

Fundamentals in diabetes. Part 2: Diabetic retinopathy

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Article points

1. Diabetes is the leading cause of blindness in people of working age in the UK.
2. Diabetic retinopathy is a progressive microangiopathy characterised by small vessel damage and occlusion.
3. Diabetic retinopathy can be classified as either non-proliferative (background and pre-proliferative) and proliferative.
4. People with diabetes should have their eyes reviewed annually as an integral part of their diabetes care management regardless of the presence of diabetic retinopathy.

Key words

- Diabetic retinopathy
- Macula
- Pathophysiology
- Risk factors
- Visual impairment

Authors' details can be found at the end of this article.

Diabetic retinopathy is a common microvascular complication of diabetes that causes significant visual impairment and blindness. People with diabetes are 25 times more likely than the general population to become blind, and from the individual's perspective, visual loss is one of the most worrying and feared potential complications that can develop as a result of poorly controlled diabetes. This article – the second in a series exploring the fundamental pathophysiology of diabetes-related complications – describes the underlying mechanisms responsible for diabetic retinopathy, and discusses how DSNs can play an important role in providing support and optimal care in reducing the risk of visual impairment for people with diabetes.

The prevalence of diabetes continues to increase significantly across the world, currently affecting almost 285 million people. In the UK alone, 2.6 million people are diagnosed with the condition, and this number is expected to reach >4 million by 2025 (Diabetes UK, 2010) – the majority of cases being type 2 diabetes associated with ageing, obesity, population growth and sedentary lifestyles (King et al, 1998).

Diabetes is the leading cause of blindness in people of working age in the UK (Department of Health, 2003), and diabetic retinopathy remains a leading cause of blindness across the world (Congdon et al, 2003; Fong et al, 2004). Diabetes immediately increases the risk of developing a broad spectrum of vascular complications, of which cataracts and diabetic retinopathy are the most common. Apart from affecting vision, diabetic retinopathy also

increases the risk of life-threatening systemic vascular complications (Donnelly et al, 2000).

This article – the second in a series on the fundamental pathophysiology of diabetes complications – explores the underlying mechanisms responsible for the development and progression of diabetic retinopathy, as well as classification, screening and the role of the DSN in caring for people with the condition.

Epidemiology

Diabetic retinopathy is the most common complication in type 1 diabetes and nearly all people with the condition will have developed some degree of retinopathy 15–20 years after diagnosis (Klein et al, 1984). Similarly, more than 60% of people with type 2 diabetes will have evidence of retinopathy during this period (Johansen et al, 1994; Aiello et al, 1998). Numerous epidemiological

Page points

1. Diabetic retinopathy is a progressive microangiopathy characterised by small-vessel damage and occlusion.
2. Chronic exposure to risk factors such as hyperglycaemia and hypertension leads to a cascade of biochemical and physiological changes that ultimately results in microvascular damage and retinal dysfunction.
3. Diabetic retinopathy can be classified as either non-proliferative (background and pre-proliferative) or proliferative.

studies – such as the Diabetic Retinopathy Study (DRS; DRS Research Group, 1981), the Wisconsin Epidemiological Study on Diabetic Retinopathy (Klein et al, 1984), the Early Treatment Diabetic Retinopathy Study (ETDRS; ETDRS Research Group, 1985), the Diabetic Retinopathy Vitrectomy Study (DRVS; DRVS Research Group, 1990), the Diabetes Control and Complications Trial (DCCT; DCCT Research Group, 1993), and the UK Prospective Diabetes Study (Kohner et al, 1993) – have reported important relevant data that have played a significant role in identifying related risk factors as well as providing guidelines for the management of diabetic retinopathy.

A review on the epidemiology of diabetic retinopathy and macular oedema has also reported that studies that are of sufficient size to stratify for age and duration of eye disease have clearly shown an increase in diabetic retinopathy in older people with long-standing diabetes (Williams et al, 2004).

Pathophysiology and classification

Diabetic retinopathy is a progressive microangiopathy characterised by small-vessel damage and occlusion (Riordan-Eva and Whitcher, 2008). The earliest pathological

changes are thickening of the capillary endothelia basement membrane and reduction of the number of pericytes (cells associated with the outer wall of small blood vessels). Chronic exposure to risk factors such as hyperglycaemia and hypertension leads to a cascade of biochemical and physiological changes that ultimately results in microvascular damage and retinal dysfunction.

