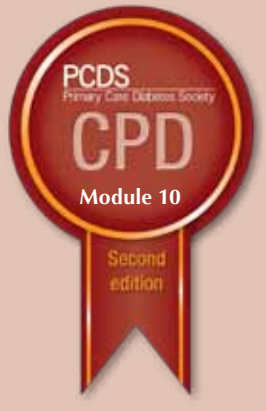
Diabetic retinopathy: Fundamentals for primary care



Deborah Broadbent

Diabetic retinopathy is a leading cause of visual impairment in the Western world. Its pathophysiology involves a complex inter-related 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.

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 the late 1980s, the WHO and International Diabetes Federation (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 ⅓ in the 5 years after 1990."

In November 2005, a European conference took place in Liverpool to review progress since the publication of the St Vincent target and to develop 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 through:

- Systematic programmes of screening reaching at least 80% of the population with diabetes.
- The use of 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 and 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 to see well enough to cook. And if they cannot see they may not be able to draw up 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 vital to consider

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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

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Box 1. Glossary of terms.

Clinically significant macular oedema – Macular oedema causing a reduction in vision (Early Treatment Diabetic Retinopathy Study Research Group, 1991a).

Fovea – The centre of the macula and 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 and 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.

Peripheral retina – 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).

the effect this can have on people's lives, their fears and their expectations. *Box 1* provides a short glossary of terms and *Figure 1* gives a schematic diagram of the eye. For an outline of the pathophysiology of diabetic retinopathy, readers are referred to the first version of this module (Broadbent, 2010).

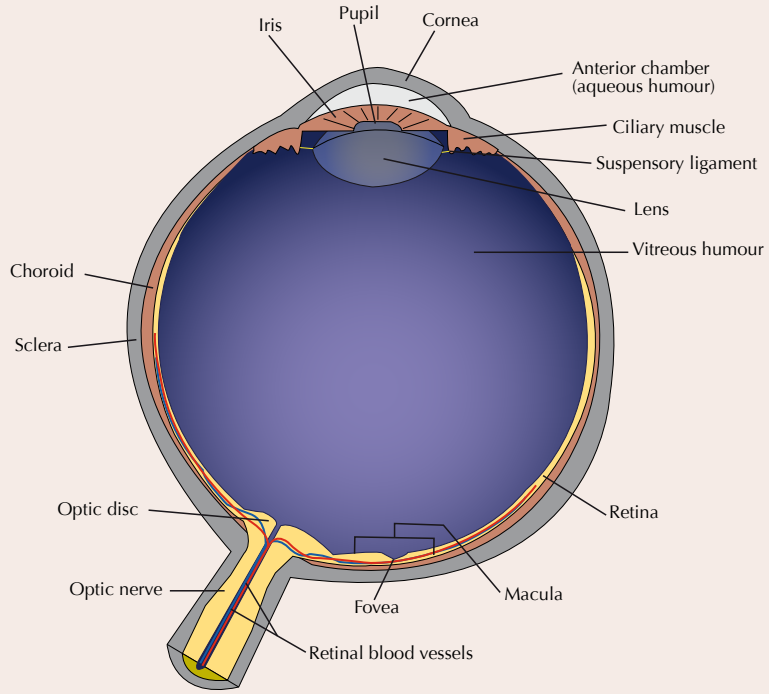

Figure 1. Schematic diagram of the human eye.

Classification

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

Many classification systems have been devised over the years. The system recognised as being the ultimate one 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 seven-field stereophotography, the Modified Airlie House Classification was instrumental for the documentation of retinal signs in the Early Treatment Diabetic Retinopathy Study (ETDRS; ETDRS Research Group, 1991b). This is still used today in research and intervention studies all over the world. However, it is extremely complicated and not suited to routine clinical use. As the "gold standard", 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. The English National Screening Programme for Diabetic Retinopathy (ENSPDR) has been renamed the NHS Diabetic Eye Screening Programme (NDESP) and the grading criteria were revised in 2012 (NDESP, 2012a). Grading is based on retinal photographs and is a reporting, rather than a clinical, classification.

