# Diabetic Retinopathy

Diabetes can be classified into type 1 diabetes mellitus and type 2 diabetes mellitus, formerly known as insulin-dependent diabetes mellitus, and non-insulin diabetes mellitus, respectively. In type 1 there is an absolute deficiency of insulin whereas type 2 has a relative insulin resistance combined with a component of insulin secretory deficiency.

Diabetes affects all organ systems in the body but we most commonly think of the major systems like cardio-vascular, cerebro-vascular , reno-vascular, neuro-vascular and retinal vascular. Each of these systems comprise the primary pathologies that we see in our patients on a daily basis. Examples of these comorbidities include myocardial infarction, cerebrovascular accidents (stroke), paresthesias, renal compromise and vision loss.

Overall, Type 1 diabetes makes up about 5-10% of patients with diabetes. Type 2 makes up the other 90-95% if diabetics. The retinopathy will have differing prevalence in these 2 groups. For instance, although 30% of type 2 diabetics will have some type of retinopathy at the time of diabetic diagnosis, it is rare to see retinopathy in type 1 diabetics at the initial diagnosis. Additionally, 50% of type 2 diabetics on no insulin will have retinopathy after 15 years but 90% of type 1 diabetics will have retinopathy after the same time period. Overall, diabetes is a common cause of blindness in the United States and is the leading cause in the 20-64 year old age group.

The cause of vision loss is traced back to the retinal vascular changes that occur at the cellular level. It is generally felt that the hyperglycemic environment leads to vascular endothelial damage manifested by basement membrane thickening and loss of pericytes. This leads to vascular leakage, capillary occlusion and ultimately retinal ischemia. The duration of diabetes and degree of hyperglycemia are important factors in the development of diabetic retinopathy. Additional systemic comorbidities can contribute to the expression of disease such as hypertension, lipid disorders, pregnancy, anemia and preexisting cardiac and renal disease.

Diabetes and diabetic retinopathy has been the subject of many important studies such as DCCT, UKPDS, DRS, ETDRS, DVS, and most recently DRCR.net. These studies represent groundbreaking studies with significant implications in the management of diabetes and diabetic retinopathy. These studies will be outlined in a later monograph.

## ***Evaluation of the Diabetic Patient in the Ophthalmology Office Setting***

History taking is an essential part of the examination for all patients. The diabetic patient requires specific attention to other organ systems specifically linked to known comorbidities. A query of cardiovascular events, diagnostic testing including carotid and cardiac studies, renal function, serum lipid profiles, hypertensive duration and degree, serum hemoglobin and hematocrit and pregnancy status are important to document.
Duration and type of diabetes can help to understand the patients' risk for retinopathy. Glycemic control as represented by blood glucose level and A1C give the care provider an understanding of the degree of recent disease control. Asking not only the most recent numbers but a detailed history of these two parameters will give the clinician a quantitative historical perspective.

Documentation of visual symptoms such as blurred vision, distortion and floaters can correlate and support the other clinical components. For instance, a phakic patient with poor glycemic control who complains of episodes of blurred vision within a timeframe of hours to days may correlate with variations in serum glucose recorded by the diabetic.

***Clinical Retinal Findings in the Diabetic Patient***

Disease progression in the diabetic patient is characterized by a spectrum of disease ranging from no diabetic retinopathy, mild NPDR, moderate NPDR, severe NPDR to Proliferative Diabetic Retinopathy (PDR).

NPDR, in its different forms, have the one common characteristic that the findings are confined to the retina and do not extend beyond the border created by the retinal internal limiting membrane (ILM). The clinical manifestations include retinal microaneurysms, hemorrhages, nerve fiber layer infarctions (CWS), exudates, edema, venous and arterial changes, and intra retinal microvascular abnormalities (IRMA). Mild, moderate and severe forms of NPDR are characterized by an increasing number of these clinical findings. The increase can indicate increasing retinal damage and therefore increasing risk to vision.

The two major threats to vision in NPDR are macular edema and macular ischemia. The anatomic vascular changes correlate with vascular basement membrane thickening and pericyte loss seen on the cellular level. This leads to increasing vascular permeability manifested by leakage of both the serous and lipid components of blood. As the vascular damage continues there is capillary closure and retinal injury. Clinically, increased permeability and capillary closure will appear as retinal thickening (edema) and retinal ischemia, respectively. The anatomic proximity and size of edema and ischemia relative to the foveola will correlate with the threat to vision.

