

BYRON J. HOOGWERF, MD, EDITOR

# Managing diabetic retinopathy

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■ Diabetic retinopathy is a leading cause of visual impairment and blindness. The disease is more likely in patients with insulin-dependent diabetes mellitus, and the incidence is higher in diabetes of long duration. In background diabetic retinopathy, the vascular changes are confined to the retina; in proliferative retinopathy, vessels grow onto the posterior vitreous surface or wedge between the retina and the vitreous. Diagnostic accuracy is more likely with an ophthalmologic consultation. A team approach between the ophthalmologist and the primary care physician is recommended for effective overall management of these patients.

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HE ADVENT of insulin therapy and resultant increased survival of diabetic patients over the last few decades has made diabetic retinopathy a leading cause of blindness and significant visual loss throughout the world. Although some degree of retinopathy develops eventually in nearly all diabetic patients, blindness is not inevitable. Early diagnosis, improved glucose control, and advances in treatment all have contributed to a better prognosis for many of these patients.

This summary reviews the demographic and medical aspects of diabetic retinopathy, the clinical features of the disease and its complications, the current treatment of this condition, and a recommended team approach for its management.

#### DEMOGRAPHIC ASPECTS

Visual impairment and loss are the main complications of diabetic retinopathy. Diabetic retinopathy can produce visual difficulties ranging from minimal visual loss to total blindness. With visual acuity between 20/20 and 20/70, driving and reading are difficult, and a variety of occupational disabilities can occur. Patients with visual acuity in the range of 20/70 to 20/200 are unable to drive and have major occupational and reading difficulties. When visual loss is between 20/200 and 5/200 (ie, approximately counting fingers at 5 feet), the patient is in the range of "legal blindness" with certain legal and economic rights. These patients have major visual difficulties, including those noted above, but they can usually ambulate well. Levels of vision less than 5/200 produce major ambulatory difficulties and vast lifestyle problems. These patients may have visual acuity adequate for light perception and distinguishing hand motion, but this is of no significant use in terms of quality of life.

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In the United States, more than 10% of new cases of blindness are caused by diabetes; between the ages of 45 and 74, the rate is 20%.<sup>1</sup> The duration of diabetes (both insulin-dependent and noninsulin-dependent) is a major predictor for the development of diabetic retinopathy. In the first 5 years of diabetes, there is little risk of retinopathy; however, the incidence of retinopathy is 25% to 50% with diabetes of 5 to 10 years' duration, and those who have had the disease for 10 to 15 years have a 75% to 95% incidence of retinopathy. Eventually, some retinopathy develops in most diabetic patients, but blindness and even significant visual impairment are not inevitable. Sex and race do not play major roles in prevalence.

### MEDICAL ASPECTS

Diabetic retinopathy is generally more severe in patients on insulin therapy than in those controlled by diet alone or oral agents,<sup>2</sup> but this reflects the more severe nature of insulin-dependent diabetes, rather than the effects of insulin per se. It is generally agreed that good glucose control may prevent the development of retinopathy or decrease its severity. Good, controlled human studies of this question are lacking, although long-term studies are underway.

The incidence of diabetic nephropathy is increased in the presence of diabetic retinopathy. Feldman and colleagues<sup>3</sup> found proteinuria, increased blood urea nitrogen, or increased creatinine in 35% of patients with symptomatic diabetic retinopathy. West and associates<sup>4</sup> found proteinuria in 58% of patients with severe diabetic retinopathy. There is an even closer correlation between the presence of retinopathy and associated nephropathy. In one study, diabetic retinopathy was confirmed in all eyes but one of patients undergoing renal transplantation because of diabetic nephropathy.<sup>5</sup>

# CLINICAL FEATURES OF DIABETIC RETINOPATHY

In addition to diabetes itself, other systemic conditions prevalent in diabetes, such as hypertensive retinopathy, hypercholesterolemia, hyperlipidemia, renal failure, renal dialysis (with or without anticoagulation therapy), renal transplant therapy, and carotid artery disease, may add to the clinical picture in patients with diabetic retinopathy.

Diabetic retinopathy has traditionally been classified as either background diabetic retinopathy (BDR) or proliferative diabetic retinopathy (PDR); this distinction is made because of the different types of complications and visual disability that may occur.

#### Background diabetic retinopathy

Background diabetic retinopathy is characterized by a spectrum of findings that range from early, often transient, changes to severe "preproliferative" changes. Early changes include venous dilation and intraretinal microangiopathy (IRMA). Many of the IRMA changes are caused by thickened capillary basement membrane and loss of pericytes. The clinical changes include dot, blot, and, more rarely, flame-shaped retinal hemorrhages. Exudates can be seen in varying amounts and in characteristic circinate patterns. As retinal capillaries close off shunt vessels, collateral and telangiectatic vessels can be seen.