The Royal College of Ophthalmologists (2012) has also recently updated its clinical guidelines on diabetic retinopathy. In this guidance, maculopathy is divided into:

- **Focal**: well-confined areas of leakage (often from microaneurysms) with hard exudates in complete or incomplete "circinate" rings (see *Figure 2*).
- **Diffuse**: generalised intraretinal oedema, often without exudates and due to capillary leakage (with or without retinal pigment epithelium pump failure or vitreomacular traction).
- **Ischaemic**: often relatively normal appearance or minimal oedema and poor vision. Fundus fluorescein angiography reveals capillary fall-out.
- **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).

Table 1 shows the classification of diabetic retinopathy used in England and Wales (ENSPDR, 2006; NDESP, 2012a).

Prevalence and incidence

The prevalence and incidence of diabetic retinopathy are explored in detail in the first version of this module (Broadbent, 2010).

Risk factors

The most important treatment for diabetic retinopathy is control of the underlying diabetes. Good management of diabetes can prevent the development, and slow the progression of, diabetic retinopathy (relevant data are explored below). Primary care physicians and practice nurses play a key role in the regular measurement and target-based treatment of modifiable risk factors.

Risk factors for the development and progression of diabetic retinopathy can be either modifiable or unmodifiable. The most important modifiable factors are glycaemia and blood pressure.

Both the DCCT (Diabetes Control and Complications Trial; DCCT Research Group, 1993; 1995a; 1995b; 2002) in type 1 diabetes and the UKPDS (UK 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 56 mmol/mol [7.3%] versus 64 mmol/mol [8.0%] 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 diabetic retinopathy (non-PDR) or PDR for those with established retinopathy at baseline.

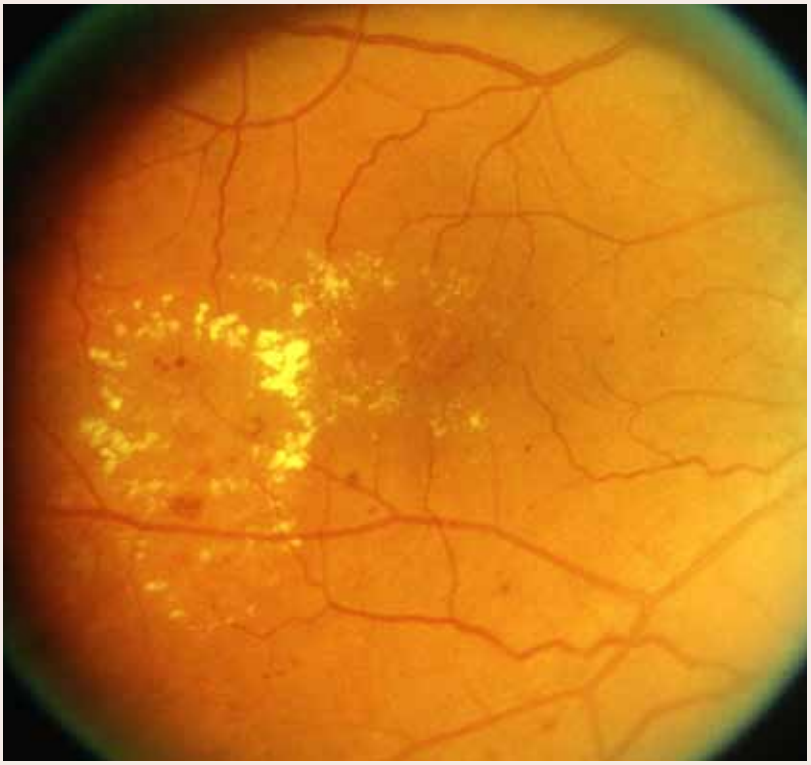

Figure 2. Circinate maculopathy. Copyright © 2001 Fundus Photograph Reading Center, Department of Ophthalmology and Visual Sciences, University of Wisconsin.

