OPTOMETRIC CLINICAL PRACTICE GUIDELINE

Care of the Patient with

Diabetes Mellitus

American Optometric Association

OPTOMETRY: THE PRIMARY EYE CARE PROFESSION

Doctors of optometry are independent primary health care providers who examine, diagnose, treat, and manage diseases and disorders of the visual system, the eye, and associated structures as well as diagnose related systemic conditions.

Optometrists provide more than two-thirds of the primary eye care services in the United States. They are more widely distributed geographically than other eye care providers and are readily accessible for the delivery of eye and vision care services. There are approximately 32,000 full-time equivalent doctors of optometry currently in practice in the United States. Optometrists practice in more than 7,000 communities across the United States, serving as the sole primary eye care provider in more than 4,300 communities.

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American Optometric Association

OPTOMETRIC CLINICAL PRACTICE GUIDELINE
CARE OF THE PATIENT WITH DIABETES MELLITUS
Reference Guide for Clinicians

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NOTE: Clinicians should not rely on the Clinical Guideline alone for patient care and management. Refer to the listed references and other sources for a more detailed analysis and discussion of research and patient care information. The information in the Guideline is current as of the date of publication. It will be reviewed periodically and revised as needed.

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INTRODUCTION

Optometrists, through their clinical education, training, experience, and broad geographic distribution, have the means to provide primary eye and vision care for a significant portion of the American public and are often the first health care practitioners to examine patients with undiagnosed diabetes mellitus (DM) or ocular manifestations of DM.

This Optometric Clinical Practice Guideline for the Care of the Patient with Diabetes Mellitus is designed to provide optometrists with examination and management protocols to reduce the risks of vision loss in patients with DM through timely diagnosis and appropriate referral and intervention.

This Guideline will assist optometrists in achieving the following goals:

- Identify patients with undiagnosed DM
- Identify patients at risk of vision loss from DM
- Preserve human vision by reducing the risk of vision loss in patients with DM through timely diagnosis, intervention, determination of future evaluation, and appropriate referral
- Improve the quality of care rendered to patients with DM
- Disseminate information and continue the education of health care practitioners regarding the ocular complications of DM and the availability of vision rehabilitation programs
- Stress availability of vision rehabilitation for those with vision loss from DM through low vision devices and psychosocial support.

I. STATEMENT OF THE PROBLEM

Diabetes mellitus is a chronic disease with long-term macrovascular and microvascular complications, including diabetic nephropathy, neuropathy, and retinopathy. It is a leading cause of death, disability, and blindness in the United States for persons 20–74 years of age.[1] Approximately 80 percent of blindness in this age group is related to diabetic retinopathy (DR). At least 50,000 Americans are legally blind from this condition. Diabetes is also responsible for 5,800, or 10 percent, of the new cases of blindness reported annually.[2]

Although DR is not totally preventable or curable, many cases of blindness can be avoided because of advances in the management of diabetes and DR. Early diagnosis, intensive treatment, and consistent, long-term follow-up evaluations for diabetic patients are essential for effective treatment, which can significantly lower the risk of blindness. Intensive treatment to maintain blood glucose concentrations close to the normal range has been shown to decrease the risk of the development of DR by 76 percent.[3]

Approximately 26 percent of patients with type 1 DM and 36 percent with type 2 DM have never had their eyes examined.[4] These patients tend to be older, less educated, and more recently diagnosed than those receiving regular eye care.[4] They also are likely to live in rural areas and to receive their health care from a family or general practitioner.[4] Furthermore, 32 percent of patients with DM who are at high risk for vision loss have never received an eye examination.[5] When examined, almost 61 percent of these patients exhibit DR, cataract, glaucoma, or other ocular manifestations of DM. These findings are particularly disturbing because the Diabetic Retinopathy Study (DRS),[6-18] Early Treatment Diabetic Retinopathy Study (ETDRS),[19-41] and Diabetic Retinopathy Vitrectomy Study (DRVS)[42-46] have demonstrated that early referral for eye care and prompt and appropriate intervention lessen the risk for and the severity of vision loss related to diabetes. Early referral is crucial for African American and Hispanic patients; 37.3 percent of

African American patients and 42.9 percent of Hispanic patients have significant DR at the initial diagnosis of DM.[47]

A. Description and Classification of Diabetes Mellitus

1. Diabetes Mellitus

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects of insulin secretion and/or increased cellular resistance to insulin. Chronic hyperglycemia and other metabolic disturbances of DM lead to long-term tissue and organ damage, as well as dysfunction, involving the eyes, kidneys, and nervous and vascular systems.[48] The definitions and categories of DM used in this document are based on the most recent classifications reported by the American Diabetes Association.[49] (See Appendix Figure 4 for ICD-9-CM classifications).

The following important changes have been made in the classification of DM.[49]

1. The designations “type 1 diabetes” and “type 2 diabetes,” using Arabic numerals, replace the terms "insulin dependent diabetes mellitus" (IDDM) and "non-insulin dependent diabetes mellitus" (NIDDM).

2. A new term, "IFG" (impaired fasting glucose), has been introduced to define glucose values that are greater than or equal to 110 mg/dl but less than 126 mg/dl.

3. The revised diagnostic criteria for DM are:

    a. Symptoms of diabetes plus casual plasma glucose concentration greater than or equal to 200 mg/dl. Casual is defined as any time of the day without regard to time since the last meal.

OR

b. Fasting plasma glucose greater than or equal to 126 mg/dl. Fasting means no caloric intake for at least 8 hours. A test yielding an abnormal result must be repeated on a different day.

OR

c. Two hour plasma glucose greater than or equal to 200 mg/dl during an oral glucose tolerance test (OGTT), using a 75-g glucose challenge, as described by the World Health Organization (WHO).[50]

a. Type 1 Diabetes Mellitus

Type 1 diabetes mellitus, which results from destruction of beta cells in the pancreas, accounts for approximately 10 percent of all patients with DM in the United States. It leads to absolute insulin deficiency. There are two forms of type 1 DM. One is an immune-mediated disease with autoimmune markers such as islet cell antibodies (ICAs), insulin autoantibodies (IAAs), and autoantibodies to glutamic acid decarboxylase (GAD65). As many as 85–90 percent of patients with fasting hyperglycemia are positive for one or more of these markers. Strong human leukocyte antigen (HLA) associations also exist. A second form of type 1 DM, now called idiopathic diabetes, has no known causes. Only a minority of patients falls into this group, which occurs mainly in individuals of African and Asian origin. Idiopathic diabetes is strongly inherited, but it lacks autoimmune markers and is not HLA associated.

Although it can occur at any age, type 1 DM is more common in those less than 30 years of age. The rate of pancreatic destruction is variable and is generally faster in infants and children and slower in adults. Patients tend to be acutely symptomatic at onset, often complaining of polydipsia, polyphagia, polyuria, unexplained weight loss, dry mouth, pruritus, leg cramps or pains, delayed healing of skin wounds, and recurrent infections of the skin, genitalia, or urinary tract. The primary

characteristic of type 1 diabetes is absolute dependence on exogenous insulin to prevent ketoacidosis.

b. Type 2 Diabetes Mellitus

Type 2 diabetes is the most common form of DM worldwide, and its prevalence is increasing. Its underlying defects can vary from predominant insulin resistance with relative insulin deficiency to a predominant insulin-secretory defect with insulin resistance. A great deal of heterogeneity exists, and most type 2 patients do not initially require insulin therapy.

