

# Diabetic Retinopathy

## A major sight threatening disease



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**D**iabetes mellitus affects several organ systems, particularly the kidneys, the peripheral nerves, and the eyes. The retinal lesions of diabetes are the leading cause of blindness in working-age patients. Much of this blindness can be prevented if the retinopathy is detected early enough for adequate treatment. Unfortunately, because visual loss is often a late symptom of advanced diabetic retinopathy, many patients remain undiagnosed even as their disease is causing severe retinal damage. As a result, many patients are examined only after the optimal time for treatment has passed.

### I- PATHOGENESIS

Normal retinal vessels, including the capillaries, are impermeable to large molecules. By contrast, in the diabetic retina, the capillaries leak proteins, complex carbohydrates, and lipids. Pericytes, cells embedded in the capillary basement membrane, are lost early in diabetic retinopathy, possibly due to the action of metabolites of the sorbitol pathway. Endothelial cells are lost later. These abnormalities are followed by the formation of microaneurysms which are leaky outpouchings of the capillary walls. Other sequelae include abnormal permeability, vascular occlusion, and neovascularization.

### II-CLASSIFICATION

The effects of diabetes on the retina are reflected in progressive stages that are defined by ophthalmoscopic criteria. In the first stage, termed nonproliferative diabetic retinopathy (NPDR), retinal blood vessels leak. If there is enough leakage into the macula - the small area of the retina

responsible for sharp central vision - visual acuity is reduced.

In the second stage, called proliferative diabetic retinopathy (PDR), progressive retinal ischemia promotes the growth of fragile new blood vessels that bleed. This neovascularization, accompanied by fibrous proliferation, grows onto the posterior surface of the vitreous. Eventually, bleeding and traction cause retinal detachment and blindness.

### III- CLINICAL SIGNS

#### 1. EARLY NONPROLIFERATIVE RETINOPATHY

In early nonproliferative retinopathy, ophthalmoscopy reveals microaneurysms, hard exudates, and intraretinal hemorrhages. Microaneurysms are usually the earliest visible manifestations of diabetic retinopathy. They appear as tiny red dots scattered in the retina posteriorly. Sometimes they are surrounded by a ring of yellow lipid, or hard exudate. Exudates are the result of vascular leakage.

Intraretinal hemorrhages appear either as small red dots or blots indistinguishable from microaneurysms or as larger flame-shaped hemorrhages.

It is the leakage from microaneurysms in the macula that is responsible for macular edema which is the most common cause of decreased vision at this stage.

The prevalence of diabetic macular edema is strongly related to the duration of diabetes. It is estimated that macular edema is present in about 5% of patients who have diabetes for 5 years or less, and in 15% of patients who have diabetes for 15 years or more. High levels of glycosylated hemoglobin are associated with a higher prevalence of macular edema.

#### 2. ADVANCED NONPROLIFERATIVE RETINOPATHY

Nonproliferative retinopathy may progress to include abnormalities that have been associated with a high risk for imminent proliferative retinopathy. Although no treatment may be necessary at this stage, the patient must understand that reevaluation within the next few months is critical.

The most easily recognized abnormalities of advanced nonproliferative retinopathy are cotton-wool spots. These are areas of capillary closure, a resultant ischemia or infarction of the nerve fiber layer of the retina. Cotton-wool spots appear in the fundus as

discrete white spots with feathery edges. More closely related to the risk of progression to proliferative retinopathy are irregular dilations of retinal veins, called venous beading, dilated tortuous intraretinal vessels and extensive retinal hemorrhages. Once these signs have appeared, approximately 50% of patients will develop proliferative retinopathy within 1 year.

### 3. PROLIFERATIVE RETINOPATHY

Proliferative retinopathy is responsible for most of the devastating visual loss in diabetes. The ophthalmoscopic changes of proliferative diabetic retinopathy are new retinal blood vessels, or neovascularization, sometimes leading to vitreous hemorrhage and fibrous proliferation. All of the nonproliferative findings, including macular edema, may also be present.

