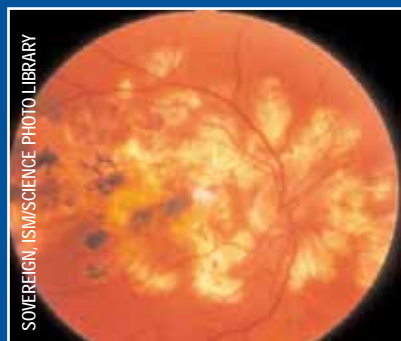




# Features of Diabetic Retinopathy and Grading Protocols

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Diabetic retinopathy is a chronic progressive sight-threatening disease of the retinal microvasculature. People with diabetes are 25 times more likely than the general population to become blind. In developed countries, diabetic eye disease represents the leading cause of blindness in adults under 65 years of age. In 2003, it was estimated that there were 194 million people, or 5.1% of the adult population worldwide with diabetes. With the epidemic of obesity that is currently being experienced in the developed world, it is predicted that this figure will rise to 333 million, or 6.3%, by 2025.

Due to the growing burden of diabetes over the past number of decades all European countries unanimously agreed the "St. Vincent Declaration" in 1989. The general goals agreed were the sustained improvement in health experience, a life approaching normal expectation in quality and quantity, and prevention and cure of diabetes, and of its complications, by intensifying research effort. A number of five-year targets were agreed, including the reduction of blindness due to diabetes by one third or more.

Screening for sight-threatening retinopathy has been shown to be effective. Screening is a simple diagnostic procedure applied to a whole population at risk to detect lesions that should be further investigated and treated. It is not a complete clinical assessment but a method to identify patients at risk who will require further examination. If a population is screened and treated, 6% of patients are prevented from going blind within a year of treatment and 34% within ten years of treatment. In addition, the costs of preventing blindness through screening for retinopathy are much

lower than those for treatment of advanced disease. The financial burden associated with the complications of diabetic visual impairment is great.

In 1989, it was estimated that an effectively managed community-based screening programme, comprising of detection, referral, treatment and follow-up could prevent 260 new cases of blindness in people with diabetes every year in those aged under 70 in England and Wales, which would represent over 10% of all cases of blindness in adults in this age group. A report in 2008 estimated this figure to have increased in England to at least 427 new cases of blindness each year.

## Diabetic Eye Disease

Ophthalmic findings in diabetic patients include a decrease in corneal sensitivity which increases the risk of corneal ulceration. There is an increased incidence of cataract formation particularly of the nuclear and cortical subtypes. A snowflake cataract is a feature occasionally observed in younger diabetic patients. In addition, a rare form of "osmotic" reversible cataract occurs in young

diabetic patients including infants. This cataract occurs due to rapid changes in fluid electrolyte balance in severe uncontrolled diabetes and there is a greater incidence of primary open angle glaucoma in diabetic patients. Cranial nerve palsies particularly sixth nerve palsies are more common in diabetic patients. In addition, asteroid hyalosis is also more common in this group (Figure 1).

The prevalence of diabetic retinopathy increases with the duration of diabetes, and nearly all patients with Type 1 diabetes and more than 60% of those with Type 2 have some retinopathy after 20 years. Diabetic retinopathy is worsened by concomitant hypertension, hyperlipidaemia, pregnancy and renal disease. Sustained hyperglycaemia increases the progression of diabetic retinopathy. Obesity, smoking and physical inactivity have been linked with the advancement of diabetic retinopathy. Age of onset of diabetes is an independent risk factor for the development of retinopathy.

Loss of vision from diabetic retinopathy may be as a consequence of either retinal neovascularisation or

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secondary to diabetic maculopathy. Growth of new vessels leads to intraocular haemorrhage, subsequent fibrosis and tractional retinal detachment. This results in profound visual loss. Maculopathy leads to a loss in central visual acuity. This is the main cause of visual loss in persons with diabetes and may be profoundly debilitating.