Accounting for approximately 90 percent of all cases of diabetes in the United States, type 2 DM occurs more frequently in adults than children, and the incidence increases with age, especially after age 40. However, the prevalence of type 2 DM in children is increasing, especially in the high-risk ethnic groups, such as Native Americans, Hispanic Americans, African Americans and Asian Americans. Most of these children are between 10 and 19 years old, have had symptoms longer, have infrequent or mild diabetic ketoacidosis, are obese, and have a strong family history of diabetes. A characteristic skin finding is acanthosis nigricans and there is an increased incidence of insulin resistance.[51]

Because the onset is frequently insidious, many patients with type 2 DM are asymptomatic and remain undiagnosed for years. Upper body obesity is a recognized risk factor because it results in peripheral insulin resistance. The beta cells compensate for this resistance by increasing insulin secretion and maintaining normal glucose tolerance. Eventually, the hyperglycemia worsens, glucose toxicity ensues, and insulin secretion and action decrease. Ultimately, the loss of beta cell mass can lead to insulin dependency. The definition of the insulin resistance syndrome has now been expanded to include glucose intolerance, hypertension, dyslipidemia (high triglycerides, low HDL cholesterol, and increased LDL), increased plasminogen activator inhibitor (PAI-1) levels, reduced sex-binding globulin, coronary artery disease, and diffuse atherosclerosis. These findings may be the basis for the marked increase in coronary heart disease reported in type 2 diabetes.

c. Impaired Glucose Tolerance

Patients with impaired glucose tolerance (IGT) have hyperglycemia at levels that are above normal but below the diagnostic criteria for diabetes, a diagnosis that can only be made with an oral glucose tolerance test. Serial testing shows that such patients may improve, remain stable, or worsen. IGT is not associated with the microvascular complications of DM but has been linked with macrovascular disease. In IGT, the fasting glucose levels are greater than or equal to 110 mg/dl but less than 126 mg/dl and the 2-hour value is greater than 140 mg/dl but less than 200 mg/dl. A new category of IFG includes those persons whose fasting glucose is greater than or equal to 110 mg/dl but less than 126 mg/dl. Most individuals with IFG and IGT are euglycemic in daily life and often have normal glycosylated hemoglobin (HbA_{1c}) levels.

d. Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first diagnosis during pregnancy. Usually diagnosed during the second or third trimester, GDM occurs in approximately 4 percent of pregnancies or 135,000 cases annually. The prevalence rate of 1–14 percent depends upon the population studied. Glucose tolerance usually returns to normal within 6 weeks after pregnancy ends, at which time the woman needs to be reclassified. Most GDM patients do not develop diabetes later in life, but some will develop IFG, IGT, type 2, or even type 1 diabetes. Because increased fetal mortality and morbidity have been associated with GDM, prompt detection and aggressive treatment are important. GDM remains a subgroup within the new classification, but the screening criteria have been revised. No longer do all pregnant women have to be screened. Women are exempted, provided all of four criteria are met: (1) less than 25 years of age, (2) normal weight, (3) no first-degree relative with diabetes, and (4) not Hispanic, Native American, Asian, or African American.

Screening is performed between 24 and 28 weeks, using a 50-g glucose load. A 1-hour value of greater than or equal to 140 mg/dl requires a full diagnostic test using 100 g of glucose. Diagnostic criteria are fasting

plasma glucose (FPG) greater than or equal to 105 mg/dl; 1-hour glucose, greater than 190 mg/dl; 2-hour, greater than 165 mg/dl; and 3-hour, greater than 145 mg/dl. A test is positive for GDM when any two of these values are exceeded.

e. Other Specific Types of Diabetes

Diabetes can also occur secondary to genetic defects in beta cell function or insulin action, pancreatic diseases or other endocrinopathies, medications, toxic chemicals, or uncommon forms of immune-mediated diabetes, e.g., "stiff man syndrome" or anti-insulin-receptor antibodies. The defects in beta cell function are better characterized since chromosome 7 has been linked to the glucokinase deficiency found in maturity-onset diabetes of the young (MODY) 2. MODY 3 is linked to chromosome 12 and MODY 1 to chromosome 20. Although few patients have DM related to these other entities, the patient's medical history must be taken into account when interpreting blood glucose screening results.

2. Treatment of Diabetes Mellitus

Diabetes mellitus is treated by one or more of the following modalities: medical nutrition therapy, exercise, oral medications, or insulin. Every patient with diabetes should be given dietary recommendations, which should be explained by a dietitian. If used early in the disease, medical nutritional therapy and weight loss may be sufficient for controlling type 2 DM in many patients. Dietary recommendations take into account the patient's total daily caloric requirements and are designed to promote weight control to achieve an ideal body weight. Optimal carbohydrate, protein, and fat intake levels usually are determined according to ADA guidelines.[52]

Insulin therapy is required for all patients with type 1 DM and for those patients whose type 2 DM is unresponsive to diet and oral medications. The goal of therapy is to maintain normal or near-normal blood glucose levels throughout the day. In addition to sulfonylurea compounds, a number of new therapies are now available for type 2 DM. These agents include biguanide (metformin), alpha glucosidase inhibitor (acarbose),

and, most recently, thiazolodinedione (troglitazone).[53] These drugs work by stimulating the beta cells and improving insulin action, reducing the increased hepatic glucose output, or reducing glucose absorption. All are directed toward one or more of the underlying metabolic abnormalities. Because of idiosyncratic liver damage and liver failure the Food and Drug Administration (FDA) removed troglitazone from clinical use in the year 2000. There are now two other compounds in clinical use, rosiglitazone and pioglitazone, which to date have had no serious adverse liver effects.

The use of combination oral therapies and oral therapies combined with insulin is increasing. A combination approach enables the patient to obtain the benefit of synergistic actions of the different medications while reducing adverse effects. Fixed dose combinations are now emerging for the treatment of type 2 diabetes. Also available are new insulin preparations such as the recently introduced basal insulin, glargine, and a new rapid-acting insulin, insulin aspart. These advances allow the initiation of more effective basal bolus insulin therapy that can result in better glycemic control.

The results of the landmark Diabetes Control and Complications Trial (DCCT) have clearly demonstrated that intensive therapy can reduce the long-term complications of type 1 diabetes.[3,54-58] This clinical trial involved the random assignment of 1,441 type 1 DM patients to intensive insulin therapy or conventional insulin therapy groups and following them for a mean of 6.5 years. The two arms of the study were designed to study primary prevention and secondary intervention for diabetes. The goal was to keep the glycosylated hemoglobin (HbA_{1c}) below 6.05 percent. Intensive therapy in the DCCT reduced the development of retinopathy by 76 percent and the progression of retinopathy by 60 percent, as well as reducing nephropathy and neuropathy by 60 percent overall. There was a threefold increase in the rate of hypoglycemia with intensive therapy, but there were no deaths. The mean 7.2 percent HbA_{1c} obtained in the intensive treatment group was 2 percent lower than that for the conventional therapy group.

The smaller, 110-subject Kumamoto Study in Japan was similar in design to the DCCT and produced similar results using intensive insulin therapy in lean type 2 diabetic patients.[59] A strong relationship between glycemic control and microvascular complications was also noted in the Stockholm Diabetes Intervention Study.[60] Although the results of the DCCT apply directly to type 1 diabetes, most clinicians felt it was reasonable to extend the findings to type 2 patients, because the genesis of microvascular disease is the same in both forms of diabetes, the only difference being in the methods used to obtain glucose control.

The landmark United Kingdom Prospective Diabetes Study (UKPDS) results were published in 1998.[61] A total of 3,867 newly diagnosed patients were followed for 9 years and randomized to conventional treatment with diet, or intensive treatment with oral therapy (sulfonylureas or metformin) or insulin. At the end of the study, the main difference was in mean HbA_{1c} values: 7.0 percent for the intensive-treatment group versus 7.9 percent for the conventional treatment group. This reduction resulted in an overall 25 percent reduction in all diabetic end points. Furthermore, the UKPDS showed a reduction in cardiovascular death with metformin treatment in a subgroup of obese patients. This study also found that 50 percent of the patients had evidence of some diabetic complication at diagnosis and that all monotherapies lost efficacy with time. This trial answers the criticism that the results of the DCCT were not applicable to type 2 patients and further emphasizes the need for earlier diagnosis and more aggressive treatment of these patients.