Retinal microaneurysms are a hallmark of early BDR and each one has a characteristic progression. If leakage from incompetent vasculature involves the macular region either locally or diffusely, macular edema can develop with varying effects on visual function. Visual acuity can range from 20/20 to 20/400, but ambulatory vision is usually not lost secondary to macular edema alone. The major causes of visual loss in BDR are the macular ischemic changes often associated with macular edema.

# Preproliferative diabetic retinopathy

In preproliferative diabetic retinopathy, all of the changes of BDR may occur, and the cumulative effects of progressive and increasing retinal ischemia and capillary nonperfusion become evident. Clinically, multiple cotton-wool spots or soft exudates, which are actually retinal microinfarcts, can be seen. Venous beading and sheathing with perivascular exudates are apparent. Venous irregularity, venous loops, and major arteriolar occlusions can be seen. Fluorescein angiography can document large areas of capillary nonperfusion.

#### Proliferative diabetic retinopathy

Proliferative diabetic retinopathy is a serious and vision-threatening stage, even though some patients may have excellent vision and be totally asymptomatic. The available data suggest that a vasoproliferative factor or factors produced by the hypoxic retina stimulate the growth, or proliferation, of new vessels. In BDR, the vascular changes are confined to the retina per se, but in PDR, the new vessels grow out of the retina and onto the posterior vitreous surface or wedge between the retina and the vitreous.

The growth of the new vessels is characterized as

either neovascularization of the disc (NVD), with growth on the disc surface, or neovascularization elsewhere (NVE), with growth in other regions of the retina. The neovascularization process can be progressive and extensive, producing varying amounts of fibrous and vascular proliferation. Changes in the vitreous cavity, such as partial or complete detachment of the vitreous gel, can create traction on the fragile new vessels and cause vitreous hemorrhages; these are usually spontaneous and not precipitated by known trauma. The affected patient may experience floaters, "spots," and blurring or loss of vision, with visual acuity ranging from relatively good to total blindness. The vitreous hemorrhages may be recurrent and disabling or they may clear slowly and spontaneously.

A more devastating complication of PDR may be retinal detachments caused by increased traction on the retina due to dense, strong vitreoretinal adhesions in regions of fibrovascular tissue. In general, visual acuity is not significantly affected unless direct traction and detachment occurs in the region of the disc and, most importantly, in the macular region. The patient may report varying degrees of visual loss, diplopia, distorted vision, and flashing lights. Macular detachment is a cause for urgent therapy.

#### TREATMENT AND COMPLICATIONS

In the last 15 years, tremendous progress has been made in the treatment of diabetic retinopathy, thanks to laser therapy and vitrectomy surgical techniques.

The Diabetic Retinopathy Study (DRS),<sup>6</sup> one of the best conducted clinical trials to date, and subsequent reports from the DRS proved that laser therapy, or panretinal photocoagulation (PRP) using either argon bluegreen laser or xenon photocoagulation therapy, effectively reduces the risk of blinding vitreous hemorrhages. The rationale for the efficacy of PRP therapy is that it destroys large areas of hypoxic retina, cutting off the production of vasoproliferative factor(s) responsible for the growth and maintenance of NVD and NVE. NVD is not treated directly, but NVE areas can be surrounded by intensive laser therapy. The involution of the active NVD and NVE vessels decreases the risk of vitreous hemorrhages. In persistent NVD or NVE, panretinal photocoagulation therapy can be extended until confluent laser burns are produced throughout the entire retina except for a small region in the macula.

Macular edema is the major complication of background diabetic retinopathy. Laser therapy delivered locally or diffusely in the macular region can benefit some patients by stabilizing their visual acuity.<sup>7</sup>

Vitrectomy surgery revolutionized ophthalmic surgery. The blinding complications of diabetic retinopathy were the chief impetus for and beneficiary of its development. With current technology, a refined microsurgical approach permits the removal of blinding vitreous hemorrhages, release of vitreoretinal traction and repair of complicating retinal detachments. Many factors determine the final outcome, but for most patients who are candidates for vitrectomy, there is no alternative treatment.