### Pathophysiology

The vascular disruptions observed in diabetic patients are characterised by abnormal vascular flow, disruptions in permeability with closure or non-perfusion of capillaries. Early diabetic changes are the formation of microaneurysms. These initial lesions are focal and located preferentially at the posterior pole of the retina. The microaneurysms form within the inner nuclear layer of the retina in capillaries linking the superficial and deep capillary networks. They range in diameter from 12 to 100 microns but only those greater than 30 microns in diameter can be detected on ophthalmoscopy.

Endothelial cells are responsible for maintaining the blood-retinal barrier. Endothelial damage results in an increased vascular permeability. When there is breakdown of the inner blood-retinal barrier, this results in an accumulation of extracellular fluid in the macula, termed macular oedema. The pericytes surrounding the microcirculation are important in autoregulation of the retinal blood supply. In diabetes, these cells become abnormal and the retinal blood supply is not correctly regulated. Loss of pericytes leads to the development of outpouchings or microaneurysms of the small vessels. Thickening of the capillary basement membrane occurs and this is secondary to an increased deposition of extracellular matrix components.

With progression of diabetic retinopathy, there is an increased number of microaneurysms observed in the venous side of the circulation. Ruptured microaneurysms, capillaries and venules are all sources of intraretinal haemorrhages, which are mostly located within the outer plexiform and the inner nuclear layers.

Diabetic Retinopathy (DR) Severity Level	Findings Observable with Dilated Ophthalmoscopy
No apparent DR	No abnormalities
Mild nonproliferative DR	Microaneurysms only
Moderate nonproliferative DR	More than "mild" but less than "severe"
Severe nonproliferative DR	Any of the following: 20 or more intraretinal haemorrhages in 4 quadrants Definite venous beading in 2 or more quadrants Prominent IRMA in 1 or more quadrants and no neovascularisation
Proliferative DR	1 or more of the following: Definite neovascularisation Preretinal or vitreous haemorrhage

➔ **Table 1**

International Clinical Diabetic Retinopathy (DR) Disease Severity Scale

Deep haemorrhages are dots and blots while superficial ones in the nerve fibre layer are flame-shaped. A predominance of flame-shaped haemorrhages indicates concomitant venous obstruction or arterial hypertension.

Important pathophysiological changes observed in diabetic retinopathy include thickening of the

basement membrane and stasis of leucocytes (white blood cells). Leucocytes become less deformable and are activated in diabetes. They then adhere to the vascular endothelium and generate superoxide radicals and proteolytic enzymes. They interact with platelets which tend to become stickier and aggregate. Erythrocytes are deformed and have



➔ **Figure 1**  
Asteroid Hyalosis



decreased oxygen transport. These factors affect retinal endothelial function, reducing retinal perfusion, increasing angiogenesis and increasing vascular permeability.

Hard exudates are extracellular collections of lipid within the outer plexiform layer, derived from leakage of serum from the abnormal vessels. They are yellowish and vary in size. They may be confluent or arranged in a circinate pattern around a cluster of microvascular abnormalities. Cotton wool spots are secondary to obstructed axoplasmic flow.

Early changes in diabetic retinopathy are primarily venous, however as the disease progresses capillaries on the arterial side of the retinal circulation also show increased cell loss and closure. Venous beading and loops develop. Beading manifests as fusiform bulges in the wall of the vein. There then follows an attenuation of vessels on the arterial side. Initially, the non-perfused area is in the midretinal periphery. As the areas of capillary non-perfusion enlarge, they are seen to be traversed by a few enlarged capillaries acting as arteriovenous shunts – intra retinal microvascular abnormalities (IRMAs) (Figure 2). As a result of capillary occlusion, retinal ischaemia stimulates a pathologic neovascularisation mediated by angiogenic factors, such as vascular endothelial growth factor (VEGF).