The epidemiologic follow-up study of the DCCT also showed that those patients who were on intensive therapy during the trial still had less diabetic retinopathy 4 years later despite convergence of HbA_{1c} levels following the conclusion of the DCCT. Four years following the DCCT, the mean HbA_{1c} of the patients who were in the control group was 8.2 percent, compared with 7.9 percent for the intensive group. The average HbA_{1c} values had been 9.1 percent and 7.2 percent, respectively. This finding strongly supports the rationale for improving glycemic control as early as possible in patients with diabetes since the benefits of early intensive control continue despite possible later less intensive control as

reflected in HbA_{1c} levels.[62] These studies also showed that there was no glycemic threshold for the development of the microvascular complications, therefore making it important for the clinician to aim for the best control possible for the patient without increasing the risks for hypoglycemia.

Insulin may be administered as conventional twice-daily injections, as multiple pre-meal and bedtime injections, or as continuous subcutaneous insulin pump infusion regimens. The most recent advance in insulin is the use of LYSPRO insulin. This recombinant deoxribonucleic acid (DNA) human insulin is very fast acting, peaking in 15–30 minutes and lasting 2–3 hours. It allows the patient to control the postprandial hyperglycemia more effectively. Most patients require some type of multiple or split dosage regimen to maintain adequate control. The recent introduction of the insulin analogue, glargine, provides the first true basal insulin. This analog can be used once daily in most patients because of the long duration of its action, which has a steady absorption profile and is without peaks. It forms the basal component of a multiple daily insulin regimen that includes rapid-acting pre-meal boluses. Daily self-monitoring of blood glucose by the patient, using a finger-prick sample with a glucose monitor, is a well-accepted practice. Such monitoring, which is absolutely necessary for intensive management programs, is encouraged for all diabetic patients.[63,64]

Appropriate action by the optometrist includes education and referral to a diabetes management team, for direction of the patient's medication changes, and self-glucose testing or consultation with an endocrinologist or diabetologist. The American Diabetes Association's (ADA) Clinical Practice Recommendations for eye care of patients with diabetes are summarized in Table 1.[52,63]

Table 1

Standards for Glucose Control

Biochemical index	Nondiabetic	Diabetic goals	Intervention indicated in diabetes
Preprandial glucose (mg/dl)	<110	80-120	<80 or >140
Bedtime glucose (mg/dl)	<120	100-140	<100 or >160
Glycosylated hemoglobin (HbA_{1c})	<6	<7	>8

B. Epidemiology of Diabetes Mellitus

1. Prevalence and Incidence

a. Diabetes Mellitus

Diabetes mellitus has been estimated to affect 16 million Americans, 50 percent of whom may be undiagnosed.[65] The prevalence of DM, estimated at 10 percent of persons over the age of 60 years, rises to 16–20 percent among those over the age of 80.[65] The overall prevalence among adults was 7.4 percent in 1995 and is expected to reach 9 percent in 2025. The annual incidence of type 1 diabetes in children from birth to 16 years of age varies with ethnicity and is approximately 3–26 new cases per 100,000 persons. For example, in African Americans in San Diego, CA, it is 3.3 per 100,000 and in whites in Rochester, MN, it is 20.6 per 100,000. Approximately 0.3 percent of the population develops the disease by 20 years of age.[66] The annual incidence of type 2 diabetes

is approximately 2.4 per 1,000 persons over age 20. By 65 years of age, 10 percent of the population may have type 2 diabetes. The prevalence is highest in Native Americans, followed by Hispanics, African Americans, and Asians.[66,67]

b. Ocular Manifestations

Diabetic retinopathy is the leading cause of new blindness in the 20- to 74-year-old population in the United States. It accounts for approximately 12 percent of all new cases of blindness each year. The prevalence of DR among patients with DM depends more on duration of the disease than the patient's age.[68-70] The actual duration of DM can be difficult to determine because the initial diagnosis may be made after a period of asymptomatic DM, especially in cases of type 2 diabetes, which has a more gradual onset. The projected ocular manifestations, by type and duration of DM, are summarized in Table 2.

Table 2

Duration of Diabetes Mellitus and Presence of Eye Disease

Type 1 Diabetes	
Duration of disease	**Ocular manifestations**
5 years	Possible ocular manifestations.
>10 years	60% have some retinopathy.
>15 years	Virtually all patients have some degree of retinopathy. 25% progress to proliferative diabetic retinopathy.
>20 years	50% progress to proliferative retinopathy.

Table 2 (Continued)

Type 2 Diabetes	
Duration of disease	**Ocular manifestations**
At diagnosis	20% have retinopathy.
>4 years	4% progress to proliferative retinopathy.
>15 years	60-80% have some retinopathy. Up to 20% progress to proliferative retinopathy.

The incidence of all ocular manifestations of DM increases with age and duration of the disease, whether type 1 or type 2. Approximately 5 percent of the population with DM develop glaucoma, compared with about 2 percent of the general population.[71] Glaucoma also has a higher prevalence in known groups at risk for DM, including African Americans, Native Americans, and older persons.

Cataracts are 2-4 times more prevalent, occur at younger ages, and progress more rapidly in patients with DM than in the general population.[70] The DCCT has shown that strict control of blood glucose can prevent or lessen the severity of ocular complications in persons with type 1 diabetes.[3,54] The United Kingdom Prospective Diabetes Study showed similar findings for persons with type 2 diabetes.[61]

2. Risk Factors

a. Screening for Diabetes Mellitus

Because of the high prevalence of type 2 diabetes and the increased morbidity and mortality associated with the disease, the ADA now recommends that all adults aged 45 years and older be screened for diabetes.[48] In individuals who are at higher risk, screening should be considered at younger ages and carried out more frequently.

The high-risk individual is one who:

- Is obese (>120% desirable body weight or body mass index > 27 kg/m^2)
- Has a first-degree relative with diabetes
- Is a member of a high-risk ethnic population (i.e., African American, Hispanic, Native American)
- Has delivered a baby weighing more than 9 pounds or has been diagnosed with GDM

[redacted]

- Is hypertensive (blood pressure >140/90)
- Has an HDL cholesterol level less than 35 mg/dl and/or a triglyceride level greater than 250 mg/dl
- Has had IGT or IFG on previous testing.

Screening is done with a FPG test after an 8-hour overnight fast, as described previously. Patients whose results are normal should be checked in 3 years.[48] Patients with positive results should be retested. Screening of urine glucose levels is not recommended, nor should the HbA_{1c} be used for screening.

b. Examination for Ocular Manifestations of Diabetes Mellitus

The clinical signs of DR can appear early in the natural history of the disease. Unfortunately, patients may not experience symptoms until relatively late, at which time treatment may be less effective. The success of appropriate intervention and management strategies depends upon accurate and timely detection of diabetic eye disease. The following individuals with DM should be examined for eye disease:[70,72]

- Any patient who is over the age of 10 and less than 30 years of age at diagnosis (generally with type 1 diabetes) should have his or her eyes examined within 3–5 years after the diagnosis of diabetes. Examination is generally not indicated before puberty. Follow-up examinations should be performed annually or as indicated by the clinical findings.
- The patient who is 30 years of age or older at diagnosis (generally with type 2 diabetes) should have an eye examination at the time of the initial diagnosis of DM. Follow-up examinations should be performed annually or as indicated by the clinical findings.
- Any patient with poorly controlled DM or proteinuria should be examined at least annually; more frequent eye examinations are likely to be needed.

[redacted]

- Any woman with previously diagnosed DM who is planning pregnancy should have an eye examination prior to conception to determine her baseline level of retinopathy. The woman with DM who becomes pregnant should have her eyes examined during the first trimester, with subsequent monitoring throughout the pregnancy as indicated by clinical findings, and examination 6–8 weeks postpartum.

- The patient with macular edema (ME), moderate to severe nonproliferative retinopathy, or proliferative retinopathy needs to be referred to an ophthalmologist skilled in treating diseases of the retina or to a retina specialist.

C. Clinical Background of Ocular Manifestations of Diabetes Mellitus

1. Natural History

Diabetic eye disease is an end-organ response to a systemic medical condition. All structures of the eye and many aspects of visual function are susceptible to the deleterious effects of DM. These effects are summarized in Table 3.

