Diabetic Retinopathy in Primary Care
Diabetes is one of the most serious challenges to health care world-wide. According to recent projections it will affect 239 million people by 2010-doubling in prevalence since 1994.

Diabetes will affect 28 million in western Europe, 18.9 million in North America 138.2 million in Asia, 1.3 million in Australasia.

Diabetes mellitus is the most common cause of blindness amongst individuals of working-age (20-65 years). The prevalence of blindness due to DR in Western Communities is estimated as between 1.6-1.9/100,000.

About 8% of UK BD8 registrations. (The World Health Organisation (1992) definition of blindness is vision less than 3/60 in the better eye with best available spectacle correction. 4th Leading cause of blindness globally-about 2 million blind.)
Regional projections of the prevalence of diabetes (millions) in 2010
Presentation

- About 2% of type 2 diabetics have macular oedema at diagnosis and 10.2% have other signs of DR already present when their diabetes is discovered.

- Mitchell and co-workers found that 15.8% of undiagnosed diabetics in an elderly Australian population had signs of DR, according to the recent *Blue Mountains Eye Study*. Indeed it may often take from 9-12 years for type 2 diabetes to be diagnosed.
Some Key facts

- About 95% reduction in rate of blindness - most treatable case of irreversible loss of vision.
- 12% of type 1 diabetics were blind after 30 years of diabetic life.
- Control of diabetes and hypertension is as important as laser therapy in prevention of blindness.
A classification of diabetic retinopathy

- Non-proliferative diabetic retinopathy (NPDR)/ BDR
  - Microaneurysms
  - Dot and blot haemorrhages
  - Hard (intra-retinal) exudates
  - PPDR

- Proliferative diabetic retinopathy
  Neovascularization of the retina, optic disc or iris
  Late DR- fibrovascular proliferation

- Maculopathy
  - Clinically significant macular oedema (CSME)
  - Ischaemic Maculopathy
  - Diffuse maculopathy
  - MACULOPATHY IS LEADING CAUSE OF BLINDNESS
Non-proliferative diabetic retinopathy (NPDR)
Pathogenesis of Diabetic Microangiopathy

- Hyperglycaemia causes-
  - BM thickening
  - non enzymatic glycosylation
  - increased free radical activity
  - increased flux through the polyol pathway
  - osmotic damage

- Haemostatic abnormalities of the microcirculation-
  - It has also been postulated that platelet abnormalities in diabetics may contribute to diabetic retinopathy. There are three steps in platelet coagulation: initial adhesion, secretion, and further aggregation. It has been shown that the platelets in diabetic patients are "stickier" than platelets of non-diabetics. They secrete prostaglandins that cause other platelets to adhere to them (aggregation) and blockage of the vessel and endothelial damage.
Microaneurysms

- DR IS A MICROVASCULAR COMPLICATION OF DIABETES-KEY LESION IS MICROANEURYSMS.

- Retinal microaneurysms are focal dilatations of retinal capillaries, 10 to 100 microns in diameter, and appear as red dots. They are usually seen at the posterior pole, especially temporal to the fovea.

- Beginning as dilatations in areas in the capillary wall where pericytes are absent, microaneurysms are initially thin-walled. Later, endothelial cells proliferate and lay down layers of basement membrane material around themselves.

- Fibrin and erythrocytes may accumulate within the aneurysm. Despite multiple layers of basement membrane, they are permeable to water and large molecules, allowing the accumulation of water and lipid in the retina.
Microaneurysms
Retinal Haemorrhages

- When the wall of a capillary or microaneurysm is sufficiently weakened, it may rupture, giving rise to an intraretinal haemorrhage. If the hemorrhage is deep (i.e., in the inner nuclear layer or outer plexiform layer), it usually is round or oval ("dot or blot")

- Dot haemorrhages appear as bright red dots and are the same size as large microaneurysms. Blot haemorrhages are larger lesions they are located within the mid retina and often within or surrounding areas of ischaemia.