➔ **Figure 2**

New vessels elsewhere (NVE) and intra retinal microvascular abnormalities (IRMA)

Neovascularisation can occur on the disc (NVD) (figure 3), the retina (NVE) or the iris (NVI). Neovascular fronds may then bleed resulting in preretinal or vitreous haemorrhages. Preretinal haemorrhage are seen as localised boat-shaped haemorrhages between the posterior hyaloid face and the internal limiting membrane of the retina (figure 4). The fronds can also fibrose and contract pulling the retina with them. A tractional retinal detachment has a concave configuration. Rubeosis iridis (NVI) may subsequently lead to the development of neovascular glaucoma.

Diabetic maculopathy occurs when there is involvement of the fovea by oedema, hard exudates or ischaemia (figure 5). Clinically significant macular oedema (CSME) is defined as the presence of one or more of the following features:

- Retinal oedema within 500 microns of the centre of the fovea
- Hard exudates within 500 microns of the fovea if associated with adjacent retinal thickening
- Retinal oedema one disc area (1500 microns) or larger, any part of which is within one disc diameter (DD) of the centre of the fovea.

## Classification

There are many different systems of classification of diabetic retinopathy - two will be discussed. The first is based on the original Airlie House/Early Treatment Diabetic Retinopathy Study (ETDRS) classifications and the second is used for population screening.

The Airlie House classification system is the gold-standard assessment. It involves the grading of seven 30° stereoscopic images of the retina (7 standard fields), with each image compared with standard photographs. A score is then assigned to each eye, ranging from 10 (no retinopathy) to 85 (advanced proliferative diabetic retinopathy), and the grades for both eyes are combined into a stepped scale.

Field 1 is centred on the macula and field 2 is centred on the optic disc. Fields 3-8 two above, two below and one nasal to the disc surround fields 1 and 2. The seven fields of view are centred around the disc and macula.

Features graded in fields 2-8 include haemorrhages and/or microaneurysms, hard exudates, cotton wool spots, venous calibre abnormalities, venous sheathing, perivenous exudates, arteriolar abnormalities, IRMAs, arteriovenous nicking, neovascularisation elsewhere (NVE), fibrous proliferation, retinal elevation, preretinal haemorrhages, and vitreous haemorrhage. This is a very vigorous grading system and suitable for clinical trials such as the ETDRS.

A simplified variation of this classification has been endorsed by the American Academy of Ophthalmology (AAO) and is now in general clinical use. It describes three stages of low risk non-proliferative retinopathy, a fourth stage of severe non-proliferative retinopathy and a fifth grade of proliferative retinopathy.

In addition macular oedema is determined as either absent or present and further subclassified on the basis of involvement of the centre of the macula (Table 1).

The National Screening Committee (NSC) has adopted a classification for use in England and Wales aimed at detection of that level of retinopathy sufficiently severe to merit referral of the patient for expert ophthalmological opinion and possible treatment. There is also a Scottish Diabetic Retinopathy Grading Scheme. The NSC classification adopts a simplified approach to grading retinopathy based on features which a non-ophthalmologist or accredited photographic grader might be faced with in a population of diabetic patients. This classification identifies four types of presentation of fundal disease, namely retinopathy (R), maculopathy (M), photocoagulation (P) and unclassifiable (U) (Table 2).

There is considerable overlap between the various classifications. They all recognise the two basic mechanisms leading to loss of vision namely retinopathy and maculopathy. The differences between classifications relate mainly to levels of retinopathy and also to the terminology used.



## Management of Diabetic Retinopathy

### Primary Interventions

Control of the metabolic abnormalities of diabetes has a major effect on the development of diabetic microvascular complications. There has been a consistent relationship between elevated levels of glycated haemoglobin (HbA1c) levels and the incidence of diabetic retinopathy. The Diabetes Control and Complications Trial (DCCT) illustrated that tight glycaemic control in Type 1 diabetics reduced both their incidence and also the progression of diabetic retinopathy. The United Kingdom Prospective Diabetes Study (UKPDS) reported similar findings in Type 2 diabetes. Any reduction of HbA1c is beneficial in reducing the development of new and progression of existing retinopathy. If retinopathy is present HbA1c should be maintained at a level below 7%.