Table 3

Ocular and Visual Complications of Diabetes Mellitus

Functional
- Tritan color vision deficiencies
- Refractive error changes
- Accommodative dysfunction
- Visual field defects

Extraocular muscle anomalies
- Mononeuropathies involving third, fourth, or sixth cranial nerves

Pupillary reflexes
- Sluggish pupillary reflexes

Conjunctiva
- Bulbar conjunctival microaneurysms

Tear film
- Tear film deficiencies resulting in dry eye syndrome

Cornea
- Reduced corneal sensitivity
- Reduced corneal wound-healing ability
- Basement membrane abnormalities resulting in increased frequency of abrasions or recurrent erosion syndrome
- Descemet's membrane wrinkling
- Endothelial cell morphology changes, often resulting in increased corneal thickness

Iris
- Depigmentation
- Rubeosis iridis, possibly with associated ectropion uvea and peripheral anterior synechiae
- Neovascular glaucoma

Table 3 (Continued)

Lens
- Higher prevalence of cataracts
- Reversible opacities and snowflake cataracts
  rarely seen in industrialized countries)

Vitreous
- Hemorrhage in proliferative retinopathy

Retina
- Nonproliferative retinopathy
- Proliferative retinopathy
- Macular edema

Optic nerve
- Papillopathy
- Ischemic optic neuropathy
- Higher incidence of open angle glaucoma

Diabetic retinopathy is the most serious sight-threatening complication of diabetes. The two broad categories of DR are nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). Moreover, diabetic ME can be present at any level of NPDR or PDR.

Although the pathophysiological processes responsible for the various lesions of DR and maculopathy are not fully understood, various individual retinal lesions indicate the risk for progression of retinopathy and vision loss. Alteration in retinal blood flow is an early change from diabetes.[73,74] Loss of intramural pericytes of the retinal capillaries, either preceding or secondary to the development of nonperfusion of retinal capillaries, weakens the capillary walls. The resulting formation of saccular outpouchings of these capillaries, called microaneurysms (Ma), is frequently the earliest clinical sign of DR.

Ruptured microaneurysms, leaking capillaries, and intraretinal microvascular abnormalities (IRMA) result in intraretinal hemorrhages. The clinical appearance of these hemorrhages reflects the architecture of the retinal level in which the hemorrhage occurs. Hemorrhages in the

nerve fiber layer of the retina have a flame-shaped appearance and coincide with the structure of the nerve fiber layer that runs parallel to the retinal surface. Hemorrhages deeper in the retina, where the arrangement of cells is more or less perpendicular to the surface of the retina, assume a pinpoint or dot shape and are more characteristic of DR.

Intraretinal microvascular abnormalities represent either new vessel growth within the retina or, more likely, pre-existing vessels with endothelial cell proliferation that serve as "shunts" through areas of nonperfusion. IRMA are frequently adjacent to cotton wool spots. Whereas multiple IRMA mark a severe stage of nonproliferative retinopathy, frank neovascularization is likely to occur on the surface of the retina or optic disc within a short time.

Venous caliber abnormalities are indicators of severe retinal hypoxia. These abnormalities can take the form of venous dilation, venous beading (VB), or loop formation. Large areas of nonperfusion can appear adjacent to these abnormal veins. VB is a significant risk factor for progression to proliferative retinopathy.

Proliferative retinopathy is marked by the proliferation of endothelial cell tubules. The rate of growth of these new vessels, either at or near the optic disc (neovascularization of the disc, or NVD) or elsewhere in the retina (neovascularization elsewhere, or NVE), varies. Adjacent to the new vessels, translucent fibrous tissue often appears. This fibroglial tissue becomes opaque and begins adhering to the adjacent vitreous.

Although PDR is responsible for the most severe vision loss, diabetic ME is the most common cause of reduced visual acuity in persons with DM. Diabetes alters the structure of the macula, thereby significantly altering its function, in any of the following ways:[70]

- The collection of intraretinal fluid in the macular portion of the retina, with or without lipid exudates and with or without cystoid changes (macular edema)
- Nonperfusion of parafoveal capillaries, with or without intraretinal fluid

- Traction in the macula by fibrous proliferation, causing dragging of the retinal tissue, surface wrinkling, or detachment of the macula
- Intraretinal or preretinal hemorrhage (PRH) in the macula
- Lamellar or full-thickness hole formation
- Any combination of the above.

Clinically, ME is retinal thickening within 1 disc diameter (DD) of the center of the macula. Retinal thickening or hard exudate with adjacent retinal thickening that threatens or involves the center of the macula is considered to be "clinically significant macular edema."

Diabetic papillopathy and acute optic disc edema having the appearance of pseudopapilledema can reduce vision, particularly in patients with type 1 diabetes. The papillopathy may present with or without an afferent pupillary defect or visual field defect.[75] Diabetic papillopathy is a distinct clinical entity that must be distinguished from papilledema or other etiologies of optic disc swelling.[76] Visual acuity is usually moderately reduced, and the prognosis for improvement upon resolution is good. Diffuse microangiopathy may be associated with the etiology of diabetic papillopathy; however, there appears to be no correlation between diabetic papillopathy and either the degree of DR or the level of clinical control of the patient's DM.[75,77]

Patients with DM are at risk for ischemic optic neuropathy, which may occur with or without evidence of DR. Diabetes-related anterior ischemic optic neuropathy usually presents with optic disc pallor, swelling and hemorrhages, sudden decreased vision, an afferent pupillary defect, and an altitudinal visual field defect. The condition often results in optic atrophy and reduced visual acuity.[78] The clinical appearance of early anterior ischemic optic neuropathy is difficult to distinguish from diabetic papillopathy.[75] Diabetic patients are also susceptible to retrobulbar ischemic optic neuropathy, although its occurrence is uncommon in DM.

2. Classification and Signs of Diabetic Retinopathy

The two broad categories of DR are nonproliferative diabetic retinopathy and proliferative diabetic retinopathy.

Appendix Figure 4 lists the ICD-9-CM classification of ocular complications of DM.

a. Nonproliferative Diabetic Retinopathy (NPDR)

Nonproliferative diabetic retinopathy is characterized by retinal Ma, intraretinal hemorrhages (blot, dot, or flame), hard exudates, soft exudates (cotton wool spots), IRMA, venous looping, and/or venous beading. VB, IRMA, and moderate to severe hemorrhage or microaneurysm (H/Ma) are significant risk factors for progression to PDR.[31]

By definition, in mild NPDR there is at least one retinal H/Ma; however, the severity of H/Ma is less than is depicted in standard photograph 2A of the modified Airlie House classification of DR.[12,29,31] No other diabetic retinal changes are present. When there is no ME and no H/Ma in the macular area, mild NPDR does not present a threat to vision. Mild NPDR has a 5 percent risk of progressing to PDR in 1 year and a 15 percent risk of progression to high-risk PDR within 5 years.

Moderate NPDR differs from mild NPDR in that in one to three retinal photographic fields the severity of H/Ma exceeds those in standard photograph 2A, or cotton wool spots, VB, or IRMA of mild degree are present. Moderate NPDR has a 12–27 percent risk of progressing to PDR in 1 year and a 33 percent risk of progressing to high-risk PDR within 5 years.[29,31] Careful examination with the indirect ophthalmoscope, fundus contact lens, or fundus lens with the biomicroscope is needed to establish the diagnosis.

Severe NPDR is defined as H/Ma more severe than in standard photograph 2A in four retinal quadrants or photographic fields, or as VB (exemplified by that in standard photograph 6B) in two quadrants, or as

moderate IRMA (greater than or equal to those in standard photograph 8A) present in at least one retinal quadrant, in the absence of frank neovascularization.[29,31] This "4-2-1" rule is an important clinical tool for determining when DR is at risk of progressing to proliferative disease. Severe NPDR has a 52 percent risk of progressing to PDR in 1 year and a 60 percent risk of progressing to high-risk PDR within 5 years.

