coherence tomography) have shown that the vitreous face is often firmly attached to the retina locally at the fovea. Traction here can cause CSMO that is resistant to laser treatment.

Leakage of red cells into the tightly packed inner layers of the retina is seen as "dot and blot" haemorrhages. Although more common in hypertension, haemorrhages in the nerve cell layer ("flame-shaped" haemorrhages) may also be present.

A procoagulant state is induced in diabetes correlating with an increase in von Willibrand factor, growth hormone and platelet-derived thromboxane A2, and leading to increased blood viscosity and microthrombus formation. There has also been much interest in the increase in leucocyte adhesion and the theory that the underlying pathology may be due to an inflammatory process (Joussen et al, 2004).

Microaneurysms are in a constant state of turnover. Some become totally occluded resulting in focal areas of capillary closure. This stimulates increased blood flow in, and dilatation of, adjacent capillaries, resulting in shear stress damage to the vessel wall, further dilatation and a vicious circle of increasing hyperperfusion and damage. It is important to remember that diabetic retinopathy is a dynamic process. Both hyperglycaemia and hypertension result in hyperperfusion of the retina, and release of angiogenic agents such as VEGF and angiotensin-II may exacerbate these effects.

Retinal signs of hypoxia are clinically referred to as "preproliferative retinopathy" (*Figure 2a*). "Cotton wool spots" are local areas of ischaemia caused by nerve fibre swelling. Venous changes include "beading", "loops" and "reduplication". Capillary fallout around the fovea results in ischaemic maculopathy and is untreatable.

Finally, increasing pericyte loss and basement membrane thickening lead to a reduction in the amount and effect of TGF-β, allowing endothelial cell proliferation. Activated endothelial cells dissolve their own basement **(*continued overleaf*)**

Box 1. Pathophysiology of diabetic retinopathy (*continued*).

membrane and proliferate as tubes of loosely connected endothelial cells under the instruction of various angiogenic growth factors.

There has been much interest in the role of growth factors. The factor receiving most attention is VEGF. Hyperglycaemia induces VEGF gene expression through a protein kinase C-dependent mechanism. VEGF is produced in endothelial cells, pericytes, smooth muscle cells and RPE cells. Its expression appears to be triggered by hypoxia, and VEGF production is implicated in both endothelial cell permeability and proliferation.

Areas of angiogenesis within the retina are referred to as intraretinal microvascular abnormalities and are classified as preproliferative changes (*Figure 2a*). When proliferating vessels breach the internal limiting membrane of the retina and grow into the potential space between the retina and the vitreous they are termed new vessels, and may occur in the peripheral retina or at the optic disc. New vessels use the vitreous face as a scaffold. Initially the new vessels are merely tubes of fenestrated endothelial cells and do not have a "coat". Consequently they leak and bleed and the resultant low resistance leads to high flow in the neovascular complex at the expense of remaining retinal vessels, promoting further ischaemia and angiogenesis.

Bleeding from new vessels between the retina and the vitreous face produces pre-retinal (classically boat-shaped) haemorrhages, and bleeding into the vitreous gel causes a sudden shower of floaters or complete blurring of vision and is termed "vitreous haemorrhage".

Fibroblasts finally become incorporated into the new vessel complexes, producing fibrovascular proliferation. Contraction of fibrous tissue may produce a traction detachment of the retina from the underlying nourishing choroid. Traction retinal detachment of the macula, if not treated surgically urgently, causes an irreversible loss of vision.

Glossary

Fovea = The centre of the macula. The part of the eye that provides fine discrimination and colour vision. Approximates to the area within 1 disc diameter radius of the centre of the macula.

Macula = Area in the retina, 3–5 mm in diameter, temporal to the optic disc (roughly the area between the major vessels).

Microaneurysm = Focal dilatation of retinal capillaries.

Optic disc = The optic nerve head. Where all the nerve fibres in the retina meet and pass to the brain. On visual field testing this is the blind spot.

Pericyte = Cell associated with the outer walls of small blood vessels.

all other grading classifications should map to the ETDRS classification.