Diabetic retinopathy can be classified as either non-proliferative (background and pre-proliferative) or proliferative. During the non-proliferative stage, early retinal damage occurs from abnormal permeability and/or non-perfusion of capillaries that leads to the formation of microaneurysms (Engerman, 1989), which results in the leaking of fluid that collects around the macula (macular oedema) (*Figure 1* gives a schematic representation of the human eye).

Proliferative diabetic retinopathy develops due to occlusion of retinal capillaries that leads to retinal ischaemia. Neovascularisation follows, whereby fragile new blood vessels proliferate on the surface of the retina causing haemorrhage. Blood then accumulates in the vitreous cavity resulting in visual impairment. *Box 1* outlines the stages of retinopathy.

Risk factors for diabetic retinopathy

A number of factors increase the risk of diabetic retinopathy:

1. *Diabetes duration* – the duration of diabetes is the major risk factor for the development of diabetic retinopathy (Klein et al, 1984).
2. *Glycaemic control* – the DCCT (DCCT Research Group, 1993) has shown that in people with type 1 diabetes, good glycaemic control reduces the risk of progression of diabetic retinopathy and delays the onset of retinopathy in those who do not have retinal changes at the time of presentation. In people with type 2 diabetes, the UKPDS (Kohner et al, 1993) has shown that good glycaemic control can also delay the progression of retinopathy.
3. *Hypertension* – studies have indicated that high diastolic blood pressure in young people (Klein et al, 1984) and higher systolic

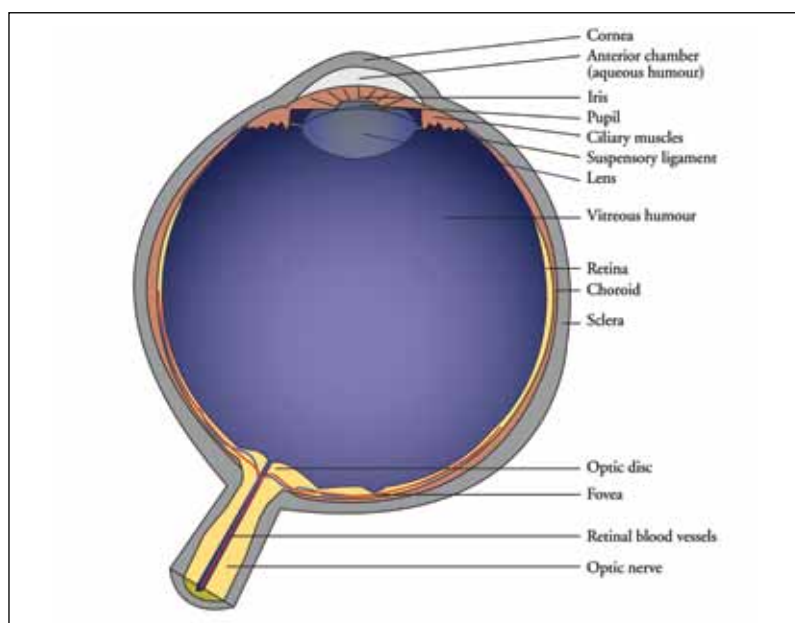


Figure 1. Schematic diagram of the human eye.

Box 1. Stages of retinopathy.

1. Background retinopathy (Figure 2)

Microaneurysms may appear as tiny red dots and hard exudates. Yellow-white shiny spots or streaks are often seen forming clusters or arcs around the macula and other points of capillary leakage on examination of the back of the eye. "Cotton wool" spots may also be seen. The vision is not usually affected if background retinopathy is diagnosed until there is macular involvement resulting in impairment of central vision to the eye (Stollery et al, 2005).

2. Pre-proliferative retinopathy (Figure 3)

Multiple, deep, round haemorrhages often appear over a short period with five or more cotton wool spots. Abnormalities of veins, including dilation, beading, looping and reduplication, and intraretinal microvascular abnormalities, are seen on examination. The eye needs close observation but is not usually treated unless regular follow-up is not possible or if the vision in the fellow eye has been lost to proliferative disease (Scott, 2011).

3. Diabetic maculopathy (Figure 4)

If the oedema or hard exudates involve the fovea and this becomes ischaemic, this is called diabetic maculopathy, and is the most common form of visual impairment in people with type 2 diabetes. Diabetic maculopathy is a sight-threatening situation, although the vision may not always be affected if it is detected early enough. Clinically significant macular oedema is a specific condition that occurs when the oedema or exudates are within certain proximity of the fovea and of a certain size. This is relevant as it requires photocoagulation treatment, regardless of the level of visual acuity.