In very severe NPDR, two or more criteria for severe NPDR are met. Very severe NPDR carries a substantial risk for progression to PDR in 1 year and to high-risk PDR within 5 years.

b. Proliferative Diabetic Retinopathy (PDR)

The most severe form of DR is PDR. Most patients with PDR are at significant risk for vision loss. Characteristics of the disease include NVD, NVE, fibrous proliferation on or within one disc diameter of the optic disc (FPD) or elsewhere on the retina (FPE), PRH, and/or vitreous hemorrhage (VH). PDR that has not reached the high-risk level has a 75 percent likelihood of becoming high risk within a 5-year period.[29,31]

c. Macular Edema

Defined as the collection of intraretinal fluid in the macular area of the retina, with or without lipid exudates or cystoid changes, ME can occur at any stage of retinopathy. When macular edema involves or threatens the center of the macula, it is considered "clinically significant." Whether present in NPDR or PDR, this edema results from Ma or other focal or diffuse vascular leakage within or near the macula. Visual acuity is generally compromised when the ME affects the fovea.

3. Early Detection and Prevention

Duration of DM is a risk factor for onset and progression of DR; therefore, early diagnosis of DM and DR is essential. Early treatment of DR with photocoagulation surgery reduces the risk of severe vision loss by at least 50-60 percent.[19,28,42,44,45,79,80]

II. CARE PROCESS

This Guideline describes the optometric care provided a patient diagnosed with or suspected of having DM. The components of patient care described are not intended to be all-inclusive; professional judgment and individual patient symptoms and findings may have a significant impact on the nature, extent, and course of the services provided. The optometrist may delegate some components of care.

A. Diagnosis of Ocular Manifestations of Diabetes Mellitus

The first diagnosis of the patient who is unaware of having a diabetic condition may be based on an eye examination. Ocular examination of a patient suspected of having undiagnosed DM should include all aspects of a comprehensive eye examination.* Particular attention should be paid to the ocular and systemic signs and symptoms of DM, as discussed in this section.

Patients with DM need regular eye examinations. The examination should include all aspects of a comprehensive eye examination, with supplementary testing as indicated to detect and thoroughly evaluate ocular complications. The frequency of examination is determined on the basis of several factors, including the type of DM, duration of the disease, age of the patient, level of patient compliance, concurrent medical status, and both nonretinal and retinal ocular findings. Due to the risk for progression of DR during pregnancy, a diabetic woman should have a baseline examination prior to a planned pregnancy or early in the first trimester of pregnancy.[81,82]

1. Patient History

a. Patients With Undiagnosed Diabetes Mellitus

The history of a person suspected of having DM should include investigation of ocular and systemic complaints and symptoms related to

* Refer to the Optometric Clinical Practice Guideline for Comprehensive Adult Eye and Vision Examination.

DM. Common ocular symptoms of undiagnosed DM include recent onset of blurred or fluctuating vision, or new-onset diplopia. Systemic symptoms may include polyuria, polydipsia, polyphagia, unexplained weight changes, dry mouth, pruritus, leg cramps or pains, impotence, delayed healing of bruises or wounds, and recurrent infections of the skin, genitalia, or urinary tract. Systemic complaints are more common in patients with type 1 diabetes. Patients with type 2 diabetes are frequently asymptomatic.

b. Patients with Diagnosed Diabetes Mellitus

The patient history should encompass both the ocular and systemic status of the patient, emphasizing in particular any new complaints or symptoms. The quality of the patient's vision should be investigated to elicit symptoms such as blurred, distorted, or fluctuating vision; diplopia; night vision problems; and flashes or floaters. Questions about previous ocular disease or surgery that might exacerbate the ocular complications from DM should be included in the patient history.

The patient's medical history should be explored carefully to determine the type and duration of the DM. Studies[68,69,83-87] confirm that the risks for ocular complications are closely related to the duration of the disease (Table 4). Age at the time of onset of DM is not as significant as the duration of the disease in the prediction of complications.[82,85] The name, address, and telephone number of the patient's primary care physician should be noted in the record to facilitate communication and coordination of the patient's care.

Table 4

Incidence of Diabetic Retinopathy by Type and Duration of Diabetes

Duration of Type 1 Diabetes	
Incidence of Diabetic Retinopathy	
0-4 years	27%
5-9 years	71%
10-14 years	54%
15+ years	38%
Duration of Type 2 Diabetes	
Incidence of Diabetic Retinopathy	
0-4 years	31%
5-9 years	32%
10-14 years	38%
15+ years	51%

A review of the patient's medical management should encompass diet, oral medications, insulin type and dosage, recent laboratory values for HbA_{1c}, the presence of microalbuminuria or overt proteinuria, lipid values, and method, frequency, and results of self-monitoring of blood glucose. This information provides insight into patient compliance with therapeutic regimens and control of the DM, which may affect the development of ocular complications.[55,56,86,88] Glycosylated hemoglobin values provide an indication of average blood glucose levels and control of the DM over the prior 6–8 weeks. The level of HbA_{1c} at baseline examination has been shown to be a strong and independent predictor of incidence and progression of any retinopathy or progression to proliferative retinopathy.[55,56,89] While laboratory values may vary, HbA_{1c} values of 5.0–7.0 percent (normal, 4.0–6.0 percent) usually indicate

adequate blood glucose control. The goal is to keep the HbA_{1c} under 7 percent or as close to normal as is practically possible.

Additional information useful for patient assessment includes a review of other medical problems, medications, and allergy history. Patients diagnosed with DM may have their blood pressure measured at the time of the eye examination because hypertension is a known risk factor for the development and progression of diabetic retinopathy and nephropathy.[90,91]

2. Ocular Examination

The ocular examination should include, but not be limited to, the following evaluations:

- Best corrected visual acuity
- Pupillary reflexes
- Ocular motility
- Visual field screening
- Refraction
- Biomicroscopy
- Tonometry
- Stereoscopic fundus examination with pupillary dilation.

Pupillary dilation with 0.5% or 1.0% tropicamide and 2.5% phenylephrine hydrochloride* is recommended, unless contraindicated, to achieve maximum visualization of the retina.[84]

3. Examination Technique

The retina should be thoroughly examined for the presence of DR by binocular indirect ophthalmoscopy with an appropriate condensing lens. Diabetic maculopathy and optic disc changes are best evaluated with

* Every effort has been made to ensure that the drug dosage recommendations are accurate at the time of publication of the Guideline. However, as recommendations change due to continuing research and clinical experience, clinicians should verify drug dosage schedules on product information sheets.

stereopsis by fundus biomicroscopy with an appropriate condensing lens, a Hruby lens, or a fundus contact lens, or by stereographic fundus photographs or validated retinal imaging. For maximum visualization of the retina, all examinations should be performed through a dilated pupil, unless contraindicated.

Stereoscopic color fundus photography through a dilated pupil is helpful in detecting and classifying DR.[29-32] Photographic grading of DR compares favorably to clinical examination by ophthalmoscopy in this process. Stereoscopic photography is particularly useful for identifying clinically significant macular edema (CSME) and for documenting retinal status.

Proper documentation of retinal status, including the use of drawings or color photographs in the patient's record, is valuable for determining any progression or stability of the retinopathy at future examinations. Use of the standard protocol for color-coding retinal drawings is recommended. It is advisable to note the presence or absence (and the severity) of neovascularization on the iris (rubeosis iridis [NVI]), retinal H/Ma, VB, IRMA, retinal neovascularization, and hard exudates or thickening in the macula. The presence of these lesions helps to determine the level of retinopathy and to diagnose ME.

When VH prevents adequate visualization of the retina or when scatter (panretinal) photocoagulation is ineffective, early vitrectomy may be indicated. In such cases, patients need to be referred promptly for evaluation, which may include ultrasound examination, and treatment. The Diabetic Retinopathy Vitrectomy Study has shown that early vitrectomy is of benefit in preserving vision in some patients.[42-46]

4. Supplemental Testing

The use of additional procedures for the diagnosis and evaluation of DR may be indicated. Such procedures include, but are not limited to:

- Color vision assessment
- Contrast sensitivity testing
- Fundus photography or validated retinal imaging

- Gonioscopy
- Macular function assessment.