#### TEAM APPROACH TO MANAGEMENT

The management of diabetic retinopathy requires close cooperation between the ophthalmologist (often a vitreo-retinal specialist) and the nonophthalmologist (endocrinologist, internist, family physician, or nephrologist). The nonophthalmic physician should be thoroughly knowledgeable about the signs and symptoms of diabetic retinopathy; some excellent reviews on the subject have been recently published.<sup>8</sup>

Several studies have shown that diagnostic accuracy is greater when based on an ophthalmologist's examination than when a nonophthalmic physician examines the patient. Accuracy also increases with the use of sophisticated examination techniques such as direct ophthalmoscopy, indirect ophthalmoscopy, dilated contact lens evaluation, fundus photography, and fluorescein angiography. Ophthalmologists and retinal specialists should make themselves available for immediate consultation in cases of suspected retinopathy.

The need for cooperation between the ophthalmologist and the primary care physician was defined recently in the American Academy of Ophthalmology's policy statement on the team approach in the management of diabetic retinopathy patients,<sup>9</sup> which includes a timetable for examinations and indications for referral.

# GUIDELINES FOR EYE CARE

The policy statement, *Guidelines for Eye Care in Patients with Diabetes Mellitus*,<sup>9</sup> recommends that people between 10 and 30 years of age who have had diabetes mellitus for 5 years have a baseline ophthalmic examination that includes history of visual symptoms, measurement of visual acuity and intraocular pressure, and ophthalmoscopic examination through dilated pupils. People with diabetes mellitus diagnosed after the age of 30 should have a baseline ophthalmic examination at the time of diagnosis. After the baseline examination,

all patients with diabetes mellitus should be examined annually unless the presence of abnormalities indicates a need for greater frequency.

# Pregnancy

The Academy suggests that any woman with pre-existing or known diabetes who becomes pregnant be examined by an ophthalmologist for retinopathy in the first trimester and thereafter at the discretion of the ophthalmologist. Furthermore, any woman with insulindependent diabetes mellitus who is planning pregnancy within 12 months should be under the care of an ophthalmologist.

# Referral

Prompt ophthalmologic referral is indicated for unexplained visual symptoms, reduced corrected visual acuity, increased intraocular pressure, retinal abnormality, and any other ocular pathology that threatens

REFERENCES

- Kahn HA, Hiller R. Blindness caused by diabetic retinopathy. Am J Ophthalmol 1974; 78:58–67.
- 2. Segal P, Treister G, Yalon M, Sandak R, Berezin M, Modan M. The prevalence of diabetic retinopathy: effect of sex, age, duration of disease, and mode of therapy. Diabetes Care 1983; 6:149–151.
- Feldman JN, Hirsch SR, Beyer MM, James WA, L'Esperance Jr FA, Friedman EA. Prevalence of diabetic nephropathy at time of treatment for diabetic retinopathy. [In] Friedman EA, L'Esperance FA, eds. Diabetic Renal-Retinal Syndrome, 2nd ed. New York, Grune and Stratton, 1982, pp. 9–20.
- West KM, Erdreich, LJ, Stober JA. A detailed study of risk factors for retinopathy and nephropathy in diabetes. Diabetes 1980; 29:501–508.

vision. Where appropriate, patients should be under the care of a retinal specialist or other ophthalmologist experienced in the management of diabetic retinopathy when preproliferative retinopathy, proliferative retinopathy, or macular edema have been identified.

### **Treatment alternatives**

Regarding treatment, the Academy policy statement notes that laser photocoagulation therapy reduces the risk of visual loss and is generally effective in the prevention of blindness in patients with high-risk proliferative retinopathy, significant macular edema, or both. Vitrectomy can restore vision in certain patients with recent traction retinal detachment or vitreous hemorrhage. Laser therapy and vitrectomy should be performed by a retinal specialist or other ophthalmologist experienced in these procedures. In some instances, it is appropriate for patients with functionally decreased visual acuity to undergo low vision evaluation and rehabilitation.

- Ramsay RC, Knobloch WH, Barbosa JJ, et al. The visual status of diabetic patients after renal transplantation. Am J Ophthalmol 1979; 87:305–310.
- The Diabetic Retinopathy Study Research Group. Preliminary report on effects of photocoagulation therapy. Am J Ophthalmol 1976; 81:383–396.
- The Early Treatment Diabetic Retinopathy Research Study Group. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study Report Number 1. Arch Ophthalmol 1985; 103:1796–1806.
- 8. Benson WE, Brown GC, Tasman W. Diabetes and its ocular complications. Philadelphia: WB Saunders, 1988.
- The Kentucky Diabetic Retinopathy Group. Guidelines for eye care in patients with diabetes mellitus. Results of a symposium. Arch Intern Med 1989; 149:769–770.