- If the hemorrhage is more superficial and in the nerve fiber layer, it takes a flame or splinter shape, which is indistinguishable from a hemorrhage seen in hypertensive retinopathy. They often absorb slowly after several weeks. Their presence strongly suggests the co-existence of systemic hypertension.

- When an ophthalmologist sees numerous splinter haemorrhages in a diabetic patient, the patient's blood pressure must be checked because a frequent complication of diabetes is systemic hypertension.
Cotton wool spots result from occlusion of retinal pre-capillary arterioles supplying the nerve fibre layer with concomitant swelling of local nerve fibre axons. Also called "soft exudates" or "nerve fibre layer infarctions" they are white, fluffy lesions in the nerve fibre layer. Fluorescein angiography shows no capillary perfusion in the area of the soft exudate. They are very common in DR, especially if the patient is also hypertensive.
Cotton Wool Spots
Hard exudates (Intra-retinal lipid exudates)

- Hard exudates (Intra-retinal lipid exudates) are yellow deposits of lipid and protein within the sensory retina. Accumulations of lipids leak from surrounding capillaries and microaneurysms, they may form a circinate pattern. Hyperlipidaemia may correlate with the development of hard exudates.
Hard exudates (Intra-retinal lipid exudates)

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Non-proliferative diabetic retinopathy (NPDR)
Late non proliferative changes-
Preproliferative DR

Intra-retinal microvascular abnormalities (IRMA) are abnormal, dilated retinal capillaries or may represent intraretinal neovascularization which has not breached the internal limiting membrane of the retina.

- They indicate severe non-proliferative diabetic retinopathy that may rapidly progress to proliferative retinopathy.
- Venous beading has an appearance resembling sausage-shaped dilatation of the retinal veins. It is another sign of severe non proliferative diabetic retinopathy.
- Blot heamorrhages +++
Late non proliferative changes
Proliferative diabetic retinopathy

- Retinal ischaemia due to widespread capillary non perfusion results in the production of vasoproliferative substances and to the development of neovascularization. Neovascularization can involve the retina, optic disc or the iris (rubeosis iridis)
Rubeosis iridis is a sign of severe proliferative disease, it may cause intractable glaucoma.

Bleeding from fragile new vessels involving the retina or optic disc can result in vitreous or retinal haemorrhage. Retinal damage can result from persistent vitreous haemorrhage.

Pre-retinal haemorrhages are often associated with retinal neovascularization, they may dramatically reduce vision within a few minutes.
Proliferative diabetic retinopathy
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Proliferative diabetic retinopathy

- Bleeding into vitreous from new vessels, a common occurrence in proliferative disease.
Iris Neovascularisation
Late Disease

- Contraction of associated fibrous tissue formed by proliferative disease tissue can result in deformation of the retina and tractional retinal detachment.
Late Complications
Diabetic Maculopathy and Macular Oedema

- Diabetic Maculopathy is now the leading cause of legal blindness in diabetics in Western Communities.
The Macula

- The macula subserves high resolution central and colour vision. It is horizontally oval, 5mm in diameter. The foveola forms the central floor. It has a diameter of 0.35mm. It is the thinnest part of the retina. Its entire thickness consists only of cone photoreceptors and it subserves the most acute vision.

- The macula has the highest concentration of photoreceptors and is the area where the RPE is most metabolically active and as a consequence most likely to suffer the consequence of enzymatic failure over time with the accumulation of metabolic debris and lipofuscin.
Macular Oedema

- Macular oedema is an important manifestation of DR because it is now the leading cause of legal blindness in diabetics.

- The intercellular fluid comes from leaking microaneurysms or from diffuse capillary leakage.
Macular Oedema
Macular Oedema
Ischaemic Maculopathy

- Maculopathy in type 1 diabetics is often due to drop out of the perifoveal capillaries with non perfusion and the consequent development of an *ischaemic maculopathy*.