The patient suspected of having DM may have his/her blood pressure measured at the time of the eye examination. Hypertension is more prevalent in persons with DM and is a known risk factor for the development and progression of DR.[9,61,91]

B. Management of Ocular Manifestations of Diabetes Mellitus

1. Basis for Treatment

Treatment decisions depend upon the extent and severity of the patient's ocular condition. Appendix Figure 1 presents a flowchart for the management of the patient with undiagnosed DM. Appendix Figure 2 presents a flowchart outlining the optometric management of the patient diagnosed as having DM.

a. Patients with Undiagnosed Diabetes Mellitus

Patients suspected of having DM should be screened for high blood glucose levels. The optometrist should refer the patient to a physician for evaluation or request a fasting blood glucose analysis. Patients with fasting blood glucose values of greater than or equal to 110 mg/dl but less than 126 mg/dl have IFG and should be retested. All patients with fasting blood glucose values of 126 mg/dl or greater should be referred to physicians for further evaluation or treatment. Most pregnant women should be screened for glucose intolerance. Because a pregnant patient is usually under medical care, her obstetrician should coordinate this examination.

Patients with undiagnosed DM who present with DR during the initial examination must be referred for treatment of their DM. The DR should be managed in accordance with accepted protocols, as outlined in section II.B.1.c of this Guideline, which focuses on retinal complications.

b. Patients with Nonretinal Ocular Complications

Management of nonretinal ocular complications of DM should be consistent with current recommendations of care for each condition. Although a comprehensive discussion of these therapy regimens is beyond the scope of this Guideline, Table 5 briefly outlines the management of nonretinal ocular complications.[92] Treatment protocols should always include patient education and recommendations for follow-up visits. As part of the proper management of DM, referrals to other appropriately licensed practitioners for concurrent care should be made when indicated.

Table 5
Management of Nonretinal Ocular Complications of DM

Category	Ocular Complications	Management*
Functional	Tritan color vision loss	Dilated fundus examination to rule out diabetic maculopathy; counseling; low vision evaluation; review of independent living aids as necessary
	Refractive error changes Accommodative dysfunction	Consultation with patient's physician regarding degree of blood glucose control; modification of spectacle prescription as necessary
	Visual field defects	Low vision evaluation; orientation and mobility training as necessary
Extraocular muscle anomalies	Mononeuropathies	Neuro-ophthalmology or neurology consultation; temporary prism spectacle prescription as needed; eye patching as indicated
Pupils	Sluggish pupillary reflexes Afferent pupillary defects	Workup to rule out optic neuropathy
Conjunctiva	Bulbar microaneurysms	Monitoring
Tear film	Dry eye syndrome	Prescription of artificial tears, ocular lubricants, and other dry eye management techniques; monitoring for corneal complications
Cornea	Reduced corneal sensitivity	Monitoring for abrasions, keratitis, or other ulcerations
	Basement membrane anomalies, recurrent corneal erosions	Prescription of NaCl solution/ointment; artificial tears; patching as necessary

Table 5 (Continued)

Cornea (continued)	Descemet's membrane wrinkling	Monitoring
	Endothelial cell changes	Monitoring Note: All corneal injuries should be monitored carefully for secondary infection or evidence of delayed wound healing. This is particularly important in patients who wear contact lenses.
Iris	Depigmentation	Monitoring; routine gonioscopy and tonometry
	Rubeosis iridis (neovascularization on the iris)	Gonioscopy to rule out anterior chamber angle involvement and neovascular glaucoma; dilated fundus examination to search for proliferative retinopathy; referral to retina specialist for possible laser surgery
Lens	Cataracts	Monitoring of both degree of lens opacification and status of any retinopathy; cataract extraction after careful preoperative retinal evaluation; surgery indicated if adequate visualization of the retina is no longer possible
Vitreous	Hemorrhage	Dilated fundus examination; consultation with retina specialist

* Patient education is an integral part of management for all conditions.

c. Patients with Retinal Complications

Five major clinical trials provide the scientific basis for standards for clinical management of DR:

- The Diabetic Retinopathy Study (DRS, 1971–1975)[6-18]
- The Early Treatment Diabetic Retinopathy Study (ETDRS, 1979–1990)[19-41]
- The Diabetic Retinopathy Vitrectomy Study (DRVS, 1977–1987)[42-46]
- The Diabetes Control and Complications Trial (DCCT, 1983–1993)[3,54-58]
- The United Kingdom Prospective Diabetes Study (UKPDS, 1977–1999)[61,91]

The DRS, ETDRS, and DRVS definitively established the efficacy of laser surgery for PDR and diabetic ME and have provided guidelines concerning the most opportune time for intervention with laser surgery and vitrectomy. The DCCT and UKPDS established the benefits of intensive control of blood glucose levels to reduce the risks of onset and progression of DR and other complications of diabetes for type 1 and type 2 DR, respectively.

The ETDRS modified and extended the Airlie House classification of DR[29,31] to assess the severity and extent of the various lesions of DR. This modification forms the basis of an overall DR severity scale[29] that ranges from the absence of DR to severe VH. Clinical approximations of these levels provide practical guidelines for the clinical diagnosis and management of DR (Table 6). The retinopathy severity scale is valuable as a description of baseline retinopathy levels and identifies the risk for progression of DR.

When indicated (generally for levels of moderate NPDR or worse, any PDR, any macular edema, neovascularization of the iris, or unexplained vision loss), the optometrist should refer the person with DM to an ophthalmologist skilled in treating diseases of the retina or a retina specialist.

Table 6
Levels of Diabetic Retinopathy

I. Nonproliferative Diabetic Retinopathy (NPDR)

A. Mild NPDR
- At least one Ma
- One or more of the following:
  - Retinal hemorrhages
  - Hard exudates
  - Soft exudates
- Definition not met for B, C and D (below) and PDR

B. Moderate NPDR
- H/Ma > standard photo 2A, or
- Soft exudates, VB, and IRMA definitely present
- Definition not met for C and D (below) and PDR

C. Severe NPDR
- One of the following:
  - H/Ma $\geq$ standard photo 2A in all four quadrants
  - VB definitely present in at least two quadrants (see standard photo 6B)
  - IRMA $\geq$ standard photo 8A in at least one quadrant
- Definition not met for D (below) and PDR

D. Very Severe NPDR
- Two or more lesions of severe NPDR (C above)

II. Proliferative Diabetic Retinopathy (PDR)

A. Mild PDR
- One or more of the following:
  - NVE
  - FPD or FPE present; NVD and NVE absent
- Definition not met for B and C (below)

Table 6 (Continued)

B. Moderate PDR
- One or more of the following:
  - NVE elevated
  - NVD < standard photo 10A
  - VH/PRH and NVE < 1/2 DA; NVD absent
- Definition not met for C (below)

C. High-Risk PDR
- One or more of the following:
  - NVD $\geq$ 1/4 to 1/3 DA (standard photo 10A)
  - NVD and VH/PRH
  - NVE $\geq$ 1/2 DA and VH/PRH

III. Clinically Significant Macular Edema (CSME)

- One or more of the following:
  - Thickening of the retina $\leq$500 microns (1/3 DD) from the center of the macula
  - Hard exudates $\leq$ 500 microns (1/3 DD) from the center of the macula with thickening of the adjacent retina
  - A zone or zones of retinal thickening $\geq$1 DA in size, any portion of which is $\leq$1 DD from the center of the macula

2. Available Treatment Options

a. Nonproliferative Diabetic Retinopathy

An annual dilated eye examination and fundus photographs, if indicated, are generally sufficient for the patient with mild NPDR, as long as there is neither ME nor a coincident medical condition, such as hypertension, renal disease, or pregnancy. The patient's primary care physician should be informed of eye examination results, even when retinopathy is minimal or not present.

For patients with moderate NPDR, fundus photography is strongly suggested, and repeat evaluation in 6–12 months is appropriate in the absence of ME or complicating medical or risk factors. Although the

patient with mild or moderate NPDR generally is not a candidate for scatter (panretinal) laser treatment, the presence of ME requires more frequent evaluation, consultation with a retina specialist, and, in the presence of CSME, probably focal laser photocoagulation. Misdiagnosis of moderate NPDR is hazardous because of significant underestimation of a patient's risk for progression to proliferative retinopathy.