Rigid control of hypertension is also effective in reducing disease progression. Hypertension has been found to be very important in determining the chances of developing retinopathy in observational studies. In Type 1 patients, antihypertensive treatment with ACE inhibitors resulted in a 23% reduction in the progression of retinopathy.

Hyperlipidemia has been linked to the presence of retinal hard exudates in patients with diabetic retinopathy. Lipid-lowering agents may also reduce the number of hard exudates and microaneurysms.

Progression of diabetic retinopathy may occur during pregnancy. The worsening retinopathy during pregnancy can be quite significant and patients may require photocoagulation whilst pregnant. This occurs more frequently in those patients with pre-existing diabetic retinopathy and if there has been poor metabolic control and concomitant hypertension.

Patients with a normal retinal examination should be re-examined annually because within one year 5-10% of patients will develop diabetic retinopathy. Existing retinopathy will worsen by a similar percentage.



➔ **Figure 3**

Preretinal gliosis and florid new vessels on the disc (NVD)

### Secondary Intervention

Laser photocoagulation is used to treat both proliferative diabetic retinopathy and diabetic macular oedema. The goal of macular laser photocoagulation is to limit vascular leakage through a series of light focal laser burns in regions of diffuse breakdown of the blood-retinal barrier (Figure 6). Treatment is normally delivered via a slit-lamp/contact lens system involving topical corneal anaesthesia and placement of a hand-held contact lens. Green or yellow laser light is used to minimise light absorption at the fovea. Blue laser light is contraindicated as it is preferentially absorbed by xanthophyll at the fovea. Macular laser photocoagulation reduces the risk of vision loss by 50% for patients with clinically significant macular oedema. A fluorescein angiogram prior to treatment helps to delineate the presence of capillary non-perfusion at the fovea. An ischaemic fovea is a contraindication to macular laser

photocoagulation. Where focal areas of leakage are identified, laser burns are directly applied to the leaking microaneurysms. However, only 15% of eyes show an improvement of visual acuity. Despite treatment, vision subsequently deteriorates in 14% of cases. Macular oedema can be quantified by using Optical Coherence Tomography.

Panretinal photocoagulation (PRP) for proliferative disease acts to ablate ischaemic areas of the peripheral retina and thereby reduce the induction of angiogenic growth factors such as VEGF. It has been shown that PRP significantly reduces the risk of severe vision loss from proliferative diabetic retinopathy by at least 50%. The extent of treatment is dependent on the severity of the proliferative diabetic retinopathy. Side effects following ablation of the photoreceptors include constriction of visual fields and difficulties with night vision. This can be severe enough to disqualify a patient



➔ **Figure 4**  
Boat-shaped preretinal haemorrhage

from driving. PRP may worsen pre-existing macular oedema and it is advised to treat any maculopathy before proceeding to PRP. Diffuse choroidal oedema is a complication of treatment and may result in a choroidal detachment.

In more severe cases of diabetic retinopathy, specifically those with tractional retinal detachment or severe non-clearing vitreous haemorrhage, vitrectomy is indicated to prevent blindness and/or severe visual loss. In addition, PRP can be applied during pars plana vitrectomy to treat the underlying proliferative diabetic retinopathy. This is typically performed intraoperatively using a fibre optic endolaser probe. Visual results following vitrectomy are dependent on the indication for vitrectomy. Approximately 70% of cases obtain a visual improvement, about 10% are made worse and the remainder have no change in vision. Factors associated with a favourable prognosis include a) good pre-operative visual function, b) young age, c) absence of pre-operative rubeosis/glaucoma and d) pre-existing PRP. The Diabetic Retinopathy Vitrectomy Study (DRVS) showed that early vitrectomy for Type 1 patients with severe vitreous haemorrhage was

beneficial. There was no advantage observed in Type 2 patients.

