BACKGROUND INFORMATION ON THE MANAGEMENT OF DIABETIC RETINOPATHY

Diabetic Retinopathy

1. Diabetic retinopathy is the commonest cause of blindness in patients of working age in developed countries. The prevalence (essentially the proportion of the population with the condition) of diabetics may vary from one community and country to another but in the United Kingdom is in the order of 2-3%. In Lambeth, Southwark, for ethnographic reasons the prevalence is higher (up to 7%), although under-reporting is suggested by wide variations in prevalence among practices (Reference 1). Individuals from black and other minority groups are up to 6 times more likely to develop diabetes and also those from low income groups are at greater risk. Of those with diabetes, approximately 1% have lost a significant amount of vision due to diabetes. Diabetes may be insulin dependent and non-insulin dependent (in a ratio of 1:9 in the national population). Those with insulin dependent diabetes tend to be diagnosed in childhood and require treatment with insulin from an early age. Those with non-insulin dependent diabetes are diagnosed in adulthood and at least initially may only require treatment with diet, or tablets. If adequate diabetic control is not achieved with oral therapy, then insulin may also be required.

2. In both types of diabetes it is recognised that the longer the duration of diagnosed diabetes, the greater the risk of developing sight-threatening complications. A classification system has been developed in order to allow recognition of the onset of sight-threatening changes within the eye due to diabetes.

Classification of Diabetic Retinopathy

1) Mild Non-Proliferative (background) Retinopathy

   This mild form of retinopathy consists of small haemorrhages or 'micro-aneurysms' (outpouchings of capillary blood vessels) but these do not in themselves pose a risk to the patient's vision and do not require treatment. Patients with this degree of diabetic retinopathy tend to be simply observed on an annual basis.

2) Moderate/Severe Pre-Proliferative Retinopathy

   This is characterised by the presence of larger and darker haemorrhages and fluffy white lesions on the retina known as 'cotton wool spots', together with irregularities in calibre and with tortuosity of the retinal blood vessels. Although the patient may have normal vision and does not require treatment, this more severe form of retinopathy does require more frequent monitoring, possibly every three to four months.

3) Proliferative Retinopathy

This is characterised by the appearance of abnormal blood vessels growing from the surface of the optic nerve (which in clinical notes are referred to as 'NVD'- "new vessels of the disc"), together with areas of peripheral retinal neovascularisation (referred to as NVE- "new vessels elsewhere"). The presence of these indicate that the patient is at significant risk of developing profound visual loss, either as a result of the blood vessels bleeding, resulting in a vitreous haemorrhage (bleeding into the vitreous jelly which fills the cavity of the eye) or due to the blood vessels undergoing transformation into scar tissue which covers the surface of the retina and as a consequence of its contractile properties causes a retinal detachment. A significant vitreous haemorrhage would of course obscure the patient's vision and if the retinal detachment involved the macular part of the retina, once again the patient's visual acuity would be reduced.

4) Diabetic Maculopathy

This is another form of sight-threatening retinopathy which can affect the macular in a number of ways:

- Oedema, in which fluid leaks from blood vessels into the macular causing retinal thickening, distortion of the intraretinal structures and visual deterioration.

- Focal Exudative Maculopathy –This refers to the development of collections of lipids and proteins, which leak from the plasma within the retinal vessels and macular microaneurysms. Once again this can cause profound central visual disturbance.

- Ischaemic Maculopathy – If the capillary blood vessels supplying the macular become constricted (a recognised consequence of diabetes) and as a result, the retina is deprived of its supply of oxygen and nutrients, resulting in photoreceptor death.

The Management of Diabetic Retinopathy

There are three key elements which are crucial to the prevention of visual loss in diabetic retinopathy: metabolic control, screening and ocular therapy.

1) Metabolic Control

1.1 It has long been recognised that maintaining good control of the levels of blood glucose, together with glycosolated haemoglobin (HbA1c, an indicator of longer term control of the condition) has a beneficial effect in reducing the incidence and severity of diabetic retinopathy, as well as of nephropathy and neuropathy. In individuals with hypertension, good control of blood pressure is also of importance. If a patient has poorly controlled diabetes, either due to failure of therapy or poor compliance (for example an inappropriate diet, failure to take medication or to attend for regular specialist review) then the risk of developing sight-threatening

retinopathy is significantly increased. The Diabetes Control and Complications Trial (DCCT) was a landmark study conducted from 1983 to 1993 designed to explore whether intensive glucose control could delay or possibly even prevent diabetes-related complications. In this study, intensive control meant keeping Hb A1c levels at 6% or less.

1.2 The study involved 1,141 volunteers, aged 13 to 39, with Type I diabetes and was conducted at 29 medical centres throughout North America. The results of the 10 year study showed that maintaining blood glucose levels in a more or less normal range can slow the onset and progression of retinopathy, as well as kidney, and nerve damage caused by diabetes. It further stated that any lowering of blood sugar levels was beneficial even when the person with diabetes had a history of poor glucose control (Reference 2)

1.3

In another landmark study, The United Kingdom Prospective Diabetes Study (UKPDS) recruited 5,102 patients with newly diagnosed type 2 who were followed for an average of 10 years to determine whether intensive use of pharmacological therapy to lower blood glucose levels and to control blood pressure would result in clinical benefits. The UKPDS results established that retinopathy, nephropathy, and possibly neuropathy are benefited by lowering blood glucose levels in type 2 diabetes with intensive therapy, which achieved a median HbA_{1c} of 7.0% compared with conventional therapy with a median HbA_{1c} of 7.9%. The overall microvascular complication rate was decreased by 25%. The study also demonstrated that lowering blood pressure to a mean of 144/82 mmHg significantly reduced strokes, diabetes-related deaths, heart failure, microvascular complications, and visual loss (Reference 3).