In the UK each devolved nation has set up a systematic national screening programme and developed similar grading classifications based on the ETDRS system. As an example, the classification for England and Wales is given in *Table 1* (English National Screening Programme for Diabetic Retinopathy [ENSPDR], 2006a). This is based on retinal photographs and is a reporting, rather than a clinical, classification.

The Royal College of Ophthalmologists (2005) also provides guidance, and for clinical purposes the features seen in preproliferative retinopathy are divided into those with a low risk of developing new vessels, and those with a high risk (*Table 2*). In the guidance, maculopathy is divided into:

- Focal: well confined areas of leakage (often from microaneurysms) with hard exudates in complete or incomplete "circinate" rings (*Figure 2b*).
- Diffuse: generalised oedema often without exudates and due to capillary leakage ± retinal pigment epithelium pump failure.
- Ischaemic: often relatively normal appearance or minimal oedema and poor vision. Fundus fluorescein angiography reveals capillary fallout.
- Tractional: local attachment of the vitreous face to the fovea.
- Mixed.

Many cases of maculopathy fall into the mixed category but it is useful for treatment purposes to classify them into the category with the most predominant features.

A simplified version of the ETDRS classification aimed at countries without systematic screening programmes has also been developed by the American Academy of Ophthalmology Guidelines Committee (Wilkinson et al, 2003).

Prevalence and incidence

A wide range of prevalence estimates have been reported, dependent on the population studied. The prevalence of retinopathy at diagnosis of type 1 diabetes is low, between 0% and 3% (Dorf et al, 1976; Frank et al, 1980; Klein et al, 1997; Wan Nazaimoon et al, 1999), while a higher proportion of those with newly diagnosed type 2 diabetes have evidence of diabetic retinopathy (6.7–30.2%) (Wirta et al, 1995; Davis et al, 1997; Aiello et al, 1998; Kohner et al, 1998), reflecting the frequent delay in diagnosis of diabetes in this group. Lower levels in later studies suggest that improved control of diabetes has reduced the prevalence of retinopathy.

The Liverpool Diabetes Eye Study (LDES; Younis et al, 2002) specifically investigated the prevalence of eye disease in people entering a

systematic screening programme. In type 1 diabetes the prevalence of any, proliferative (PDR) and sight-threatening diabetic retinopathy (STDR) was 45.7%, 3.7% and 16.4%, respectively. The corresponding results in people with type 2 diabetes were 25.3%, 0.5% and 6.0%. STDR was significantly correlated with duration in both type 1 and 2 diabetes and with insulin use in type 2 diabetes.

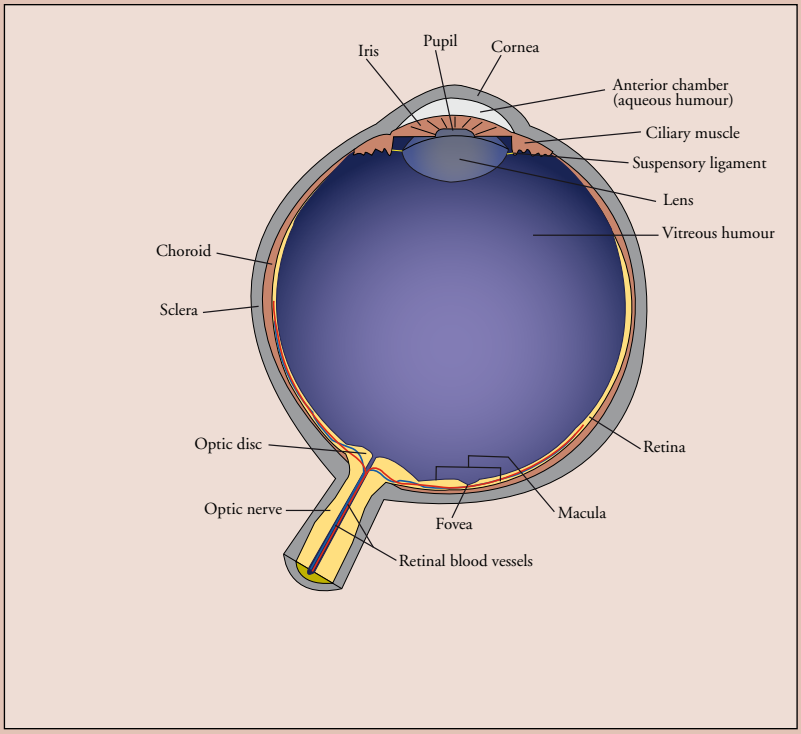
A recent study in the UK has reported a higher prevalence of STDR in people of south Asian descent than in white European people (45% vs. 37%), suggesting that ethnicity may also be a contributing factor in diabetic retinopathy (Raymond et al, 2009).