Intravitreal triamcinolone acetonide (IVTA) is increasingly being used as an off-label adjunctive treatment of diabetic macular oedema. Sustained release devices delivering intravitreal corticosteroids are also in use. Corticosteroids may work through multiple mechanisms of action. In addition to their well-known anti-inflammatory effects, corticosteroids may cause downregulation of VEGF. Complications of IVTA include cataract, raised intraocular pressure and the risk of endophthalmitis. The beneficial effect of IVTA is quick in onset but is transient in nature.

Bevacizumab (Avastin) is a full-length recombinant humanised antibody active against all isoforms of VEGF-A. It was developed as an adjunctive systemic treatment for metastatic colorectal cancer. A small number of studies report it to be effective in the treatment of proliferative diabetic retinopathy and oedema. Its effects are not sustained.

Ranibizumab (Lucentis) is a recombinant, humanised fragment of a monoclonal IgG antibody containing the antigen binding sequence capable of binding and inhibiting all isoforms of

VEGF-A by preventing VEGF-A molecules from binding normally to their receptors on endothelial cells. It was developed for the treatment of choroidal neovascular changes in AMD. Avastin and Lucentis are both derived from the same murine monoclonal IgG antibody against VEGF-A. The main difference at the molecular level between Avastin and Lucentis is that Avastin is a full length antibody engineered from a humanised Fab (antigen binding) fragment. Avastin is therefore a larger molecule (150kd) with two antigen binding sites (Fab) and Lucentis is a much smaller molecule (48kd) with one binding site. Pegaptanib (Macugen) may also be used as an anti-VEGF agent.

In patients with diabetic macular oedema not responsive to photocoagulation, either IVTA or an intravitreal anti-VEGF agent may be considered as second-line treatments. In patients with complications of proliferative diabetic retinopathy not amenable to photocoagulation, intravitreal anti-VEGF agents may produce short-term stabilisation or regression of iris and/or retinal neovascularisation. In most patients, however, photocoagulation will eventually be necessary.

## Screening & Grading

Screening for diabetic retinopathy fulfils the Wilson and Jungner criteria for a screening programme. These criteria have formed the basis of the UK NSC criteria for appraising the viability, effectiveness and appropriateness of a screening programme. It is recognised that screening for diabetic retinopathy is different from screening for other diseases because screening is to prevent the development of complications in existing patients rather than detection of early disease in healthy populations. However, it still comes under the remit of the NSC.

The Liverpool Declaration from 2005 declares that "European countries should reduce the risk of visual impairment due to diabetic retinopathy by 2010 by systematic programmes of screening reaching at least 80% of the population with diabetes; using trained



**Retinopathy (R)**

*Level 0*

- None

*Level 1 Background*

- Microaneurysm(s)
- Retinal haemorrhage(s) ± any exudate

*Level 2 Proliferative*

- Venous beading
- Venous loop or reduplication
- Intraretinal microvascular abnormality (IRMA)
- Multiple deep, round or blot haemorrhages (Cotton wool spots - careful search for above features)

*Level 3 Proliferative*

- New vessels on disc (NVD)
- New vessels elsewhere (NVE)
- Preretinal or vitreous haemorrhage
- Preretinal fibrosis±tractional retinal detachment

**Maculopathy (M)**

- Exudate within 1 disc diameter (DD) of the centre of the fovea
- Circinate or group of exudates 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 VA of (if no stereo) 6/12

**Photocoagulation (P)**

- Focal grid to macula
- Peripheral scatter

**Unclassifiable (U)**

➔ **Table 2**

National Guidelines on Screening for Diabetic Retinopathy

professionals and personnel; and universal access to laser therapy". The main goals when screening for diabetic retinopathy are the detection of the first signs of early retinopathy to evaluate the progression of retinopathy and, above all, to detect severe treatment-requiring lesions. With early identification, prompt incorporation into the health care system, adequate education of the patient, regular lifelong evaluation, appropriate referral, and timely treatment, the vast majority of severe visual loss can be prevented. Screening is a process which requires reporting and quality assurance and is not a function of the GOS sight test.