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 (the 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 (Diabetic Retinopathy Candesartan Trials) programme has 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 WESDR (the Wisconsin Epidemiological Study of Diabetic Retinopathy) and the Hoorn study (van Leiden et al, 2002) have shown a correlation between high blood cholesterol levels and risk of retinopathy in people with diabetes. A theoretical role for lipids in the development of retinopathy has been proposed and a clearing of retinal exudates has been observed in people receiving statins, but it is not yet completely clear whether this is 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 with type 2 diabetes (37% reduction in laser overall, 31% for first laser for maculopathy, and 30% for PDR]) receiving fenofibrate (Keech et al, 2007; Wright and Dodson, 2011). This occurrence appeared to be independent of a lipid-lowering effect, and a protein kinase C (PKC) inhibition mechanism was proposed. The ACCORD (Action to Control Cardiovascular Risk in Diabetes) Eye study also showed a significant reduction in diabetic retinopathy progression in the fenofibrate group independent of glycaemia and a 40% reduction in odds of having progression in diabetic retinopathy over 4 years with fenofibrate versus placebo (ACCORD Study Group and ACCORD Eye Study Group, 2010; Chew and Ambrosius, 2011; Wright and Dodson, 2011). However, fenofibrate does have an effect on creatinine, the mechanism for which is unclear at present. Practically, if an individual is to be considered for fenofibrate because of sight-threatening diabetic retinopathy he or she should be on the maximum tolerated statin dose before the fibrate is prescribed and then renal and liver function should be monitored closely.

Table 1. The NHS Diabetic Eye Screening Programme grading classification (English National Screening Programme for Diabetic Retinopathy, 2006; NHS Diabetic Eye Screening Programme, 2012c).

Level	Grade	Features
RETINOPATHY		
R0	None	–
R1	Background	● Microaneurysm(s), retinal haemorrhage(s) ± any exudate not within the definition of maculopathy ● Venous loop
R2	Preproliferative	● Venous beading ● Venous reduplication ● Intraretinal microvascular abnormality ● Multiple blot haemorrhages (cotton wool spots are not included, but if seen should promote a careful search for features of R2 above)
R3A	Proliferative (active)	● Newly presenting vessels on disc ● Newly presenting vessels elsewhere ● Previous laser treatment not deemed stable ● New features indicating reactivation of proliferation or potentially sight-threatening change from fibrous proliferation ● Pre-retinal or vitreous haemorrhage.
R3S	Proliferative (stable)	● Evidence of previous laser treatment and stable retinopathy ● Stable pre-retinal fibrosis ± tractional detachment
MACULOPATHY		
M0	None	–
M1	Maculopathy	● Exudate within 1 disc diameter (DD) of the centre of the fovea ● Group of exudates ≥½ disc area entirely 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		
P0	None	–
P1	Photocoagulation	● Evidence of focal or grid laser to macula ● Evidence of peripheral scatter laser
UNCLASSIFIABLE		
	Unclassifiable	● Unobtainable or ungradable

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. It is very probable that there is a genetic explanation for this. Not surprisingly, there have been extensive studies; however, to date, no single gene has been identified (Hanis and Hallman, 2006). The biological processes underlying the development of retinopathy are complex and inter-related. It would be foolish to suppose that there would not be similarly complex relationships between many genes, with small inter-related effects, and the environment.

One of the recommendations of the Liverpool Declaration was to promote joint working between ophthalmologists, diabetologists and primary care. A joint meeting was held in Liverpool in November 2007. Consensus guidelines for management of risk factors were developed and are presented in *Table 2*. However, it should be recognised that there is a need for individualised targets based on an assessment of relevant risks and benefits.

Screening

Screening for diabetic retinopathy in the UK meets the requirements set out in the World Health

Organization document titled *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 [March] 2006, 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%) – as described by Taylor et al (1998) – and allows appropriate quality assurance. Screening, however, is a "sieve". No method currently achieves 100% sensitivity and specificity, although screening can reduce the risk of vision loss to an acceptable rate. For this reason, quality-assurance targets for the process have been set (NDESP, 2012b) and programmes must meet Key Performance Indicators (NDESP, 2012c). Quality assurance is the safety net that underpins any screening programme, and all programmes are measured against service objectives.

The management of screen-positive cases in England and Wales is provided in *Table 3*.

Currently, all people with diabetes aged 12 years and over in the UK are eligible for annual screening unless they have no perception of light in either eye.