- Ischaemic maculopathy is not uncommon in type 2 diabetics, maculopathy in this group may show both changes due to ischaemia but also retinal thickening.
Ischaemic Maculopathy
Flourescein Angiography
The current consensus of opinion from Europe and the United States is that screening for DR by suitably trained and experienced practitioners is cost effective and results in reduced morbidity due to blindness.

All diabetics over the age of 12 years should have their fundus examined annually.

www.diabetic-retinopathy-screening.nhs.uk/
Studies from the UK have shown sensitivity levels for the detection of sight-threatening diabetic retinopathy of 41-67% for general practitioners, 48-82% for optometrists, 65% for an ophthalmologist, and 27-67% for diabetologists and hospital physicians using direct ophthalmoscopy.
The direct ophthalmoscope enables adequate examination of only the posterior pole whilst the indirect ophthalmoscope provides insufficient magnification.

Slit lamp examination (using either indirect ophthalmoscopy with a convex aspheric lens or diagnostic contact lens) yields much more information by providing stereoscopic assessment of retinal thickening and proliferative retinopathy.
**Screening for DR**

- Photoscreening will not always detect subtle signs of DR, such as retinal thickening, but a success rate of 80-92% in detecting DR is claimed by researchers.
- Annual digital fundus photography is now the recommended modality of screening.
A protocol for diabetic screening and Monitoring

Type 2 diabetic patients without retinopathy should be assessed at the time of diagnosis and annually thereafter.

- Patients with diabetes and mild non-proliferative retinopathy should be assessed every 12 months by a suitably experienced practitioner.

- Screening doctors should always look, in particular, for the onset of macular oedema.

- Type 1 diabetics rarely develop retinopathy until after eight years of diabetic life. The current recommendation is that type 1 diabetics should be screened after puberty or age 12 years.
Primary ocular care of diabetics

- Just as effective as laser therapy in reducing blindness.

- Eye is the window of the soul—factors which prevent retinopathy also prevent other multi-system complications of diabetes.

- In particular there is a strong relationship between DR and nephropathy—marovascular complications may also be prevented.
Primary ocular care of diabetics

- Factors that can worsen diabetic retinopathy- and indeed the general prognosis of diabetes, include poor diabetic control, obesity, systemic hypertension, hyperlipidaemia, cigarette smoking, diabetic nephropathy, anaemia, pregnancy and cataract surgery
Glycaemic control

- It is now proven that good diabetic control may slow the development and progression of diabetic retinopathy in both type 1 and type 2 diabetes.

- Overall there was a 30% reduction in microvascular end points in the group exhibiting good glycaemic control.
The HbA1C test is currently one of the best ways to check diabetes is under control.

Coincidentally the sugar/HbA1C numbers for good control are rather similar though: sugar levels 5.5-6.5 mmols/l half an hour before meals versus 5-7% HbA1C.

When should the HbA1C be measured?

If diabetes is controlled (an HbA1C lower than 7%), every 3-6 months.
Glycated haemoglobin in relation to the risk of retinopathy in conventionally treated (top) and intensively treated patients.
Aetiology and pathogenesis of the development of obesity and non-insulin dependent diabetes mellitus
American Heart Association
Recommendations 2000

- At least five servings of fruits and vegetables daily.
- Six or more servings of whole grains and legumes (beans).
- Six ounces of lean meat or poultry per day.
- At least two servings of fatty fish, such as tuna or salmon per week.
- No more than one alcoholic drink per day for women and two for men, for those who consume alcohol.
- To prevent weight gain, the new guidelines also recommend at least 30 minutes of brisk walking daily. The walking can be done all at once or in segments throughout the day.
- The guidelines also stress the importance of preventing obesity, which research has shown can contribute to medical problems such as diabetes, high blood pressure and heart disease. The association's diet plan recommends a gradual weight loss no more than one to two pounds per week using a simple process of cutting calories and increasing exercise.
Tightening of glycaemic control may initially produce worsening of retinopathy. The postulated mechanism includes lowering of retinal blood low or overproduction of IGF-1 by the liver.