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) has provided the most comprehensive data on the incidence of diabetic retinopathy over the past 25 years. In 1989 the group reported the 4-year incidence of any retinopathy in people with type 1 diabetes at 59% and people with type 2 at 34% (insulin-requiring, 47.4%) (Klein et al, 1989). Progression to PDR was 10% over 4 years in people with type 1 diabetes, and 7% and 2% in people with type 2 diabetes treated with or without insulin, respectively.

In type 1 diabetes, insulin-treated type 2 diabetes and non-insulin-treated type 2 diabetes, the 4-year incidence of CSMO was 4%, 5% and 1%, respectively, and the incidence of legal blindness was 1.5%, 3% and 2.5%, respectively (Klein et al, 1990). The 10-year incidence of any retinopathy, CSMO or visual loss was 90%, 20% and 9% in type 1 diabetes, 79%, 25% and 33% in insulin-treated type 2 diabetes and 67%, 14% and 21% in non-insulin-treated type 2 diabetes, respectively (Klein et al, 1996). More recently, 25-year incidences have been published that show a recent reduction in incidence in the study population, which may well reflect a survival bias (Klein et al, 2008; 2009).

Data on 10-year incidence from the LDES in people with type 2 diabetes enrolled in a systematic screening programme suggested that a 3-yearly screening interval could be safely adopted for those with no retinopathy at baseline, but yearly or more frequent screening was needed for individuals with higher grades of retinopathy or insulin use (Younis et al, 2003a). Similar results were shown for type 1 diabetes (Younis et al, 2003b).

Figure 1. Schematic diagram of the human eye.



Risk factors

Risk factors for the development and progression of diabetic retinopathy are modifiable and unmodifiable. The most important modifiable factors are glycaemic and blood pressure control.

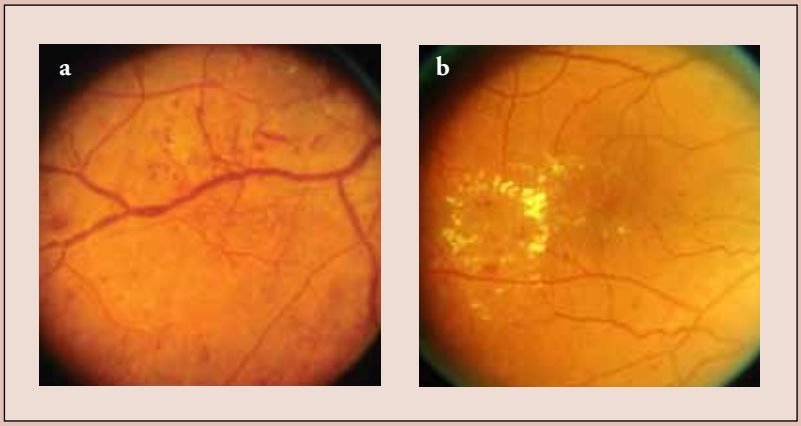


Figure 2. (a) Preproliferative retinopathy (intraretinal microvascular abnormalities and beading) and (b) Circinate maculopathy. Copyright © 2001 Fundus Photograph Reading Center, Department of Ophthalmology and Visual Sciences, University of Wisconsin.

Both the DCCT (Diabetes Control and Complications Trial; DCCT Research Group, 1993; 1995a; b; 2002) in type 1 diabetes and the UKPDS (United Kingdom Prospective Diabetes Study; UKPDS Group, 1998) in type 2 diabetes have shown a clear relationship between the duration of diabetes and glycaemic control in the development of retinopathy.

In the DCCT (1993), intensive glycaemic control (mean HbA_{1c} level of 7.3% [56 mmol/mol] vs. 8% [64 mmol/mol] in the conventional group) conferred a 76% risk reduction in development of retinopathy in those without retinopathy at baseline, and a 47% reduction in progression to severe non-proliferative retinopathy or PDR for those with established retinopathy at baseline.