Exclusions from screening include the following groups of people (NDESP, 2012d):

- Those who have made a written informed choice to opt out of NDESP. These people should be contacted again by the screening programme after 3 years to ascertain whether they still wish to be opted out of screening.
- Those who would never be able to receive or benefit from treatment owing to another existing condition. This includes people who are terminally ill.

Table 2. Recommendations for risk factor control in diabetic retinopathy (Broadbent, 2010).

Risk factor	Management
HbA_{1c} level	● The person with diabetes and the clinician should jointly agree the target ● Generally, a target of <48 mmol/mol (6.5%) is the aspiration; however, <53 mmol/mol (7.0%) or <64 mmol/mol (8.0%) may be acceptable ● Per cent reduction over a specified time is an alternative approach ● Watch carefully for worsening of diabetic retinopathy if there is a drop in HbA_{1c} level ≥33 mmol/mol (3.0%)
Blood pressure	● If there is coexisting diabetic retinopathy, aim for a target blood pressure of 130/80 mmHg ● In the presence of coexisting nephropathy, aim for a lower blood pressure
Lipids	● Aim for total cholesterol <5.0 mmol/L (ideally <4.0 mmol/L) ● Aim for low-density lipoprotein cholesterol <3.0 mmol/L (ideally <2.0 mmol/L) ● Aim for triglycerides <2.3 mmol/L ● Commence statins in all individuals >40 years, or >19 years if there is coexisting retinopathy

- Those who have been assessed by the clinical lead for the local screening programme as never being able to be screened by digital photography or slit-lamp biomicroscopy.

People who are excluded are not invited for screening and are not screened or assessed for diabetic retinopathy.

Eligible people who continue to have their retinas checked for diabetic retinopathy can be suspended from screening if they are in one of the following states:

- Under the care of the hospital eye service (HES) for the management or treatment of diabetic retinopathy.
- Under surveillance for diabetic retinopathy in either a slit-lamp biomicroscopy clinic (those who have ungradable images) or a digital imaging surveillance clinic (commonly referred to as an ophthalmic photographic diabetic review [OPDR] clinic). (OPDR clinics allow people with early disease [pre-treatment] to be monitored more frequently than annually. This is at the discretion of the ophthalmic clinical lead.)

People who are suspended should be monitored through the fail-safe system in the screening programme.

In general, all screening programmes are now expected to implement fail-safe mechanisms. Fail-safe is a back-up mechanism so that when

Page points

1. Screening programmes should provide local solutions to mobility issues, such as arranging direct referral to a slit-lamp biomicroscopy clinic.
2. People with diabetes who are currently in prison in the UK should be included in the screening programme of the clinical commissioning group responsible for healthcare in that facility.
3. The recommendation is that people should be given two opportunities to attend. If 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 suspended from screening.

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 (NHS Commissioning Board, 2012).

Pregnancy and comorbidities

Pregnant women with either type 1 or type 2 diabetes should be offered digital photography in an OPDR clinic at (or soon after) their first antenatal clinic visit and again at 28 weeks' gestation. If background diabetic retinopathy is found to be present, an additional screen should be performed at 16–20 weeks and for at least 6 months post-partum. If sight-threatening diabetic retinopathy develops during the pregnancy, the individual should be referred to the HES (NDESP, 2013b).

People with diabetes and comorbidities visiting an ophthalmologist should be photographed separately (unless there is a reason why this is likely to be unsuccessful), through which they may be "screened" for diabetic retinopathy as part of their routine ophthalmic appointment (NDESP, 2012d).

Mobility issues, prisons and non-compliance

Confusion often arises with regard to house-bound 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) are covered as part of the exclusion criteria (NDESP, 2012d).

People with diabetes who are currently in prison in the UK should be included in the screening programme of the clinical commissioning group responsible for healthcare in that facility. These individuals pose particular problems with regard to mobility of the population and confidentiality. Ideally, prison populations should be screened every 6 months to ensure adequate coverage (NDESP, 2012d).