In 2000, Garvican, Clowes and Gillow reported the findings of a group commissioned by the NSC to develop a model and cost estimates for a comprehensive national risk-reduction

programme for diabetic retinopathy. A systematic national programme based on digital photography was proposed. Digital fundus photographs have the advantage that they can be obtained at minimal cost and inconvenience for the patient. Disadvantages of screening and grading encountered using digital photography compared to slit lamp examination include media opacities or small pupil size. There is also a difficulty in distinguishing retinal thickening without hard exudates in nonstereoscopic digital images - the direct ophthalmoscope is limited in this respect as it offers a two-dimensional view. In addition, the small field of view offered by a direct ophthalmoscope also limits its usefulness as a screening tool.

Systematic screening programmes using digital fundus photography are now in place across England, Scotland, Wales and Northern Ireland. The NSC has determined that the method of screening for England and Wales is digital photography through dilated pupils. Scotland has adopted a non-mydriatic protocol with the option of pupil dilatation if images are poor. There is a recommended threshold of a minimum 80% sensitivity and 95% specificity for detecting mild

retinopathy. Screening should be offered on an annual basis to all diabetic patients over the age of 12 years. Patients who become pregnant need more frequent screening. The scale of the management task for handling retinal photographs for the English Screening Programme alone is huge. There will be approximately 2,000,000 retinal image sets that require grading each year.

In order for a screening programme to be effective, it has to meet stringent National Clinical Standards to ensure safety and quality. These include that the screening test must comprise digital photography, the screening staff should be appropriately trained and a clinical lead and programme manager are required to be in place. Positive screening tests must be appropriately followed-up and there must be good links to both hospital and primary care. People with diabetes have to be invited to screening annually and the uptake rate must be at least 70%. A screening programme must cover at least 12,000 people with diabetes. There needs to be a call and recall process from a comprehensive managed list of those covered by the programme. The digital imaging must be of an appropriate standard, with suitable viewing, storage



➔ **Figure 5**  
Advanced maculopathy



➔ **Figure 6**  
Large laser photocoagulation scars with foveolar damage

and compression. Finally, a diabetic screening programme must participate in quality assurance.

A mobile retinal photography service can provide an acceptable screening service. The "gold standard" consists of seven 30-degree fields using stereoscopic pairs. This requires two frames from each field to simulate a stereoscopic view; thus fourteen frames from each eye are needed. It has been shown that reducing this to two 45-degree fields per eye does not significantly alter the results whilst reducing the cost, complexity and the time spent. The photographs can be taken by a mobile unit with a camera and a technician and be later assessed by a trained reader or may be taken in a fixed unit. Mobile units are useful for rural areas. In the community, the optometrist is ideally placed to be involved in the screening process as he/she can be both a screener and a grader. The Scottish criteria for an appropriately taken photograph include a 45 degree view, the entire optic disc to be displayed and that the fovea is two DDs from the edge of the image. The clarity of the photograph must be sufficient so that the third generation of branching vessels are visible around the fovea. In England, Northern Ireland

and Wales, the requirement is that there are both a disc centred image as well as a macula centred image taken. In the macular image, the centre of the fovea should be  $\leq 1$ DD from the centre of the image, and the vessels should be clearly visible within 1DD of the centre of the fovea, as well as vessels visible across  $>90\%$  of the image. In the disc centred image, the centre of the optic disc should be  $\leq 1$ DD from the centre of the image. There should be fine vessels clearly visible on the surface of the disc as well as vessels visible across  $>90\%$  of the image.

In primary grading, the responsibility is to detect retinopathy and to flag any other gross conditions such as glaucoma or choroidal tumours. In secondary grading, all of the images graded as containing signs of retinopathy, together with 10% of those graded as normal are graded by the secondary grader. Tertiary grading is performed by an ophthalmologist. The Level 3 Certificate in Diabetic Retinopathy Screening is awarded by City and Guilds. It contains three mandatory units and a further three units which can be chosen from a group of six units. Exemptions from certain units are awarded to optometrists.