Table 1. The English National Screening Programme for Diabetic Retinopathy grading classification.

Retinopathy		
Level	*Grade*	*Features*
R 0	None	N/A
R 1	Background	• Microaneurysm(s), retinal haemorrhage(s) ± any exudate not within the definition of maculopathy.
R 2	Preproliferative	• Venous beading. • Venous loop or reduplication. • Intraretinal microvascular abnormality. • Multiple deep, round or blot haemorrhages. (Cotton wool spots not included, but if seen should promote a careful search for above features).
R 3	Proliferative	• New vessels on disc. • New vessels elsewhere. • Pre-retinal or vitreous haemorrhage. • Pre-retinal fibrosis ± tractional detachment.
Maculopathy		• Exudate within one disc diameter (DD) of the centre of the fovea. • Circinate or group of exudates within the macula. • Retinal thickening within 1 DD of the centre of the fovea (if stereo available). • Any microaneurysm or haemorrhage within 1 DD of the centre of the fovea only if associated with a best visual acuity of ≤6/12 (if no stereo).
Photocoagulation		• Evidence of focal/grid laser to macula. • Evidence of peripheral scatter laser.
Unclassifiable		• Unobtainable / ungradable.

From: English National Screening Programme for Diabetic Retinopathy (2006a)

In the UKPDS, tight control of blood pressure resulted in a 37% reduction in microvascular complications (UKPDS Group, 1998).

The UKPDS did not find any difference between the use of beta-blockers and angiotensin-converting enzyme (ACE) inhibitors. EUCLID (European Controlled Trial of Lisinopril in Insulin-dependent Diabetes; Chaturvedi et al, 1998) suggested that blockade of the renin-angiotensin system (using ACE inhibitors) might be superior to beta blockade. However, the study was not designed to specifically address this question and was consequently under-powered.

The selective effect of an angiotensin receptor blocker is theoretically superior to ACE inhibition. The DIRECT studies have suggested that candesartan can reduce the incidence of any retinopathy in people with type 1 diabetes and induce regression of retinopathy in people with type 2 diabetes, although the study just failed to reach statistical significance (Chaturvedi et al, 2008; Sjølie et al, 2008).

Both the WESDR and Hoorn (van Leiden et al, 2002) studies have shown a correlation between high blood cholesterol levels and risk of retinopathy in the diabetes population. A theoretical role for lipids in the development of retinopathy has been proposed and a clearing of retinal exudates has been observed in people on statins, but it is not yet clear whether this is merely an unloading effect or a therapeutic effect. The more recent FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) study did show a significant reduction in the need for laser treatment in people on fenofibrate (Keech et al, 2007). This effect appeared to be independent of a lipid-lowering effect and a PKC inhibition mechanism was proposed.

Anecdotally, practitioners can all recount individuals with immaculate metabolic control and aggressive retinopathy, and conversely individuals with many years of poor control and no retinopathy. There has to be a genetic explanation. It is not surprising that there have been extensive studies but, to date, no single

gene has been identified (Hanis and Hallman, 2006). The biological processes underlying the development of retinopathy are complex and interrelated. It would be foolish to suppose that there would not be similarly complex relationships between many genes with small interrelated effects and the environment.

One of the recommendations of the Liverpool Declaration was to promote joint working between ophthalmologists, diabetologists and primary care. In England a joint meeting was held in Liverpool in November 2007 (ENSPDR, 2007). Consensus guidelines for management of risk factors were developed and are given in *Table 3*. However, it should be recognised that targets should be individualised to the patient based on an assessment of relevant risks and benefits.

Screening

Screening for diabetic retinopathy meets the requirements set out in the World Health Organization document *Principles and Practice of Screening for Disease* (Wilson and Jungner, 1968).

Following the St Vincent Declaration and a joint workshop of the UK National Screening Programme and the Royal College of Ophthalmologists in October 1999, recommendations for the implementation of national screening programmes for diabetic retinopathy in the UK were made. The National Service Framework for diabetes, stated that "by 2006 (March), a minimum of 80% of people with diabetes are to be offered screening for the early detection (and treatment if needed) of diabetic retinopathy as part of a systematic programme that meets national standards, rising to 100% coverage of those at risk of retinopathy by end 2007" (Department of Health, 2003).