It is therefore recommended that monitoring of retinopathy is increased if major changes to glycaemic control are made particularly in previously poorly controlled diabetics. Ideally glycated haemoglobin (HbA1c) should be maintained below 7%.
Recent literature indicates that there is a striking correlation between the presence of systemic hypertension and progression of diabetic retinopathy.

It is important to note that many type 2 diabetics will need a combination of anti-hypertensive agents to lower their blood pressure.
Hypertension
Systemic hypertension and DR in type 2 diabetes

- The hypertension in diabetes study was launched within the original UKPDS study in 1987.

- The study compared diabetics whose blood pressure was tightly controlled (BP < 150/85) with ACE inhibitors and beta blockers with a cohort whose blood pressure was less tightly controlled. (BP < 180/95) Median follow up was 8.4 years.

- The reduction of macrovascular events was significant with a 32% reduction in diabetes related deaths. There was a 44% reduction in stroke and a 34% reduction in overall macrovascular disease.

- UKPDS is a unique study in that it also looked at microvascular end points in type 2 diabetics. Overall the tight control group had a 37% reduction in microvascular disease.

- This effect was manifested as a reduction of the risk of having to undergo laser photocoagulation by 34%.
Systemic hypertension and DR in type 2 diabetes

- The risk of reduction of visual acuity was lowered by 47%.

- Atenolol and Captopril were equally effective in reducing the risk of progression of retinopathy in type 2 diabetics.

- The Hypertension Optimal Treatment (HOT) study indicates that the lowest incidents of cardiac events occurs when blood pressure is lowered to 82.6 mmHg diastolic and 136 mmHg systolic.
Systemic hypertension and DR in type 2 diabetes

- Each 1 mmHg of blood pressure rise causes a 1.3% increase in the number of problems that may develop.
- Target BP 130/80
Angiotensin Converting Enzyme (ACE) inhibitors in Type 1 diabetes

- The EUCLID study is currently investigating the prophylactic treatment of type 1 diabetics with the Angiotensin Converting Enzyme (ACE) Inhibitor Lisinopril and the progression of nephropathy and other microvascular disease including DR. Preliminary reports are of a specific benefit are encouraging, with a claimed 50% reduction in progression of DR in type 1 diabetics.

- The study did not look at maculopathy - so that implications are unclear for type 2 diabetics, although no specific advantage of ACE inhibitors (Captopril) over Atenolol was seen in UKPDS.(31)
Hyperlipidaemia and diabetic maculopathy

- There is evidence in the literature that diabetics who have exudative maculopathy with extensive lipid exudes benefit from active treatment of hyperlipidaemia.
- Statins are very helpful.
Diabetic nephropathy accelerates the progression of retinopathy, especially macular oedema, *inter alia* via increased levels of fibrinogen and lipoprotein and associated hypertension.

The visual prognosis is often better if the nephropathy is treated by renal transplantation rather than by dialysis.

Any anaemia resulting from renal disease must be aggressively treated.

Diabetic retinopathy is a common prelude to the development of renal disease.
Diabetic nephropathy

Investigations

- U+E’s Creatinine
- Proteinuria
- Morning Albumin/Creatinine ratio
- Formal 24h creatinine clearance
Diabetic retinopathy may worsen during pregnancy. Screening should therefore be undertaken at confirmation of pregnancy and every two months during pregnancy if no retinopathy is present, or monthly, if retinopathy is present.

Retinal status should not preclude pregnancy since contemporary methods of management can result in satisfactory ocular and pregnancy outcomes even in the presence of advanced diabetic microvascular disease providing sufficient care is taken.
Pregnancy may accelerate the progression of diabetic retinopathy. Frequency of monitoring NPDR should therefore be increased.

