Diabetes and the eye

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Early intervention and
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absolutely crucial.

Diabetes is a major public health problem — various estimates of the extent of the problem put the number of diabetics at present at approximately 135 million worldwide. This number is rising rapidly and expected to reach about 240 million in the developing world alone by the year 2010. The ocular complications of this condition are a major cause of morbidity and are of extreme importance for the general practitioner or primary care physician for several reasons.

Firstly, various studies have shown that after 20 years of diabetes nearly all patients with insulin-dependent diabetes mellitus (IDDM), and more than 60% of those with non-insulin dependent diabetes mellitus (NIDDM) have some degree of retinopathy. Furthermore the incidence of proliferative diabetic retinopathy in patients with IDDM is approximately 60% after 30 years. While this figure is probably not as high in the group with NIDDM, these patients are probably more likely to develop macular complications at an earlier stage of their disease. The importance of this information lies in the fact that the 5-year risk of severe visual loss from proliferative retinopathy may be as high as 60%, while the risk of moderate visual loss from macular complications may be as high as 25 - 30%, making diabetic retinopathy the most common cause of legal blindness in individuals between the age of 20 and 65 years in many developed countries.

Secondly, the early changes in this condition are usually completely asymptomatic and as such the patient is unlikely to consult an ophthalmologist. It is obviously important that these patients be followed up carefully by someone with experience in the management of these complications, but it is just not logistically feasible for all diabetics to be seen by an ophthalmologist especially when they have no ocular involvement at all.

Thirdly, many studies have shown that early intervention and appropriate therapy in the earlier phase of complications can reduce ocular morbidity in diabetics by over 90%. Consequently the involve-
Ocular complications

Diabetics are prone to develop many different ocular complications, including:

- an increased incidence of superficial and deep infections, such as blepharitis, preseptal and orbital cellulitis; a rare, but particularly serious and life-threatening form of orbital cellulitis secondary to mucormycosis occurs almost exclusively in diabetics
- early onset of cataracts
- rapid refractive changes, which are usually reversible, during periods of particularly poor control; this may be secondary to changes in the sugar alcohols of the lens, resulting in alterations of lens refractive power
- neuro-ophthalmological complications, such as III, IV or VI nerve palsies with the sudden onset of diplopia and strabismus
- bilateral optic neuropathy, a relatively uncommon complication in younger diabetics
- neovascular glaucoma secondary to new vessel growth on the iris which presents as a loss of vision in a painful red eye and is often associated with advanced diabetic retinopathy
- diabetic retinopathy.

The remainder of this article concentrates on diabetic retinopathy as it is here that the role of the general practitioner as primary care physician is really invaluable to the effective management of these patients. Diabetic retinopathy may present either as a gradual or a sudden onset of visual loss in a painless usually white eye. However it is critical that patients be examined while still asymptomatic according to the following guidelines.

Guidelines for follow-up

The guidelines for the follow-up of these patients have been established by general consensus and include the following:

- It is probably unnecessary to examine the fundi of patients with IDDM regularly until the condition has been present for 5 years, at which stage regular annual fundal examinations are indicated.

Patients with retinopathy are often asymptomatic until they lose vision suddenly secondary to haemorrhage from the new vessels into the vitreous cavity, while patients with maculopathy are usually aware of a gradual decrease in their visual acuity.

- In the case of patients with NIDDM, however, annual fundal examination is essential from the time of diagnosis. This is probably because in a significant majority of these patients the hyperglycaemic state has been present for a significant period of time before the diagnosis is made.
- Diabetics considering pregnancy should have an examination before falling pregnant and then early in each trimester or more frequently as indicated.

The family practitioner responsible for the management of the patient's diabetes should see to it that each patient is informed of the possibility of the development of retinopathy with or without the prior development of symptoms and the associated threat of visual loss. The natural course and treatment of diabetic retinopathy should be discussed and the importance of routine examinations stressed. This should include as a minimal baseline:

- a visual acuity test
- a dilated fundal examination.

In addition the following measures have been shown to have a beneficial effect on the progression of diabetic retinopathy and should be carefully checked and discussed with each patient:

- Good metabolic control was a controversial issue in the past, but it has been shown fairly definitely that this is of value in delaying the onset of and slowing the progression of retinopathy. It must be stressed that it is only of value if the good control is long term. If control has been sub-optimal for some time, the sudden institution of very tight control may result in an initial aggravation of retinopathy, but this is usually transient in nature.
- Good control of hypertension — this is especially important and may reverse certain components of maculopathy even in the short term.
- The management of anaemia, as this may aggravate ischaemia.