Non-compliance with screening can be a major problem. Leese et al (2008) identified an association between non-attendance at screening with living in socially deprived areas, poor glycaemic control, higher blood pressure, smoking, longer duration of disease and earlier age, although a recent paper exploring screening in three South London boroughs suggested that socio-economic inequality might be smaller than reported in earlier studies (Gulliford et al, 2010). In this study, the highest non-attendance rates were in adults aged 18–34 (32%) and in the people 85 years and older (28%). Psychological factors clearly play a large part and although mechanisms to improve uptake can be effective they require intense effort and resources. The recommendation is that people should be given two opportunities to attend. If 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 suspended from screening. Appointments will be offered again in the next screening year (NDESP, 2012d).

Practical aspects

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 more than distance vision, but people should be advised not to drive during this time. In the HES setting, and occasionally in screening, longer-acting eye drops are needed, blurring vision for 6–12 hours. There is a small risk of provoking angle-closure glaucoma by dilating the pupils in susceptible individuals, and all attendees are given a warning letter about this, but glaucoma is not a contra-indication to screening (Wolfs et al, 1997).

Table 3. Management after grading in the NHS Diabetic Eye Screening Programme (NHS Diabetic Eye Screening Programme, 2012e).

Level	Action
Retinopathy	**R0:** Annual screening **R1:** Annual screening *and* inform diabetes carer **R2:** Refer to HES **R3A:** Fast-track referral to HES **R3S:** Monitor in OPDR
Maculopathy	Refer to HES or OPDR clinic depending on decision of ophthalmic clinical lead
Unclassifiable	Refer to dedicated slit-lamp biomicroscopy clinic
Other lesions	Local arrangements – refer to HES or inform primary physician

HES=hospital eye service; OPDR=ophthalmic photographic diabetic review.

Evidence for benefits

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).

Also in Sweden, biennial screen intervals have been adopted for people without retinopathy for some time (Stefansson et al, 2000). A recent study carried out in Malmö (Agardh et al, 2011) prospectively followed people with type 2 diabetes and no retinopathy and concluded that it appeared safe to adopt 3-year intervals as suggested by the Liverpool group (Younis et al, 2003a; 2003b). However, the participants were compliant (only 9% did not attend for follow-up), they had a short duration of diabetes (6 ± 6 years [mean ± standard deviation]) and good control (HbA_{1c}, 46.0 ± 16.4 mmol/mol [6.4 ± 1.5%] at baseline and 45.0 ± 14.2 mmol/mol [6.3 ± 1.3%] at 3-year follow-up), and consequently it might be unwise to recommend 3-year intervals for all people with diabetes, without further studies. Additionally it is vital to ensure that grading is highly accurate in order to ensure that the appropriate screen interval is chosen. However, it is likely that, in the future, economic drivers will lead to the introduction of biennial screening in individuals with no retinopathy, or, more safely, screen intervals based on individual risk.

Quality and Outcomes Framework

Recognising the effectiveness of screening for diabetic retinal disease in the detection of unrecognised sight-threatening retinopathy, diabetes mellitus indicator 011 in the Quality and Outcomes Framework covers the percentage of people with diabetes, on the register, who have a record of retinal screening in the preceding 12 months (NHS Employers, 2013).

Public health considerations

Local strategies to promote awareness of the programme and the importance of screening and to highlight the benefits of attendance, thus encouraging the uptake of appointments, should be an integral part of any systematic screening programme.

A public health-orientated service specification for the NDESP has recently been published (NHS Commissioning Board, 2012). This document states clearly the essential elements to be met by every screening programme in the NDESP. Further guidance on commissioning is available on the NDESP website (NDESP, 2009). However, it should not be forgotten that primary care health professionals have an equally important role to play. They should:

- Provide the screening programme with accurate and timely updates on the demographic data of their diabetes population (e.g. newly diagnosed, died, moved away).
- Regularly monitor risk factors in the people with diabetes they see and strive for optimal control (as in *Table 2*).
- Monitor non-compliance with screening and actively encourage engagement.
- Be in regular communication with the screening programme and assist in developing service improvements.