PDR is characterized by retinal vascular pathology that extends outside the internal limiting membrane. This extraretinal fibrovascular proliferation evolves through stages and the grading system of PDR is stratified into early, high risk or advanced PDR. The criteria for this system, depends on the components of neovascularization on or near the disc (NVD), elsewhere (NVE) and the presence of hemorrhage in the vitreous or preretinal space. The threat to vision at this stage is additive to the edema and ischemia that is seen in NPDR. Hemorrhage into the preretinal or vitreous space by the fragile new vessels can lead to floaters or if severe, loss of vision. Fibrovascular proliferation with contraction of membranes can cause traction retinal detachments, combined rhegmatogenous/traction retinal detachment and ultimately loss of vision if allowed to proceed along its natural course. When the ischemia is sufficient, the development of NV of the iris (NVI) or trabecular meshwork (NVA) in the anterior segment can also occur. It is important to discover these findings early since secondary glaucoma and anterior segment scarring complications can be avoided with early detection and treatment.

***Clinical Diagnostic Studies for Diabetic Retinopathy***

Fundus Photography is a noninvasive method to document the wide spectrum of retinal and vascular changes in the posterior pole and midperiphery of the posterior segment. Comparative sequential photographs are a helpful tool to document and estimate rate-of-change over time. Comparison of current clinical findings to initial photographs can help to determine effectiveness of treatment and provide guidance for further interventions.

Fluorescein Angiography (FA) is a retinal vascular diagnostic study currently requiring the injection of an intravascular dye. This study can be done in the office with a good safety profile for the patient and an excellent yield of information pertinent to the stage and degree of retinal vascular compromise. It is suited to look at the retinal vascular system with digital imaging not involving x-ray radiation. It yields information about the choroidal circulation during the early portion of the study and the retinal circulation in all phases of the study. The retinal vascular injury is illustrated on the FA with changes in the conformation of the arteries and veins, the presence of microaneurysms and the non-leaking IRMA seen in more advanced NPDR. In nonproliferative diabetic retinal disease there is injury to blood vessels resulting in edema and ischemia. These are demonstrated on the FA as increasing diffuse hyperfluorescence, and as areas of hypofluorescence, respectively.

Optical Coherence Tomography (OCT) is a structural analysis of the preretinal space, retina, subretinal space and RPE. The resolution and depth of study is improving with advancements in technology and continues to evolve. OCT in its current form is a non-invasive method to study the presence or absence of fluid within or beneath the retina. It can also reveal if there is distortion of the RPE and subRPE space. With higher resolution, the study of the retinal layers and even individual cells are becoming possible. Currently, OCT provides easily accessible, quantifiable measurements of subretinal fluid, retinal thickness and overall retinal elevation among many parameters. The presence of edema as intraretinal fluid can be characterized and used to document the need for treatment as well as the tissue response to treatment.

***Treatment of Diabetic Retinopathy***

The treatment of diabetic retinopathy is quickly evolving regarding both the systemic management and locally, in the eye. The original DCCT and UKPDS gave us initial guidance on the importance of glycemic control. These studies illustrated that glycemic control had a positive impact on ocular and nonocular tissues such as neuropathy and nephropathy. Our understanding of the impact of systemic management of disease has evolved so that now our history includes documentation of not just blood sugars and A1C, but also BMI, lipid profile, blood pressure, cholesterol and renal function. Communication with primary care providers, endocrinology, cardiology, nephrology and other subspecialists has become standard in the care of diabetic patients. This result emphasizes that the management of diabetic eye disease includes a coordinated systemic management of risk factors.

Since macular edema is a primary cause of decreased vision much study has been devoted to the treatment of diabetic macular edema. Early on, the ETDRS guided our use of macular laser. Treatment guidelines were introduced and prognostic guidance was provided. More recently, the use of injectable agents including steroids and anti-VEGF agents has been shown to be beneficial and the recommendations are quickly being updated and intravitreal injections are a mainstay of treatment. Pars plana vitrectomy has been used in the past for diabetic macular edema and its use is still being studied. The DRCR.net has shown using PPV for edema reduced mean retinal thickness but that median visual acuity was unchanged over the follow up period.