2) Ophthalmic Management

2.1 All patients with diabetes require regular examination of their eyes. This may be performed in the community by the patient's optometrist or General Practitioner and in addition there are a number of community and hospital based screening services for this purpose. If the patient is felt to be at risk of developing significant retinopathy then referral would be made for a specialist's opinion by an ophthalmologist with an interest in the management of diabetic retinopathy. The patient attending a diabetic retinopathy clinic will undergo a detailed ocular examination. Visual acuities would be measured and the eyes examined at what is known as a 'slit lamp microscope' which allows a detailed and magnified assessment to be made of structures of the eye, from the front to the back, and in particular the retina ("fundoscopy"). The examination will also include a measurement of the pressures within the eyes (in order to investigate the possibility of glaucoma) and also an observation of the state of the crystalline lenses within the eyes to investigate the possibility of cataract formation. Additional investigations include fundus fluorescein

angiography (and over the past few years, OCT scanning). While all patients undergo slit lamp biomicroscopy, fluorescein angiography tends to be reserved for those patients in whom more subtle degrees of neovascularisation or macular oedema are suspected, which is not clearly visible on fundoscopy. A more absolute indication for fluorescein angiography is if macular ischaemia is suspected as this investigation remains the best method for confirming the presence of capillary closure in the macular region. Fluorescein angiography does have a recognised morbidity, for example an anaphylactic reaction, cardiovascular collapse and death.

2.2 If retinopathy is present, it will be graded according to the standard classification and a decision made regarding management. The first line of treatment for sight-threatening retinopathy is laser photocoagulation.

2.3 The beneficial effects of laser photocoagulation for proliferative retinopathy have been recognised for many years.

2.4 The Diabetic Retinopathy Study (DRS) defined a number of risk factors which put eyes at an increased risk of visual loss, which included optic disc new vessels, peripheral new vessels of one half disc diameter or more and the presence of vitreous or preretinal haemorrhage (Reference 4). The DRS found that panretinal photocoagulation (PRP) to eyes with such risk factors effected neovascular regression and reduced the overall rate of severe visual loss over a two year period from 26% in untreated eyes to 11% in treated eyes.

2.5 While the DRS employed a standard protocol of 1200 burns in treated patients, in practice one applies the number of burns necessary to achieve a positive therapeutic outcome. On the other hand, it is recognised that if a large number of burns is applied in a single session then there is a greater incidence of laser-related side effects such as exudative retinal detachment, choroidal detachment and macular oedema.

2.6 It is therefore standard practice to perform the laser treatment in divided sessions with fewer than1000 being applied in each session. The accepted protocol for panretinal photocoagulation requires burns being applied outside of the vascular arcades (and therefore external to the macula) and for the intensity of the burns to be light in appearance. There are a variety of laser delivery systems available, including a slit-lamp mounted modality and a head-mounted laser indirect ophthalmoscope.

2.7 Unfortunately, even after full and appropriate panretinal photocoagulation, a diabetic vitreous haemorrhage and retinal detachment may occur. In this situation, if the blood does not clear sufficiently to allow laser therapy to be performed, then surgery in the form of a vitrectomy is the only therapy available. A vitrectomy is a lengthy and complex procedure, involving the use of a number of instruments that are inserted in the eye, supplementary laser therapy and the use of intraocular gas or oil as a ‘tamponading’ agent to keep the retina attached.

2.8 A subset of proliferative diabetic retinopathy has been identified, which is termed ‘florid diabetic retinopathy’ (FDR). FDR is characterised by rapid progression of the retinopathy to vitreous haemorrhage, retinal detachment and blindness. A study of the management of FDR determined that extensive and early panretinal photocoagulation and early vitrectomy where significantly reduced the risk of visual loss (Reference 5).

2.9 Gestational diabetes may also result in progression of retinopathy and screening and more frequent review of such patients is mandatory. The presence of sight-threatening retinopathy is an indication for urgent retinal laser photocoagulation. A vitreous haemorrhage, or retinal detachment may require a vitrectomy depending on the stage of pregnancy. Early induction, or a Caesarian section may be performed, to allow stabilisation of the diabetes and management of its complications (Reference 6).

2.9

With regards to diabetic maculopathy, The Early Treatment Diabetic Retinopathy Study (ETDRS) reported that if untreated, 25-30% of patients with clinically significant macular oedema exhibited doubling of the visual angle within three years (essentially significant visual loss). Focal macular laser therapy reduces the risk of such visual loss by approximately 50% (Reference 7).

2.10 The outcome of clinical trials conducted by the Diabetic Retinopathy Vitrectomy Study DRVRS Research Group clearly established the benefit of performing early vitrectomy for both severe diabetic vitreous haemorrhage and also severe proliferative diabetic retinopathy, as opposed to deferring vitrectomy for one year. With regards to patients with vitreous haemorrhage, of the early vitrectomy group in patients with Type 1, early onset diabetes 36% of eyes had reasonable vision as against only 12% in the deferral group. In the patients with severe proliferative retinopathy (advanced neovascularisation), 44% of eyes had good vision in the early vitrectomy group, versus 28% in the deferral group. The clinically relevant data arising from these studies were published between 1985 and 1990, leading to rapid adoption of their recommendations among retinal specialists (References 8 to 11).

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