National programmes with this aim but slightly different operational procedures have now been implemented in all four devolved nations. All use digital photography as the method of choice as this is the only method that meets the Exeter targets for sensitivity (80%) and specificity (95%) (Taylor et al, 1998) and allows appropriate quality assurance. Screening, however, is a "sieve". No method currently achieves 100% sensitivity and specificity but screening reduces the risk of vision loss to an acceptable rate. For this reason quality assurance targets for the process have been set (ENSPDR, 2009a). Quality assurance is the safety net that underpins any screening programme. All programmes are measured against service objectives. An example of management of screen-positive cases is given in *Table 4*.

Currently, all people with diabetes aged 12 years and over are recalled for annual screening. The only exception to this is

Table 2. Guidelines for classification of diabetic retinopathy: Background, non- or preproliferative retinopathy.

Features with a low risk of developing new vessels:

- Mildly dilated veins.
- Microaneurysms.
- Dot haemorrhages.
- Exudates.
- Occasional cotton wool spots.

Features with a high risk of developing new vessels:

- Intraretinal microvascular abnormality.
- Venous beading and "omega" loops.
- Clusters of large "blot" or "blotch" haemorrhages.
- Multiple cotton wool spots.

From: Royal College of Ophthalmologists (2005)

Table 3. Recommendations for risk factor control in diabetic retinopathy.

Risk factor	Management
HbA_{1c} level	• Patient and physician to jointly agree target. • <6.5% (<48 mmol/mol) is the aspiration; however, <7.0% (<53 mmol/mol) or 8.0% (64 mmol/mol) may be acceptable. • Per cent reduction over a specified time is an alternative approach. • Watch carefully for worsening of diabetic retinopathy if drop in HbA_{1c} level ≥3.0% (≥33 mmol/mol).
Blood pressure (BP)	• If coexisting diabetic retinopathy, target BP=130/80 mmHg. • In presence of coexisting nephropathy aim for lower BP.
Lipids	• Total cholesterol <5.0 mmol/L (ideally <4.0 mmol/L). • LDL-cholesterol <3.0 mmol/L (ideally <2.0 mmol/L). • Triglycerides <2.3 mmol/L. • Commence statins in all patients >40 years or >19 years if coexisting retinopathy.

Adapted from: English National Screening Programme for Diabetic Retinopathy (2007)

Page points

1. People with diabetes and comorbidities attending an ophthalmologist may either be photographed separately (unless there is a reason why this is likely to be unsuccessful) or may be "screened" for diabetic retinopathy as part of their routine ophthalmic appointment.
2. People with diabetes who are currently in prison in the UK should be included in the screening programme of the PCT responsible for health care in that prison.
3. People attending for screening should bring all their current glasses and, particularly on sunny days, a pair of dark glasses for use until the drops wear off.

women with diabetes who are pregnant. Recommendations are that fundus examinations should be performed pre-pregnancy, at diagnosis of pregnancy, at the end of each trimester, and 9–12 months postnatally. Exclusions from screening include the following groups of people (ENSPDR, 2006b):

- A person with diabetes who has made his or her own informed choice that he or she no longer wishes to be invited for screening.
- A person with diabetes who does not have perception of light in either eye.
- A person with diabetes who is terminally ill.
- A person with diabetes who has a physical or mental disability preventing either screening or treatment.
- A person with diabetes who is currently under the care of an ophthalmologist for the treatment and follow-up of diabetic retinopathy, and then only for that period.

People with diabetes and comorbidities attending an ophthalmologist may either be photographed separately (unless there is a reason why this is likely to be unsuccessful) or may be "screened" for diabetic retinopathy as part of their routine ophthalmic appointment.

Confusion often arises with regard to housebound individuals. Screening programmes should provide local solutions to mobility issues, such as arranging direct referral to a slit-lamp biomicroscopy clinic. Those who are physically unable to comply with treatment for diabetic retinopathy (i.e. unable to attend an ophthalmic clinic) form part of the exclusion criteria.