Ophthalmic treatment

Laser treatment

The conventional treatment for diabetic retinopathy to date has been peripheral scatter laser treatment. To be effective, this must be given at the optimal stage of the disease process. Laser treatment can stabilise the retinal changes but is rarely able to restore vision that has been lost. However, studies have shown that in imminent or early proliferative retinopathy, it will prevent severe sight loss in over 90% of 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 for retinopathy, specifically, is to apply a large number of laser spots (1500–3000 in total) to the peripheral retina. The recently introduced PAtterned SCAnning Laser (PASCAL) system allows semi-automated application of arrays of gentle laser burns, reducing the treatment time and

Page points

1. It is likely that, in the future, economic drivers will lead to the introduction of biennial screening in individuals with no retinopathy, or, more safely, screen intervals based on individual risk.
2. Recognising the effectiveness of screening for diabetic retinal disease in the detection of unrecognised sight-threatening retinopathy, diabetes mellitus indicator 011 in the Quality and Outcomes Framework covers the percentage of people with diabetes, on the register, who have a record of retinal screening in the preceding 12 months.
3. Local strategies to promote awareness of the programme and the importance of screening and to highlight the benefits of attendance, thus encouraging the uptake of appointments, should be an integral part of any systematic screening programme.
4. The conventional treatment for diabetic retinopathy to date has been peripheral scatter laser treatment.

Page points

1. The Driver and Vehicle Licensing Agency (DVLA) has set standards of visual field function that are required for permission to hold a driver's licence. It is the individual's responsibility to inform the DVLA that he or she has had laser therapy for diabetic retinopathy.
2. Although laser treatment can be effective, worldwide the search for newer, more effective or less destructive treatments continues.
3. On 27 February 2013, NICE approved ranibizumab for the treatment of diabetic retinopathy in people with visual impairment and significant oedema. The Scottish Medicines Consortium, shortly before this, brought in similar guidance for Scotland.

increasing patient comfort. Most people do notice a problem with night vision after laser treatment but few notice a change in their field of vision.

In the UK, the Driver and Vehicle Licensing Agency (DVLA) has set standards of visual field function that are required for permission to hold a driver's licence (DVLA, 2013). 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 the treatment for maculopathy, gentle laser burns are applied close to the centre of the fovea. A much lower exposure to laser is required than for retinopathy. Complications for this type of treatment are rare (NDESP, 2013a).

Although laser treatment can be effective, worldwide the search for newer, more effective or less destructive treatments continues.

Pharmacological approaches

A number of important studies have shown that injections of steroid drugs, such as triamcinolone and fluocinolone, directly into the eye, are effective at treating diabetic maculopathy (Rudnisky et al, 2009). However, the effect wears off and injections need to be repeated every 6 months. Important potential side effects of this treatment are the development of glaucoma and cataract. There is a development rate for glaucoma of 25–40%, with a peak at 2 months. In most cases, intraocular pressure returns to normal at 4–6 months; however, around 2% will need glaucoma surgery (for a review of this topic see Razeghinejad and Katz [2012]).

Anti-vascular endothelial growth factor (anti-VEGF) agents have been investigated for some time as an alternative to conventional laser treatment, particularly for diabetic maculopathy. Oral PKC inhibitors have been studied and shown to have an effect in certain groups of people (Aiello et al, 2006), but the main focus is now on the intravitreal injection of anti-VEGF agents (ranibizumab, bevacizumab and aflibercept). Results are temporary, requiring repeated injections at monthly intervals, but these agents have been shown to be superior to laser treatment when the vision has been affected (Elman et al, 2010; 2012; Mitchell et al, 2011).

On 27 February 2013, NICE approved ranibizumab for the treatment of diabetic macular oedema in people with visual impairment and significant oedema (≥400 µm on optical coherence tomography). The body suggested monthly injections until the vision was stable for 3 months and resumption if the vision dropped again (NICE, 2013). The Scottish Medicines Consortium (2012) brought in similar guidance for Scotland shortly before this.

However, with anti-VEGF therapy there is a risk of promoting arterial thromboembolic events and caution must be exercised in people with a recent history of a cardiovascular event. The agents are also contraindicated in pregnancy (e.g. electronic Medicines Compendium, 2013). Finally, all injections directly into the eye hold a small risk of the development of endophthalmitis (a serious infection inside the eye). This risk has been estimated to be approximately 0.05% in a meta-analysis of over 100 000 injections (Ueta et al, 2009).