4. Proliferative retinopathy (Figures 5 and 6)

Proliferative retinopathy is the main cause of visual impairment in people with type 1 diabetes. It can occur soon after type 2 diabetes is diagnosed, possibly because the diabetes has gone on longer undetected. The appearance of new vessels as fine fronds or arcades of abnormal structure are seen usually arising on the optic nerve head. This is described as neovascularisation of the disc. New vessels are associated with haemorrhage, retinal detachment and glaucoma. Laser therapy, if required, can be given for this in outpatient clinics and aims to prevent neovascularisation occurring. Scotomas (blind spots) present cause little visual impairment (Early Treatment Diabetic Retinopathy Study Research Group, 1985).

5. Advanced diabetic eye disease (Figure 7)

Advanced disease is end-stage damage that usually leads to blindness. Vitreous and preretinal haemorrhages occur as new vessels grow forward from the retina and enter the vitreous where they bleed easily. Retinal detachment occurs when the retina is pulled off the underlying choroid by strands of fibrous tissue associated with the formation of new vessels or previous haemorrhages. Rubeosis iridis, whereby new vessels grow on the iris, can be seen or they cause a diffuse reddening of the iris; this is often complicated by glaucoma due to obstruction of the filtration angle in the anterior chamber. Early vitrectomy and also treating neovascular glaucoma (involvement of iris with major risk of acute glaucoma) improves visual recovery in people with proliferative retinopathy and severe vitreous haemorrhage (Mohamed et al, 2007).

blood pressures in older people (Kohner et al, 1993) can worsen diabetic retinopathy. Recommended target blood pressure levels are $\leq 130/80$ mm/Hg for people with type 2 diabetes and $\leq 135/85$ mmHg for people with type 1 diabetes (NICE, 2005; 2009); however, targets may vary according to local guidelines and protocol.

4. *Pregnancy* – this has been associated with worsening of diabetic retinopathy, therefore dilated retinal examination is essential during the course of pregnancy. Intrinsic hormonal changes in pregnancy and the need for rapid tightening of glycaemic control throughout pregnancy has also been found to have a strong association with worsening retinopathy. Various factors influence the progression of diabetic retinopathy in pregnancy, including: being in a pregnant state; duration of diabetes; degree of retinopathy at conception; presence of existing hypertension and metabolic control before and during pregnancy (Klein et al, 1990; DCCT Research Group, 2000).

5. *Hyperlipidaemia* – data from the ETDRS suggest that lipid-lowering may reduce the risk of visual loss in people with diabetic retinopathy (Chew et al, 1996). Target total cholesterol levels of < 4 mmol/L are now recommended for people with type 2 diabetes (NICE, 2009).

6. *Cigarette smoking* – this an additional risk factor and its effect on cardiovascular disease is well known.

7. *Age* – retinopathy is uncommon in type 1 diabetes before the age of 13 years. The onset of puberty may influence retinopathy, although the duration of diabetes is a significant factor. In those with older onset type 1 diabetes there is an increased frequency of retinopathy in those aged < 50 years (Klein et al, 1984). Approximately 21% of people with type 2 diabetes have retinopathy at diagnosis, and their retinopathy is believed to have begun at least 6.5 years before diagnosis of diabetes (Harris et al, 1992).

8. *Ethnicity* – data from population-based studies suggest that the prevalence and severity of diabetic retinopathy are both

Figure 2. Background diabetic retinopathy with microaneurysms, haemorrhages and exudates. Copyright 1st Retinal Screening Ltd.



Figure 3. Pre-proliferative diabetic retinopathy with cotton wool spots, intraretinal microaneurysm and multiple blot haemorrhages. Copyright 1st Retinal Screening Ltd.



Figure 4. Diabetic maculopathy with haemorrhages and circinate exudates and multiple blot haemorrhages. Copyright 1st Retinal Screening Ltd.



Figure 5. Proliferative diabetic retinopathy with pre-retinal and vitreous haemorrhages. Copyright 1st Retinal Screening Ltd.



higher in African American, Hispanic and south Asian people than in white people, and are not fully accounted for by differences in the distribution of retinopathy risk factors (Wong et al, 2006; Raymond et al, 2009). For example, in the UK Asian Diabetes Study (Raymond et al, 2009) of 1035 people with type 2 diabetes (421 south Asian and 614 white European), the authors showed that after controlling for retinopathy risk factors, south Asian people were more likely to have diabetic retinopathy than white people.