People with diabetes who are currently in prison in the UK should be included in the screening programme of the PCT responsible for health care in that prison. These individuals pose particular problems around mobility of the population and confidentiality. Ideally prison populations should be screened 6-monthly to ensure adequate coverage.

Non-attendance for screening is a major issue. The factors affecting non-compliance are many and common in people with long-term conditions. Recommendations are that people should be given two opportunities to attend. Should they fail to keep these appointments the GP should be informed and advised that further appointments will not be routinely offered and the individual will be temporarily excluded from screening. Appointments will be offered in the next screening year.

People attending for screening should bring all their current glasses and, particularly on sunny days, a pair of dark glasses for use until the eye drops wear off. Usually only a short-acting eye drop is used to dilate the pupils. This wears off after 2–3 hours. Near vision is affected worse than reading vision, but people should be advised not to drive during this time. In the hospital eye service, and occasionally in screening, longer acting eye drops are needed, blurring vision for 6–12 hours.

All screening programmes are now expected to implement fail-safe mechanisms. Fail-safe is a back-up mechanism so that when something goes wrong in a system, processes are in place to identify what is going wrong and action follows to ensure that there is a safe outcome. Responsibilities for all stakeholders in national screening programmes have been identified. The principal responsibilities for primary care providers in England are given in *Table 5* (Garvican and O'Leary, 2008).

Table 4. Management after grading in the English National Screening Programme for Diabetic Retinopathy.

Retinopathy	
Level	*Action*
R 0	Annual screening.
R 1	Annual screening / inform diabetes carer.
R 2	Refer to HES.
R 3	Fast-track referral to HES.
Maculopathy	Refer to HES.
Photocoagulation	
New screen / unstable	Refer to HES.
Quiescent post-treatment	Annual screening.
Unclassifiable	Refer to dedicated slit-lamp biomicroscopy clinic.
Other lesions	Local arrangements – refer to HES or inform primary physician.

HES = hospital eye service.

From: English National Screening Programme for Diabetic Retinopathy (2009b)

An article from Sweden in 2007 demonstrated that a reduction of blindness due to diabetes can be achieved, but that it requires a combination of careful screening for diabetes, effective screening for diabetic retinopathy and good medical management (Olafsdottir et al, 2007).

The most important treatment for diabetic retinopathy is to control the underlying hyperglycaemia. As discussed earlier, good management of diabetes can prevent the development, and also slow the progression of, diabetic retinopathy. Primary care physicians and practice nurses play a key role in the regular measurement and treatment of modifiable risk factors according to targets in *Table 3*. They also need to ensure that people with diabetes attend regularly for screening.

Treatment

The conventional treatment for diabetic retinopathy is laser treatment to stabilise the changes in the retina. To be effective, this must be given at the optimal time. Laser treatment does not aim to restore vision that has been lost, but studies have shown that in imminent or early proliferative retinopathy, it will prevent severe sight loss in over 90% cases (Diabetic Retinopathy Study Research Group, 1981). In most cases it is possible to preserve reading and driving vision. Laser treatment for focal and diffuse maculopathy is not as successful as that for proliferative retinopathy, but still prevents serious sight loss in 60–70% of cases (ETDRS Research Group, 1985). Laser treatment is ineffective in ischaemic maculopathy.

Laser treatment is given at an outpatient clinic, and may involve a single visit or more than one visit before the eye changes are controlled. Treatment is usually only given to one eye at a time, and each session lasts between 15 and 30 minutes. Treatment for retinopathy, specifically, is to apply a large number of laser spots to peripheral retina. Most people notice a problem with night vision after this treatment but few notice a change in their field of vision.

In the UK, the Driving and Vehicle Licensing Agency (DVLA, 2009) has set standards of visual field function that are required for permission to hold a driver's license. In the UK, it is the individual's responsibility to inform the DVLA that he or she has had laser therapy for diabetic retinopathy. If this is not possible, then the individual's next of kin or GP should inform the DVLA of the person's visual status.

In treatment for maculopathy, gentle laser burns are applied close to the centre of the fovea. Much less laser is required than for retinopathy. Complications for this type of treatment are rare.