Surgical vitrectomy

Surgical vitrectomy has been the treatment of choice for people with advanced retinopathy (vitreous haemorrhage and traction retinal detachment). It has also been shown to have good results in tractional diabetic maculopathy (Haller et al, 2010). An area of increasing interest lies in the possibility of giving an injection into the eye to produce a chemical vitrectomy, particularly for maculopathy, and this is being actively researched.

Treatment summary

In summary, peripheral scatter laser treatment remains the treatment of choice for imminent or early proliferative retinopathy. A rational approach to treatment for diabetic maculopathy is:

- Monitor closely if there is good vision and the individual is asymptomatic.
- Consider laser treatment for sight-threatening maculopathy with good vision or minimal reduction in visual acuity and minimal oedema.
- If there is reduced vision and significant oedema, inject an intravitreal anti-VEGF agent for 3 months, assess response and consider further anti-VEGF or laser treatment.
- If pseudophakic (post-cataract surgery), consider intravitreal steroid.

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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"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."

Online CPD activity

Visit www.diabetesonthenet.com/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. A short explanation of the correct answer is provided. 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 learnt in practice. The new CPD centre keeps a record of your CPD activities and provides the option to add items to an action plan, which will help you to collate evidence for your annual appraisal.

1. According to World Health Organization estimates from 2009, on a global scale what proportion of cases of blindness are NOT preventable or curable?

   Select ONE answer only.

   A. 0%
   B. 25%
   C. 50%
   D. 75%
   E. 100%

2. Which of the following item or items were NOT listed in the Liverpool Declaration as a factor for European countries to address in order to reduce the risk of visual impairment due to diabetic retinopathy?

   Select ONE answer only.

   A. Laser therapy access
   B. Use of trained individuals
   C. Government awareness.
   D. Systematic screening programmes
   E. All of the above

3. Roughly, what is the diameter of the macula?

   Select ONE answer only.

   A. 1–2 mm
   B. 2–3 mm
   C. 3–5 mm
   D. 5–7 mm
   E. None of the above

4. Which of the following items are modifiable risk factors for the development and progression of diabetic retinopathy?

   Select ONE answer only.

   A. Glycaemic control
   B. Blood pressure control
   C. Duration of diabetes
   D. A and B
   E. A, B and C

5. What was the odds ratio in the ACCORD Eye study for progression to diabetic retinopathy over 4 years in the fenofibrate group compared with the placebo group?

   Select ONE answer only.

   A. 40%
   B. 0.40
   C. 60%
   D. 0.60
   E. 4.0

6. What is required of screening programmes by the Exeter targets?

   Select ONE answer only.

   A. A proportion of true positives among total positives of 80% and true negatives among total negatives of 95%
   B. A proportion of true positives among total positives of 80% and true negatives among total negatives of 85%
   C. A proportion of true positives among total positives of 90% and true negatives among total negatives of 95%
   D. A proportion of true positives among total positives of 90% and true negatives among total negatives of 85%
   E. A proportion of true positives among total positives of 85% and true negatives among total negatives of 90%

7. In the context of diabetic retinopathy screening, what does OPDR stand for?

   Select ONE answer only.

   A. Ophthalmic photographic diabetic review
   B. Ophthalmic prospective diabetic review
   C. Optical photographic diabetic review
   D. Optical prospective diabetic review
   E. None of the above

8. In the NHS Diabetic Eye Screening Programme, what is the recommended action if the grading is "unclassifiable"?

   Select ONE answer only.

   A. Standard hospital eye service referral
   B. Fast-track hospital eye service referral
   C. Slit-lamp biomicroscopy clinic referral
   D. Annual screening
   E. Biannual screening

9. What does VEGF stand for?

   Select ONE answer only.

   A. Venous epithelial growth factor
   B. Venous endothelial growth factor
   C. Vascular epithelial growth factor
   D. Vascular endothelial growth factor
   E. None of the above

10. In the meta-analysis of Ueta et al (2009), what was the risk found to be for endophthalmitis from injections directly into eye?

    Select ONE answer only.

    A. 5 in 100
    B. 5 in 1000
    C. 5 in 10 000
    D. 5 in 100 000
    E. 5 in 1 000 000