If no abnormalities are noted, annual follow-up by the family practitioner is recommended. If abnormalities are seen, it is probably advisable to refer these patients to an ophthalmologist. Although the frequency of follow-ups by the ophthalmologist will vary somewhat, they should be done biannually to annually for background diabetic changes, and approximately every 3 months or even sooner once
the changes of preproliferative retinopathy are visible.

**Pupillary dilatation**

It is possible to make a superficial assessment of the fundus without a dilated pupil in some patients and non-mydriatic fundus cameras are being used in some sophisticated centres in the USA to transmit images to central reading centres where trained technicians decide whether further evaluation is necessary. However, an adequate evaluation for the presence or absence of diabetic retinopathy requires dilatation of the pupil in the majority of patients. In many young patients this might be possible in a suitably darkened room, but often this is inadequate and pharmacological dilatation is indicated.

The primary care physician should be comfortable with this procedure and be aware of the associated risks. Some patients may find that because of the resultant paralysis of accommodation, they are unable to drive home or back to work with dilated pupils. This should be considered before pupillary dilatation is undertaken. In the general practice situation a drop of tropicamide (Mydriacyl; Alcon), applied 2 or 3 times, 5-10 minutes apart, is probably the ideal method as it has a fairly rapid onset of action and its effect has usually worn off by the next day. Atropine drops should not be used in this situation as their effects may persist for up to 2 weeks. Before dilatation is undertaken the eyes should be checked for the presence of a shallow anterior chamber. The eclipse test should be used, as the possibility exists of precipitating an attack of acute angle closure.

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Pupillary dilatation begins at the optic nerve head. Then follow the blood vessels, especially the ones that define the temporal arcades, but including those in the nasal retina as well, taking note of the surrounding retina. Finally, concentrate on the area of the macula.

**Pathology**

An appreciation of the pathology responsible for the changes found in diabetic retinopathy will facilitate an understanding of the signs of this complication as well as the rationale behind the therapy. The primary pathology is that of microangiopathy. The details of the pathology are fairly complex and still a matter of some debate but exhibit features of both a microvascular occlusion as well as that of increased microvascular permeability. The occlusion results initially in retinal ischaemia and hypoxia. This leads to the formation of arteriovenous shunts and ultimately, because of the release by the ischaemic retina of angiogenic substances, the development of retinal neovascularisation or new vessels both at the disc and at distant sites on the retina and occasionally elsewhere in the eye. New vessels may even occasionally develop on the iris leading to neovascular glaucoma, another major complication of diabetes. The increased microvascular permeability is closely related to the loss of pericytes, the cells that surround the capillaries and which are thought to be responsible for their structural integrity. Therefore this is initially manifest by the appearance of increased microvascular permeability.
of small capillary micro-aneurysms with the subsequent development of retinal haemorrhages and oedema.

The changes in the retina can usefully be divided into:
- retinopathy, further subdivided according to severity into background, preproliferative (where clues are present for progression) and proliferative
- maculopathy which may be further subdivided into focal exudative, diffuse exudative, or ischaemic.

Patients with retinopathy are often asymptomatic until they lose vision suddenly secondary to haemorrhage from the new vessels into the vitreous cavity, while patients with maculopathy are usually aware of a gradual decrease in their visual acuity.

Clinical features of retinopathy

The clinical features of background diabetic retinopathy (Fig. 1) are:
- micro-aneurysms, which appear as small round red dots which vary in size, and are usually distinguishable clinically from small round haemorrhages on the basis of size
- intra-retinal haemorrhages which may have a dot or blot shape if they are in the middle layers of the retina or may be flame shaped if they are situated more superficially in the nerve fibre layer of the retina
- hard exudates which are yellow-white in appearance and composed of lipoprotein and lipid-laden macrophages and are usually found associated with leaking micro-aneurysms, often surrounding them in a circular pattern
- retinal oedema resulting in a thickened retina which is often very difficult to pick up with the monocular direct ophthalmoscope.

The features of preproliferative retinopathy (Fig. 2) are those which suggest that the ischaemic process is fairly advanced. They include:
- cotton wool spots (Fig. 3) — fluffy whitish lesions with blurred margins which represent thickened opaque ischaemic areas of the retinal nerve fibre layer
- intra-retinal microvascular abnormalities (IRMA) — these may sometimes be confused with new vessels by the inexperienced, but their intra-retinal location and their failure to cross major retinal blood vessels are important distinguishing features
- venous changes such as beading (Fig. 4), looping or sausage-like segmentation — evidence of advancing ischaemia
- large dark blot haemorrhages which may represent haemorrhagic retinal infarcts.

Fig. 1. Early background diabetic retinopathy with a few scattered micro-aneurysms, and a ring of hard exudates.