Worldwide, the search for newer, more effective or less destructive treatments continues. Anti-VEGF agents have been investigated as an

Table 5. Responsibilities for primary pare providers in the English National Screening Programme for Diabetic Retinopathy.

Principal responsibilities of PCT Screening Programme Leads

- Ensure that robust processes are in place to provide a strategic steer, performance management and clinical governance.
- Commission a retinal screening programme to national quality standards.
- Ensure that all GPs are taking part in retinal screening.
- Ensuring that GPs provide the retinal screening programme with updated practice registers.

Principal responsibilities of GPs

- Referring all their patients to a single screening programme.
- Maintaining an up-to-date practice register of people with diabetes.
- Ensuring that children with diabetes are referred to the screening programme when they reach the age of 12.
- Informing all their people with diabetes of the importance of regular retinal screening.
- Identifying exclusions to screening.
- Ensuring that a person who is considering opting out of the programme has received sufficient information to enable him or her to make an informed choice.
- Acting on non-responder notifications received from the screening programme.

Treatment of diabetic retinopathy

The effective management of diabetic retinopathy relies on a number of factors:

- The identification of people with the condition before the vision has been affected and at a stage when treatment is likely to be most effective.
- The timely investigation and treatment of people with retinopathy by an eye specialist (ophthalmologist).
- Good management of the underlying diabetes.
- Effective communication between screening programmes, GPs, diabetes specialists and ophthalmologists.

Adapted from: Garvican and O'Leary (2008)

Page points

1. A number of important studies have shown that injections of steroid drugs, such as triamcinolone, into the eye are effective at treating diabetic maculopathy. However, the effect also wears off after about 6 months, meaning that repeated injections are needed.
2. Injections directly into the eye also hold a small risk of the development of endophthalmitis (a serious infection inside the eye).
3. Patient information leaflets on screening, diabetic retinopathy and laser treatment can be found at: www.retinalscreening.nhs.uk.

alternative to conventional laser treatment. Oral PKC inhibitors have been studied and shown to have an effect in certain groups of people (Aiello et al, 2006), but research has also centred on the injection of anti-VEGF agents directly into the eye (Huang et al, 2009; Nguyen et al, 2009). Results are temporary, requiring repeated injections at regular intervals. While, spectacular results for both retinopathy and maculopathy have been obtained, the long-term effects of this treatment are, as yet, unknown.

Additionally, a number of important studies have shown that injections of steroid drugs, such as triamcinolone, into the eye are effective at treating diabetic maculopathy (Rudnisky et al, 2009). However, the effect also wears off after about 6 months, meaning that repeated injections are needed. An important side-effect of this treatment is the development of glaucoma. Injections directly into the eye also hold a small risk of the development of endophthalmitis (a serious infection inside the eye).

A final area of interest is the possibility of giving an injection into the eye to produce a chemical vitrectomy, particularly to remove traction on the central retina, without the need for surgery, and this is being actively researched.

Patient information leaflets on screening, diabetic retinopathy and laser treatment can be found at: www.retinalscreening.nhs.uk.

Conclusion

Diabetic retinopathy is one of the most feared complications of diabetes, but evidence clearly shows that the risk of visual impairment can be significantly reduced with good control of diabetes, regular screening and timely treatment.

Primary care practitioners play a key role in the regular measurement and treatment of modifiable risk factors for diabetic retinopathy, and in ensuring that people with diabetes attend regularly for screening. ■

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"Primary care practitioners play a key role in the regular measurement and treatment of modifiable risk factors for diabetic retinopathy, and in ensuring that people with diabetes attend regularly for screening."

CPD module

Online CPD activity

Visit www.diabetesandprimarycare.co.uk/cpd to record your answers and gain a certificate of participation

Participants should read the preceding article before answering the multiple choice questions below. There is ONE correct answer to each question. After submitting your answers online, you will be immediately notified of your score. A pass mark of 70% is required to obtain a certificate of successful participation; however, it is possible to take the test a maximum of three times. Before accessing your certificate, you will be given the opportunity to evaluate the activity and reflect on the module, stating how you will use what you have learned in practice.

1. It is important to screen for diabetic retinopathy (DR) for which one of the following combinations of reasons? 1. Sight-threatening retinopathy may have no visual symptoms; 2. Treatment for DR is most effective before vision is affected; 3. All people with DR require treatment; 4. People with DR and normal vision do not need treatment. Select ONE option only.