Follow up every 2–3 months in consultation with a retina specialist is advisable for patients with severe or very severe NPDR. Scatter laser photocoagulation may be indicated, depending on the clinical judgment of the retina specialist. Studies also suggest that type 2 diabetic patients are more likely to benefit from scatter photocoagulation prior to the development of high-risk PDR.[36,93] Severe and very severe NPDR (as well as PDR that is not high risk) may require early scatter laser surgery, particularly when neovascularization of the disc has occurred or elevated new vessels are present.

Patients with moderate NPDR or worse should be considered for focal laser treatment of ME, whether the ME is clinically significant or not, in preparation for the possible future need for scatter photocoagulation. Focal laser surgery for CSME is strongly indicated for patients with severe NPDR because of the risk for the development of PDR and high-risk PDR.[90] Consultation with a retina specialist is indicated.[94]

b. Proliferative Diabetic Retinopathy

Proliferative diabetic retinopathy is marked by new vessel growth on the optic disc or elsewhere on the retina, or by the proliferation of fibrous tissue. Proliferative retinopathy that has not reached the high-risk level has a 75 percent likelihood of becoming high-risk PDR within a 5-year period. Scatter laser photocoagulation may be indicated, and even when ME is not clinically significant, the patient with PDR may benefit from treatment. Prompt referral to a retina specialist is indicated.

The DRS and ETDRS conclusively demonstrated that scatter (panretinal) laser photocoagulation surgery significantly reduces the risk for severe

vision loss from PDR. Furthermore, these studies identified specific retinal lesions that pose a significant threat of vision loss.[29,31]

Patients with high-risk PDR require immediate referral to a retina specialist for scatter laser photocoagulation. High-risk PDR is characterized by any one or more of the following lesions:[8]

- NVD approximately one-fourth to one-third disc area (DA) or more in size (i.e., $\geq$ NVD in standard photo 10A)
- NVD less than one-fourth DA in size when fresh VH or PRH is present
- NVE greater than or equal to one-half DA in size when fresh VH or PRH is present.

To identify high-risk PDR, the examiner must pay attention to the presence or absence of retinal neovascularization, the location and severity of any neovascularization, and the presence or absence of preretinal or vitreous hemorrhages. The risk for severe vision loss can be reduced by at least 50 percent by initiating scatter laser surgery for eyes with high-risk PDR; consequently, any patient who demonstrates high-risk PDR should be referred immediately (within 24–48 hours) to a retina specialist.

Eyes in which PDR has not advanced to the high-risk stage should be considered analogous to eyes with high-risk PDR. Many retina specialists perform scatter laser photocoagulation in eyes with less than high-risk PDR, particularly when there are extenuating circumstances, such as patient noncompliance, the development of cataracts, difficulty in managing DM or associated medical conditions (e.g., hypertension, nephropathy), or pregnancy. These same considerations pertain to patients with severe or very severe NPDR.[36,93] Patients with type 2 diabetes or type 1 diabetes of long duration may benefit from earlier laser treatment, prior to the development of high-risk PDR.[93]

The goal of laser surgery is to induce regression of neovascularization without VH or fibrovascular proliferation that results in traction retinal detachment or macular dragging. Any patient with PDR should be referred to a retina specialist promptly for further evaluation and photocoagulation treatment, as clearly supported by the DRS and ETDRS. Timely and appropriate laser and vitrectomy surgery can significantly reduce the 5-year risk for severe vision loss from PDR. In the ETDRS, 4 percent of eyes with PDR that were treated had severe vision loss within 5 years, and 1 percent of patients had such loss. Only 5 percent of ETDRS patients with PDR became legally blind.

c. Macular Edema

Management of patients with ME involves consideration of both the significance of the edema and the nature of any other retinopathy present. ME is divided into two categories, the less severe of which, nonclinically significant ME, usually does not require laser surgery. Such patients should be re-examined within 3–4 months in consultation with a retina specialist. Followup can be more frequent if required for proper management of the retinopathy. Referral for fluorescein angiography (FA) may be indicated to identify treatable lesions, although FA generally is not needed for diagnosis.[19,20,22,24]

As defined by the ETDRS, clinically significant macular edema includes any one of the following lesions:[19,21]

- Retinal thickening at or within 500 microns (one-third DD) from the center of the macula, or
- Hard exudates at or within 500 microns (one-third DD) from the center of the macula, if there is thickening of the adjacent retina, or
- An area or areas of retinal thickening at least 1 DA in size, at least part of which is within 1 DD of the center of the macula.

Patients with CSME should be referred promptly for FA and focal laser photocoagulation treatment.[19] Follow-up examination should be

scheduled 3-4 months after treatment. If the retina consultant defers treatment, the retina consultant's follow-up examination generally occurs within 3 months.

The management of diabetic papillopathy and ischemic optic neuropathy may require consultation with a neuro-ophthalmologist or neurologist to rule out all other potential etiologies, such as space-occupying lesions.

The clinical appearance of the nerve fiber layer may be affected by scatter (panretinal) photocoagulation to treat the microvascular complications of DR; however, no significant change in the optic disc contour or cup-to-disc ratio has been documented.[89] Optic disc pallor without increased cup-to-disc ratio may result from quiescent PDR, whether occurring spontaneously or following scatter (panretinal) laser photocoagulation.[83]

3. Patient Education

Virtually all patients with DM will develop some form of DR at some point during the course of the disease. Therefore, it is important for them to learn about the disease process and the risks for developing ocular signs and symptoms that may result in vision loss. Optometrists should inform patients that retinopathy may exist even when vision is good. Patients should be encouraged to report all ocular symptoms (e.g., blurred vision, flashes, and floaters), inasmuch as DM may be the underlying etiology. Optometrists should help patients understand that timely follow-up examinations and management are critical for early diagnosis and intervention, when indicated, to reduce the risk of vision loss from DR. Patients also should be informed about their higher risk for other nonretinal ocular complications, such as cataracts, neovascular glaucoma, and open angle glaucoma.[95]

Optometrists should inform their patients about the relationship between the level of control of diabetes and the subsequent development of ocular and other medical complications. Specific emphasis should be placed on the benefit of any reduction in elevated HbA_{1c} in lowering the risk of damage. A 1 percent rise in HbA_{1c} (from 7 to 8 percent) increases the

progression of nonproliferative retinopathy by 44 percent over a 10-year period. For the patient with proliferative retinopathy, the same 1 percent increase in HbA_{1c} results in 145 percent progression over 10 years.[96] Special care is needed in the approach to elderly patients; because their risks and benefits may be different, the discussion and instruction will have to be individualized.[97]

Patients should be informed that diabetic nephropathy, as manifested by microalbuminuria, requires aggressive early treatment. Treatment modalities include improved glycemic control and the timely use of the angiotensin converting enzyme (ACE) inhibitors. The captopril type 1 diabetes study showed that ACE inhibitors reduce by 50 percent the progression to end-stage renal disease, which necessitates dialysis or kidney transplantation, and can result in death.[98] Similar data are now available for type 2 diabetes.[99] Proper monitoring and timely treatment can result in subsequent saving of sight for persons with diabetes mellitus.

Finally, all patients should be advised about organizations that provide resources and support for patients with DM. (A list of organizations is available from the AOA Clinical Care Group.)

4. Prognosis and Followup

All patients with DM are at risk for the development of ocular-related complications. Compliance with treatment recommendations to maintain close control of their blood glucose levels is a significant factor in slowing the development and progression of ocular complications of DM.

Diabetic patients who do not have DR should be re-examined annually. The follow-up examination of patients with DR should be scheduled in accordance with the clinical trials protocols. Proper diagnosis is crucial because misdiagnosis by just one level underestimates a patient's risk of developing PDR in 1 year by 50 percent or more (Appendix Figure 3).