Fig. 2. Composite drawing of the clinical features of preproliferative diabetic retinopathy, including venous beading, venous loops, cotton wool spots, large blot haemorrhages and intra-retinal microvascular abnormalities.

Fig. 3. Cotton wool spots can be distinguished from hard exudates by their whiter appearance and fluffy, less distinct margins.

Fig. 4. Venous beading with early new vessel formation on the optic disc.

The end result of all the above changes is the development of proliferative diabetic retinopathy. Here new vessels are seen to grow from the disc (Fig. 5), the major temporal vascular arcades (Fig. 6) and occasionally in other areas of the retina. These vessels may occasionally lie flat on the surface of the retina in a fine fibrillary meshwork but often grow forward into the vitreous cavity. It is this fact that makes them liable to easy rupture with the development of spontaneous vitreous haemorrhages and sudden visual loss.

Patients with maculopathy, on the other hand, report a gradual loss of vision. In the exudative types this is due to the accumulation of fluid within the retina resulting in retinal thickening. In these patients fundal examination reveals the signs of background diabetic retinopathy, such as micro-aneurysms, haemorrhages and significant hard exudates involving the fovea and parafoveal area. In patients with
different form depending on whether the problem is primarily proliferative retinopathy or maculopathy. In the case of proliferative retinopathy a technique referred to as pan retinal photocoagulation (PRP) is performed. Here the peripheral retina outside the vascular arcades is lasered in order to decrease the ischaemic stimulus for the formation of new vessels by destroying the ischaemic retina. This may create a slight decrease in the peripheral field, but it is very rarely a significant problem to these patients. In the case of exudative maculopathy the laser is applied in a more directed fashion at the micro-aneurysms responsible for the leakage or in a grid-like pattern if the leakage is more diffuse. Laser treatment is usually fairly atraumatic, performed as an outpatient procedure with topical anaesthetic while the patient is seated at the slitlamp.

The value of laser treatment, especially if applied timeously, has been clearly proven by many excellent trials. However if patients present later after vitreous haemorrhage or once the fibrovascular membranes that have grown into the vitreous begin to create tractional detachments of the retina, vitreoretinal surgery may be indicated and the prognosis is much more guarded. It is for this reason that these patients need to be identified up in the asymptomatic phase of their disease when the results of intervention are optimal.

Pregnancy
A few additional words about the management of diabetic retinopathy in pregnant women are important as the presence of proliferative diabetic retinopathy was considered by many to be an absolute contraindication for a diabetic to fall pregnant only several decades ago before the proven value of laser therapy. When pregnancy is being considered a very careful fundal examination is indicated as laser therapy should be considered at an earlier stage of retinopathy and should be instituted before the patient falls pregnant. Several

IN A NUTSHELL

The ocular complications of diabetes and particularly the consequences of diabetic retinopathy are a major cause of morbidity.

The role of the general practitioner in the evaluation and follow-up of the eyes of asymptomatic diabetic patients is critical.

The general practitioner’s assessment should include a measurement of the visual acuity, a dilated fundal examination, a careful review of the degree of both metabolic and blood pressure control and management of any underlying anaemia.

The primary pathology in diabetic retinopathy is a microangiopathy which exhibits features of both a microvascular occlusion and increased permeability.

Diabetic retinopathy may result in both a sudden painless loss of vision secondary to vitreous haemorrhage or a gradual painless loss of vision as a result of diabetic maculopathy.

Laser treatment is the mainstay of therapy once retinopathy is established and if applied timeously can result in a significant reduction in morbidity.

Diabetic patients considering pregnancy require careful fundal evaluations and appropriate therapy before falling pregnant.
authors have shown that diabetic retinopathy may progress more rapidly during pregnancy and so these patients should have their fundi carefully monitored at least once during each trimester. There are at present no firm data on the risk of vitreous haemorrhage in proliferative retinopathy during vaginal delivery. Proliferative retinopathy per se is not considered an indication for caesarean section, but it should probably lower the threshold for this decision if any other problems are anticipated.

Conclusion
With appropriate and timely intervention and long-term care the significant ocular morbidity which results from diabetes can be reduced by more than 90%. This is an extremely valuable contribution to the health of our patients. The role of the general practitioner as the kingpin in this endeavour is critical and should be more widely appreciated.

I would like to thank Mr Jack Kanski (Consultant Ophthalmic Surgeon at King Edward VII Hospital) for kind permission to make use of his photographs.

FURTHER READING


When pregnancy is being considered a very careful fundal examination is indicated as laser therapy should be considered at an earlier stage of retinopathy and should be instituted before the patient falls pregnant.