A. 1 and 4.
B. 1 and 2.
C. 2 and 3.
D. 3 and 4.
E. 2 and 4.

2. Which of the following combinations should be graded as preproliferative DR? 1. Cotton wool spots; 2. Microaneurysms; 3. Venous beading; 4. Macular exudates. Select ONE option only.

A. 1 and 4.
B. 2 and 3.
C. 2 and 4.
D. 1 and 2.
E. 1 and 3.

3. Which one of the following combinations is true about the effectiveness of digital imaging at detecting DR? 1. All people requiring referral will be detected; 2. All people not requiring referral will be detected; 3. Some people requiring referral will be missed; 4. Some people not requiring referral will be referred. Select ONE option only.

A. 3 and 4.
B. 1 and 2.
C. 1 and 4.
D. 2 and 3.
E. 2 and 4.

4. Which of the following is not true of treatment for DR? Select ONE option only.

A. The conventional treatment for DR is laser treatment.
B. All people should have intraocular injections of anti-VEGF drugs.
C. People must inform the DVLA if they have had laser treatment.
D. The most important treatment is good control of the underlying diabetes.
E. Laser treatment for focal and diffuse maculopathy is not as successful as that for proliferative retinopathy.

5. Which of the following is true of diabetic maculopathy? Select ONE option only.

A. Loss of vision may be caused by ischaemia.
B. It is not usually associated with macular microaneurysms.
C. The fovea is spared from exudate deposition.
D. Leakage is caused by retinal pigment epithelial disease.
E. A and D.

6. Which of the following requires most urgent referral? Select ONE option only.

A. Optic disc new vessels and a visual acuity (VA) of 6/6.
B. Maculopathy and a VA of 6/36.
C. Optic disc new vessels, a pre-retinal haemorrhage and a VA of 6/5.
D. Venous beading and intraretinal microvascular abnormalities in all quadrants and a VA of 6/60.
E. Cotton wool spots and VA of 6/18.

7. A 26-year-old woman with type 1 diabetes becomes pregnant. She has preproliferative DR in both eyes and no maculopathy. Her blood glucose ranges between 3 and 15 mmol/L and her HbA_{1c} level is 10.3% (89 mmol/mol). Which of the following statements is not true? Select ONE option only.

A. She should have her eyes screened at the end of each trimester.
B. Rapid tightening of glycaemic control may lead to worsening of her DR.
C. Treatment for DR can safely be given during pregnancy.
D. Women who have DR should not become pregnant.
E. She should aim for good management of her diabetes during pregnancy.

8. A 52-year-old woman with type 2 diabetes is going to attend her first laser therapy session. Which of the following should you not include in her education plan? Select ONE option only.

A. She should consider taking sunglasses to prevent glare afterwards.
B. She should not drive for a number of hours after treatment.
C. Advice on driving should be clarified as some services use longer-acting drops.
D. She will not need to take her current glasses as they do not test eye sight and they may be misplaced.
E. Laser therapy does not restore sight that has been lost.

9. A 20-year-old man with type 1 diabetes presents after screening has detected background DR. His blood pressure (BP) is 140/90 mmHg, his HbA_{1c} level is 10.6% (92 mmol/mol) and his total cholesterol is 5.0 mmol/L. Which course of action is most likely to prevent progression of this DR? Select ONE option only.

A. Aim for a target BP of 130/80 mmHg.
B. Aim for a reduction in HbA_{1c} to 6.5% (48 mmol/mol) over the next 2 years.
C. Commence treatment with a statin.
D. A, B and C.
E. Only B and C.

10. A 37-year-old woman has type 1 diabetes, which has been poorly controlled for several years. Her HbA_{1c} level is 9.3% [78 mmol/mol] and her BP is normal, but her last retinal screening 2 years ago showed proliferative retinopathy. She presents with sudden unilateral blindness. Which of the following is the most likely diagnosis? Select ONE option only.

A. Cataract.
B. Transient ischaemic attack.
C. Open angle glaucoma.
D. Age-related macular degeneration.
E. Vitreous haemorrhage.