The delicate new vessels that form on the surface of the retina resemble a tangle of hair or a fishnet. Neovascularization originating from the area around the optic nerve head is referred to as new vessels at the disk (NVD). If originating elsewhere on the retina, the neovascularization is called new vessels elsewhere (NVE).

As these fragile new vessels grow, they may bleed into the vitreous cavity, a condition called vitreous hemorrhage. Vitreous hemorrhage may be very mild, perceived by the patient as a sudden shower of dark dots or floaters, or more severe, filling the vitreous with blood and decreasing the patient's visual acuity to light perception. Patients reporting any of these symptoms should be examined urgently by an ophthalmologist.

Neovascularization in diabetes is not always confined to the retina. The retinal ischemia may cause new vessels to grow on the surface of the iris as well. Iris neovascularization is sometimes referred to as rubeosis iridis because of the reddish color change. These vessels may cause adhesion between the iris peripherally and the trabecular meshwork. The adhesion interferes with the normal drainage of aqueous fluid from the eye and may lead to glaucoma.

Fibrous proliferation generally accompanies neovascularization because the proliferating fibrocytes contain contractile proteins. The fibrovascular stalk shrinks, sometimes causing tearing or detachment of the retina. Even if the retina does not detach, the fibrovascular membrane may wrinkle and distort the retina, causing visual loss.

The prevalence of proliferative retinopathy is related to both the duration of the disease and the patient's age at the time of diagnosis. Insulin-using diabetic patients diagnosed before age 30 experience almost no proliferative retinopathy within the first 5 years after diagnosis. However, after 15 years duration of disease, 25% develop proliferative retinopathy; after 20 years, 55% develop proliferative retinopathy. In diabetic patients diagnosed after age 30, proliferative retinopathy is uncommon among noninsulin-using patients 20 years after diagnosis.

## IV-DIAGNOSIS AND TREATMENT

### 1- DIAGNOSIS:

Careful and detailed ophthalmoscopic examination through a dilated pupil is required to identify the initial presence of diabetic retinopathy, the stage of the disease, and the need for treatment.

Fundus photographs and fluorescein angiograms can document areas of vascular leakage, nonperfusion, and neovascularization. Fluorescein angiography also is useful in guiding laser surgery for macular edema.

### 2-TREATMENT:

The principal method used in treatment of diabetic retinopathy is laser photocoagulation surgery. In specific cases with the use of intraocular injection of antiangiogenesis factors.

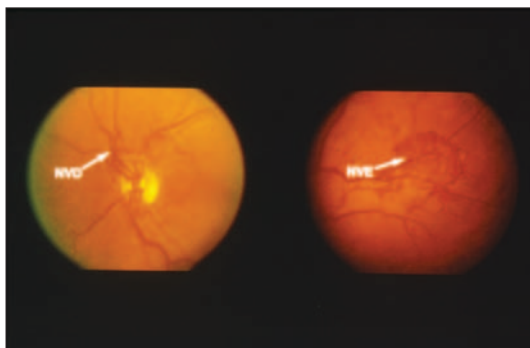
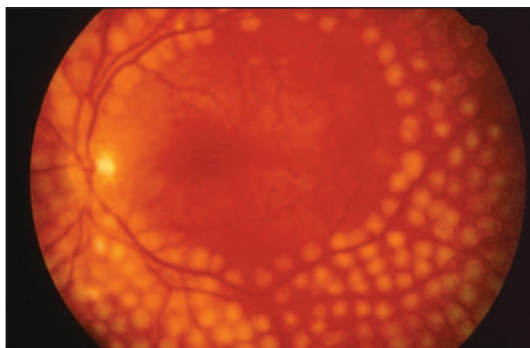
**Photocoagulation for proliferative retinopathy:** To treat proliferative diabetic retinopathy, the physician directs the laser beam into the eye and places burns a fraction of a millimeter in size in an evenly distributed scatter-pattern across the entire retina except at the macula. This panretinal photocoagulation causes the proliferating vessels to regress. A current hypothesis is that the ischemic retina elaborates a substance called angiogenesis factor. Photocoagulation eliminates the source of the angiogenesis factor by ablating the ischemic retina.