Screening

Current screening recommendations are that all people aged >12 years with diabetes need to be invited for annual screening (Scanlon, 2008). Digital retinal photography with mydriasis (dilating the pupil using eye drops – usually tropicamide 1% – prior to retinal photography) should be used as the gold standard screening test to detect diabetic retinopathy. There should also be an appropriate referral service in place whereby if any abnormalities are detected these can then be addressed either in hospital clinics or in primary care.

The screening programme may vary in its delivery regionally depending on the availability of resources and patterns of provision. It may involve GPs, optometrists, hospital physicians and other healthcare professionals. The UK National Screening Committee is responsible for screening programmes in each region.

Management and implications for diabetes nurses

People with diabetes should have their eyes reviewed annually as an integral part of their diabetes care management regardless of the presence of diabetic retinopathy. Emphasis should focus more on prevention and monitoring than treatment. This comes with highlighting the importance of education in relation to diabetes and lifestyle issues surrounding its management.

Following initial assessment of the individual with diabetic retinopathy, the following elements should be covered in the consultation:

Figure 6. Proliferative diabetic retinopathy with new vessels at the optic disc. Copyright 1st Retinal Screening Ltd.



Figure 7. Advanced retinopathy – fibrous proliferation. Copyright 1st Retinal Screening Ltd.



- Glycaemic control.
- Blood pressure.
- Lifestyle (including smoking cessation, basic dietary review, physical activity and alcohol consumption).
- Current medication.
- Baseline biomedical parameters (HbA_{1c} level, renal function, lipid profile and urine albumin excretion).
- Provision of individual diabetes education, including self-monitoring of blood glucose.

The risk of visual impairment and blindness may be reduced by advising people with diabetes on self-care strategies and enrolling them on structured education programmes (NICE, 2003). Programmes such as DESMOND (Diabetes Education and Self-management for Ongoing and Newly Diagnosed) for people with type 2 diabetes and DAFNE (Dose Adjustment for Normal Eating) for those with type 1 diabetes, have been designed to enable these individuals to self-manage their condition successfully. Currently, no topical pharmaceutical preparations

are available for the treatment of diabetic retinopathy, although research is still ongoing.

Setting up a diabetes eye clinic service is an innovative and challenging venture, and can prove to be a new learning curve for DSNs. It can also help develop management and interpersonal skills as well as create good working relationships within both the ophthalmic and diabetes clinics. *Box 2* highlights how this service can be implemented within a clinical area.

Conclusion

Diabetic retinopathy is a chronic but treatable complication of diabetes. DSNs can play a key role in targeting these screened-positive individuals who present with high but modifiable risk factors (poor glycaemic control, cardiovascular risk).

The increasing prevalence of diabetes is already having an impact on financial constraints in the NHS. Screening for diabetic eye disease and early detection at a time when it is asymptomatic when followed by interventions can lead to improved outcomes and also play an important part in reducing healthcare costs and improve quality of life for people with diabetes. ■

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Box 2. Implementing a diabetes eye clinic service.

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|----------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Patient capture/recruitment | <ul style="list-style-type: none"> ● From retinal screening clinic. ● Existing retinal clinic patient. ● Communicate with other doctors in both the eye and diabetes clinics. |
| One-stop clinic/partnership | <ul style="list-style-type: none"> ● Identify a key ophthalmologist with special interest in diabetic retinopathy and key consultant diabetologist to run the service for continuity of care. ● Decide on the local referral protocol. |
| Follow-up, treatment protocol and guidelines | <ul style="list-style-type: none"> ● Follow local and national consensus guidelines on glycaemic, lipid, microalbuminuria and blood pressure management. |
| Resources | <ul style="list-style-type: none"> ● Secure location and times of clinic. ● Ensure relevant IT teaching package has been installed (the Clinical Workstation is used in Leicester). |
| Audit of results | <ul style="list-style-type: none"> ● IT package (as above) to record and analyse interventions. |
| Staff training/development | <ul style="list-style-type: none"> ● Skills and qualification should be aligned to meet competencies as outlined by the TREND UK (2011) competency framework and Skills for Health (2009). The nurse should also ensure that the clinic is run in line with the Nursing and Midwifery Council (2004) code of conduct and accountability. ● Have a mentor for advice/support in managing people's diabetes treatment. |

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