Women who begin a pregnancy with no retinopathy, the risk of developing diabetic retinopathy is about 10%.

Women who begin pregnancy with poorly controlled diabetes and who are suddenly brought under strict control frequently have severe deterioration of their retinopathy and do not always recover after delivery.
The role of the ophthalmic hospital

- Monitoring DR
- Liasing with other health professionals
- Education
- Specialist therapeutics
Laser Therapy

- Laser photocoagulation causes a retinal burn which is visible on fundoscopy.
- Retinal and optic disc neovascularization can regress with the use of retinal laser photocoagulation.
Panretinal laser photocoagulation for proliferative DR

- The mainstay of treatment of diabetic retinopathy is retinal laser photocoagulation.
- Laser therapy is highly effective; the rate of severe visual loss at 2 years due to proliferative disease can be reduced by 60%.
- Rubeosis iridis requires urgent panretinal photocoagulation to prevent ocular pain and blindness from glaucoma.
Panretinal laser photocoagulation for proliferative DR
The indications for laser therapy now include CSME which is treated with a macular laser grid or treatment of focal lesions such as microaneurysms.

Early referral and detection of disease is important as treatment of maculopathy is far more successful if undertaken at an early stage of the disease process.

There is a reduction in the rate of loss of vision by 50% at 2 years with macular grid therapy.
Macular laser therapy
Complications of laser photocoagulation

Although laser therapy can be highly effective in preventing blindness, it is associated with numerous complications.

- Retinal vein occlusion can follow inadvertent photocoagulation of a retinal vein. Rarely, there may be loss of central acuity from inadvertent photocoagulation of the fovea.
- Vitreous haemorrhage can follow photocoagulation of retinal or choroidal vessels.
- There may be visual field restriction, decreased contrast sensitivity, impaired night vision or impaired colour vision.
- Visual field constriction may impair fitness to drive although ophthalmologists increasingly strive to avoid this most undesirable problem, for example by avoiding confluent laser burns.
- A recent study indicates that 88% of diabetics who have undergone laser photocoagulation would pass the Esterman binocular field test which is the legal criterion for fitness to drive in the United Kingdom, even if both eyes were treated. 42% of uniocular fields failed to make the criterion of a 120 degree horizontal field. Patients who have already lost the sight in one eye therefore have a significant chance of failing to meet legal parameters for fitness to drive in the United Kingdom.
- Headache can sometimes follow laser therapy. The headache is usually relieved with rest and simple analgesia. Glaucoma must be excluded if the headache is severe or persistent.
Cataract surgery may lead to progression of pre-existing macular oedema and proliferative diabetic retinopathy. However, cataracts may impede fundoscopy and therefore interfere with the treatment of diabetic retinopathy.

If possible, diabetic retinopathy should be treated prior to cataract surgery.
VITRECTOMY IN DIABETIC PATIENTS

- Vitrectomy, plays a vital role in the management of severe complications of diabetic retinopathy.

- The major indications are nonclearing vitreous hemorrhage, traction retinal detachment, and combined traction/rhegmatogenous retinal detachment.
BDA recommends treatment which aims for the following:

- Blood pressure levels of 140/80 mm Hg or below
- HbA1c levels of 7.0% or below
- Fasting blood glucose levels of 4 - 7 mmol/litre
- Self monitored blood glucose levels before meals between 4 and 7 mmol/
Primary care is just as effective as laser therapy in reducing blindness.

All diabetics over the age of 12 years should have their fundus examined annually.

Factors that can worsen diabetic retinopathy include poor diabetic control, obesity, systemic hypertension, hyperlipidaemia, diabetic nephropathy.
Web Sites

- www.diabeticretinopathy.org.uk
- www.eyetextbook.org.uk

Screening
- www.diabetic-retinopathy-screening.nhs.uk/

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