PDR, with the development of neovascularization secondary to ischemia and the potential for subsequent complications of vitreous hemorrhage and neovascular glaucoma, has been clinically responsive to laser photocoagulation. The DRS showed that there is a reduction in severe vision loss in eyes treated with laser when compared to no treatment. This is still

the mainstay of treatment. If there is non-clearing vitreous hemorrhage precluding the use of laser for PDR, laser can be combined with pars plana vitrectomy (PPV). When tractional elements occur in association with traction retinal detachments, PPV with membrane dissection and release and laser photocoagulation is indicated.

***Diabetic Eye Examinations***

Pt education regarding their ocular and systemic health is important and should be a part of their encounter with each of their healthcare providers. Coordination and communication between providers allows better care and the potential for optimized outcomes.

Currently, Type 1 diabetics should be seen 3-5 years after initial diagnosis and then annually. If there is mild to moderate NPDR then the interval decreases to every 6-12 months with shorter intervals (2-4 months) if there is macular edema or if scatter PRP needs to be considered. Type 2 diabetics should have the initial exam at the time of diagnosis and then annually if there is no diabetic retinopathy. Once there is diabetic retinopathy, the same schedule should be followed as for Type 1 diabetics. In pregnancy, the diabetic should be seen in the first trimester and then if mild-NPDR or greater, at 1-3 month intervals dependent on the degree of severity.

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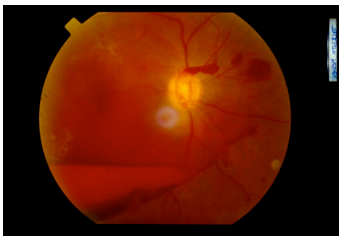

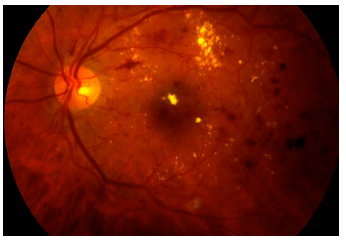

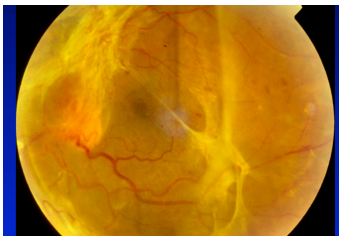

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**Answer Questions, scan and e-mail to: debbieosborn36@yahoo.com for CME:**

1) Diabetic retinopathy is a multisystem disease that affects the:
- heart
- kidney
- retina
- brain
- all of the above

2) Diabetic management includes coordinating care with:
a) no other providers
b) primary care providers
c) legislators
d) friends and neighbors

3) Important parameters to follow in diabetic patients is/are:
a) Hgb A1C
b) daily blood sugar
c) lipid profile
d) blood pressure
e) all of the above

4) True or False. The patient History is an integral part in the evaluation of the diabetic patient.
a) True
b) False

5) NPDR is associated with all of the findings except:
a) microaneurysm
b) retinal hemorrhages
c) neovascularization
d) IRMA

6) One of the primary reasons for vision decline in the NPDR patient is:
a) macular ischemia
b) tractional retinal detachment
c) severe neovascular glaucoma
d) IRMA

7) PDR is associated with:
a) early Type 1 diabetes
b) good control of diabetes and disease duration of less than 3 years
c) cataracts
d) new vessels that extend beyond the internal limiting membrane

8) Important components of patient education include all of the following except:
   a) glucose control
   b) management of serum lipids
   c) optimizing systemic hypertension
   d) keeping follow up appointments
   e) all of the above choices are important

9) The recommended eye examination schedule includes:
   a) no particular time for initial examination
   b) there is no variance for the presence for macular edema
   c) Type 2 diabetics should have an initial examination at the time of diagnosis
   d) Type 1 and Type 2 diabetics have exactly the same recommended schedule

10) True or False. Diabetes is the leading cause of blindness in the 20-64 year old age group.
   a) True
   b) False

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