**Photocoagulation for macular edema:** The photocoagulation technique used to treat macular edema differs from that used to treat proliferative retinopathy. The leaking microaneurysms are treated directly with the argon laser to seal them and prevent further vision loss. As the edema is gradually resorbed, visual acuity may actually improve if the macula has not been badly damaged.

**Intravitreal anti VEGF agents:** In patients with extensive macular edema and severe PDR, laser photocoagulation can be combined with the use of intravitreal injections of antiangiogenesis factors primarily anti VEGF agents (Lucentis, Avastin). The goal is to decrease the vascular leakage and obtain the regression of neovascularization.

**Vitrectomy.** For patients whose retinal complications are not amenable to photocoagulation surgery, vitrectomy (removal of the vitreous) is a treatment option for removing vitreous hemorrhage and for treating or preventing retinal detachment associated with diabetic retinopathy.

Vitrectomy is a complex procedure in which the vitreous is simultaneously removed by suction and replaced by infusion of a



modified saline solution. An intraocular fiberoptic light source is introduced, and fibrous bands are cut. Intraocular laser photocoagulation, called endophotocoagulation, may also be performed to destroy the retinal new vessels.

### 3- DIABETS CONTROL:

The Diabetes Control and Complications trial (DCCT), 1400 Patients with demonstrated that good glucose control

reduces the development and progression of diabetic retinopathy. Intensively treated patients with mild to moderate NPDR showed a 54% reduction in the progression of retinopathy, a 47% reduction in the development of severe NPDR or PDR, and a 56% reduction in the need for laser surgery.

Recent findings show special interrelationships between proliferative diabetic retinopathy (PDR) and cardiovascular disease. The presence of PDR was observed to be an important risk indicator for the development of myocardial infarction, stroke, and amputation. In addition, patients with PDR are at higher risk of developing diabetic nephropathy.

Diabetic retinopathy often worsens considerably during pregnancy. Diabetic patients who wish to become pregnant should discuss the risks with their primary care physician and their ophthalmologist. During pregnancy, patients should be examined at frequent intervals, especially if the retinopathy has already been detected.

### V-Screening Guidelines

Based on current knowledge of the natural history of diabetic retinopathy and the efficacy of treatment, the following screening guidelines are suggested:

- 1- Patients with diabetes diagnosed before age 30 who are generally insulin users, should be evaluated annually by an ophthalmologist through dilated pupils, beginning 5 years after diagnosis or at age 10 if the diagnosis was made before age 5. Earlier evaluation is not necessary because retinopathy tends not to occur before puberty and is rare before 5 years' duration of the disease.
- 2- Patients with diabetes diagnosed after age 30 should be evaluated by an ophthalmologist through dilated pupils at the time of the initial diagnosis. After the initial screening examination, patients should be examined yearly or more frequently if the severity of the retinopathy warrants.
- 3- Ideally, diabetic women who are planning a pregnancy should be examined before conception to obtain a baseline view of the retina and to discuss the risks of developing or exacerbating retinopathy. Pregnant diabetic patients should be examined by an ophthalmologist during the first trimester and at least every 3 months thereafter until delivery.

### CONCLUSION

In most patients, diabetic retinopathy can be treated successfully with methods developed and refined within the last 20 years. Unfortunately, many diabetic patients come to medical attention after they have experienced visual loss, when it is often too late for the most effective treatment. The best solution is better screening.

Diabetes mellitus and its complications can be expected to become an increasing public health problem as the percentage of older people increases and diabetes becomes more prevalent. Screening is a costeffective way to reduce the incidence of blindness from diabetes.

To help patients and communities realize these benefits, all physicians must familiarize themselves and their patients with diabetic ocular complications, appropriate examination schedules, treatment options, and screening guidelines. With such an effort, perhaps diabetic