One of the earliest uses of computers

to aid the clinician in retinal screening was proposed in 1964 by Monnier et al who analysed the response of the retina to different frequencies of light. The techniques needed for automatic retinal screening using digital retinal images have now progressed substantially. The replacement of manual grading with automated software has been proposed.

## Conclusion

Diabetic retinopathy is becoming more prevalent in our population. Screening for diabetic retinopathy significantly reduces the risk of sight threatening disease. It is important that patients are educated to understand the need for annual ophthalmic examinations. By controlling their blood glucose, blood pressure and cholesterol levels, patients will have less severe diabetic eye disease. The diabetic screener has an important role in patient education.

## About the author

Louise O'Toole is a consultant medical ophthalmologist in the Mater Private Hospital, Eccles Street, Dublin.

## Further Reading

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## Module questions

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Please note, there is only one correct answer. Enter online or by the form provided

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- 1) Which one of the following is correct?
- almost 1% of the adult population have diabetes
  - people with diabetes are 5 times more likely than the general population to become blind
  - screening has been shown to reduce 34% of patients from becoming blind over a ten year period
  - there are 42 new cases of blindness related to diabetes per annum
- 2) Ocular features of diabetes include all of the following except:
- snowflake cataract
  - oil drop cataract
  - asteroid hyalosis
  - an increased risk of primary open angle glaucoma
- 3) All of the following increase the risk of diabetic retinopathy progression except:
- pregnancy
  - duration of disease
  - renal disease
  - aspirin
- 4) Which one of the following is incorrect? In diabetic retinopathy, there is:
- a loss of pericytes
  - an increase in VEGF levels
  - thickening of basement membranes
  - infiltration of giant cells into the vessel wall
- 5) Which one of the following is correct regarding diabetes?
- the Airlie House classification is based on a single macula centred fundus image
  - background retinopathy is the last stage in the International Clinical Diabetic Retinopathy Disease Severity Scale
  - changes in venous calibre do not carry any significance
  - two photographs per eye are required to allow classification and grading in England
- 6) Which one of the following is correct regarding laser treatment?
- blue light is favoured for parafoveal laser
  - treatment is mandatory for all ischaemic foveas
  - treatment is reversible
  - in focal areas of leakage, laser burns are applied directly to the leaking microaneurysms
- 7) Which one of the following is incorrect? Anti-VEGF agents are:
- used in the treatment of age related macular degeneration
  - injected into the vitreous
  - used in the treatment of diabetic eye disease
  - injected into the arm
- 8) Common complications of intravitreal triamcinolone include all of the following except:
- endophthalmitis
  - cataract
  - glaucoma
  - uveitis
- 9) Side effects associated with panretinal photocoagulation include all of the following except:
- constriction of visual fields
  - difficulties with night vision
  - choroidal detachment
  - rubeosis
- 10) Which one of the following is incorrect regarding diabetic maculopathy?
- hard exudates have been linked to hyperlipidaemia
  - diabetic maculopathy may be ischaemic
  - diabetic maculopathy may be worsened by panretinal photocoagulation
  - maculopathy is not a feature of Type 2 Diabetes
- 11) Which one of the following is incorrect? Clinically significant macular oedema is defined as:
- retinal oedema within 500 microns of the fovea
  - retinal oedema 1000 microns or larger, any part of which is within one disc diameter of the fovea
  - hard exudates within 500 microns of the fovea is associated with retinal thickening
  - retinal oedema and exudates within 500 microns of the fovea
- 12) Which one of the following is incorrect? In diabetic screening:
- patients should be screened annually
  - digital photography is the preferred method
  - there is a recommended threshold of 80% sensitivity and 95% specificity
  - patients under the age of 10 years should be included

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