Focal laser photocoagulation for CSME reduces the risk of moderate vision loss (i.e., a doubling of the visual angle) from nearly 30 percent to approximately 12 percent. Scatter (panretinal) laser photocoagulation reduces the risk of severe vision loss (best visual acuity $\leq$ 5/200) to less than 2 percent. Laser surgery, therefore, greatly improves the prognosis for maintaining useful vision.

Following successful treatment, patients with PDR should be re-examined every 2–4 months. A peripheral visual field examination may be performed approximately 6 months after treatment. Color photography also may be useful in monitoring post-treatment status. The management of patients with PDR needs to be coordinated with the recommendations of the retina specialist.

Appropriate communication with the patient's primary care physician (as with any referral consultant) is critical for proper coordination of the patient's care. Due to the nature of DM, a multidisciplinary approach to patient management is essential. All health care personnel involved with the patient's care should be aware of the patient's overall medical status. Written letters or reports are useful in accomplishing this task. These letters also provide permanent documentation for the patient's record. The patient's primary care physician must be involved in all aspects of the health care.

The patient with diabetic ME, or with suspected diabetic ME, should be referred promptly, usually within 2–4 weeks, to a retina specialist for evaluation. The patient with high-risk PDR should be referred to a retina specialist immediately, usually within 24–48 hours, for consideration of scatter (panretinal) laser surgery. Patients whose PDR is less than high risk or who have signs of severe or very severe NPDR should be referred for consultation with retina specialists because they may require laser surgery. The optometrist should communicate with the diabetic patient's primary care physician following each eye examination.

5. Management of Patients with Severe, Irreversible Vision Loss

Patients with DR are at risk for both permanent loss of visual acuity and loss of functional vision, including:

- Reduced central visual acuity and central scotoma from diabetic maculopathy
- Loss of peripheral visual field
- Difficulty with vision in dim light, secondary to retinal ischemia or panretinal laser photocoagulation
- Vision loss secondary to residual effects from vitreous hemorrhage, preretinal hemorrhage, or traction retinal detachment.

Because standard corrective eyeglasses and contact lenses may not alleviate the functional vision problems associated with DR, patients with DR may need low vision rehabilitation entailing orientation and mobility training, nonoptical aids, and other independent living aids or devices. For example, optical aids alone may be inadequate for patients who need to manage their medication regimens or to self-monitor blood glucose. Due to acquired color vision defects, diabetic patients have particular difficulty using color-comparison systems for self-monitoring blood glucose levels,[100] and may require a self-monitoring system with a digital display meter or voice response. Another problem for the DM patient is loss of tactile sensation related to peripheral neuropathy. This loss may affect the patient's ability to perform routine tasks safely, such as meal preparation, dialing the telephone, and writing.

When a standard corrective prescription or a less complex low vision device cannot satisfy the visual requirement, the patient's rehabilitation may necessitate a specialized low vision consultation or appropriate patient counseling. Patients should be evaluated to determine their potential to benefit from comprehensive low vision rehabilitation that would reduce the debilitating effects of vision loss.[*]

Patients with significant reduction of visual acuity or functional vision loss may be unable to continue their usual employment. Occupational or vocational rehabilitation may help patients achieve more fulfilling, self-

[*] Refer to the Optometric Clinical Practice Guideline on Care of the Patient with Low Vision.

sustaining lifestyles.[101] Referrals should be made only after discussion with the patients regarding their willingness to participate in such consultations.

The fear of vision loss associated with DR can result in a high level of anxiety for any patient with retinopathy, including the patient with good functional vision.[102,103] Even patients without retinopathy or other ocular complications may have personal concerns about DM (e.g., problems accepting the disease, adapting to it, and adjusting to emotional and social changes). Referral for psychosocial counseling is indicated for any patient who may have difficulty dealing with the issues associated with DM or DR. An early counseling visit may be beneficial for a family with a child who has DM. Educational literature and a list of support agencies and other resources should be made available to the patient.

CONCLUSION

Until modalities are in place to prevent or cure DR and other complications of DM, emphasis must be placed on identification, careful followup, and timely treatment, including laser photocoagulation, for patients with DR and diabetic eye disease. Proper care will result in reduction of personal suffering for those involved, and a substantial cost savings for the involved individuals, their families, and the country as a whole. Therefore, strict guidelines have been established for the ocular care of people with diabetes.[72,104]

Optometrists should inform all diabetic patients of the possibility of developing retinopathy, with or without symptoms, and of the associated threat of vision loss. The results of the DCCT and UKPDS should be discussed and patients should be encouraged to see their diabetes care providers to work toward achieving the goals for control published by the American Diabetes Association. The natural course and treatment of DR should be discussed with the patient, and the importance of routine eye examinations should be stressed.

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IV. APPENDIX

Figure 1
Optometric Management of the Patient
With Undiagnosed Diabetes: A Brief Flowchart

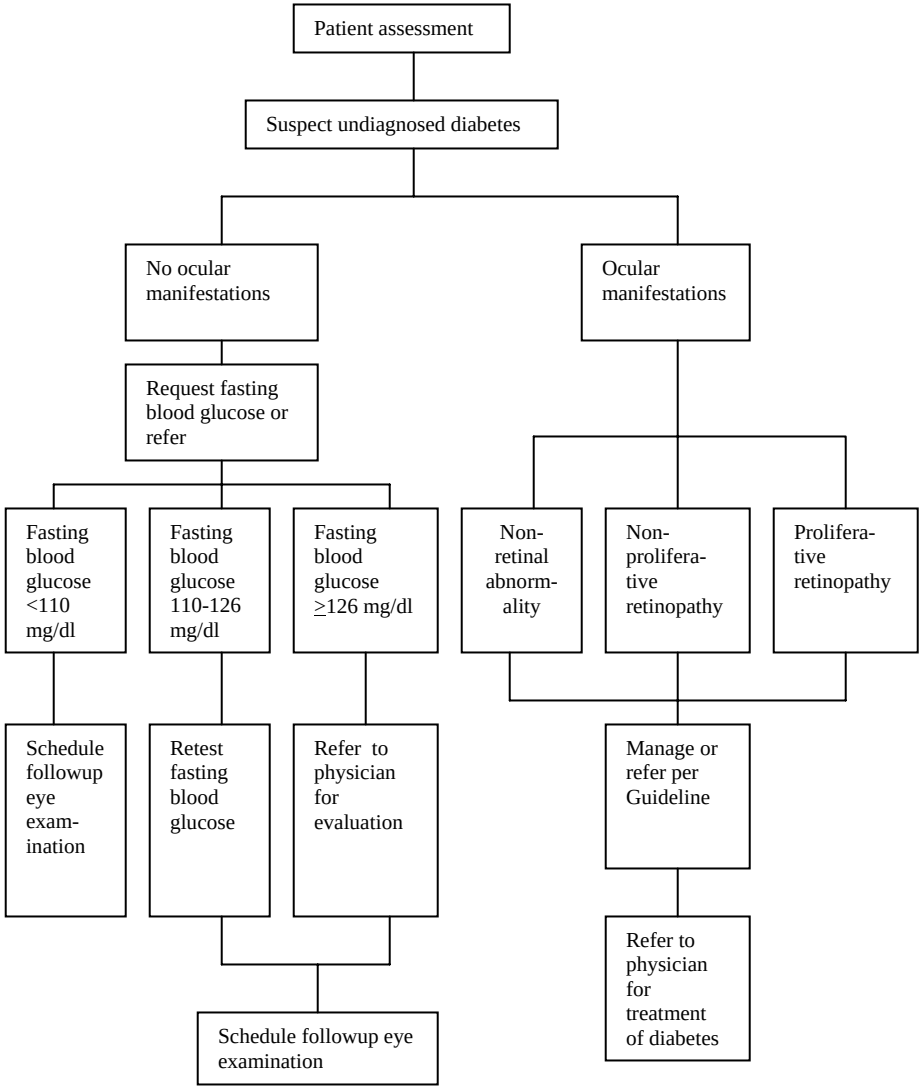

Figure 2
Optometric Management of the Patient
With Diagnosed Diabetes Mellitus: A Brief Flowchart

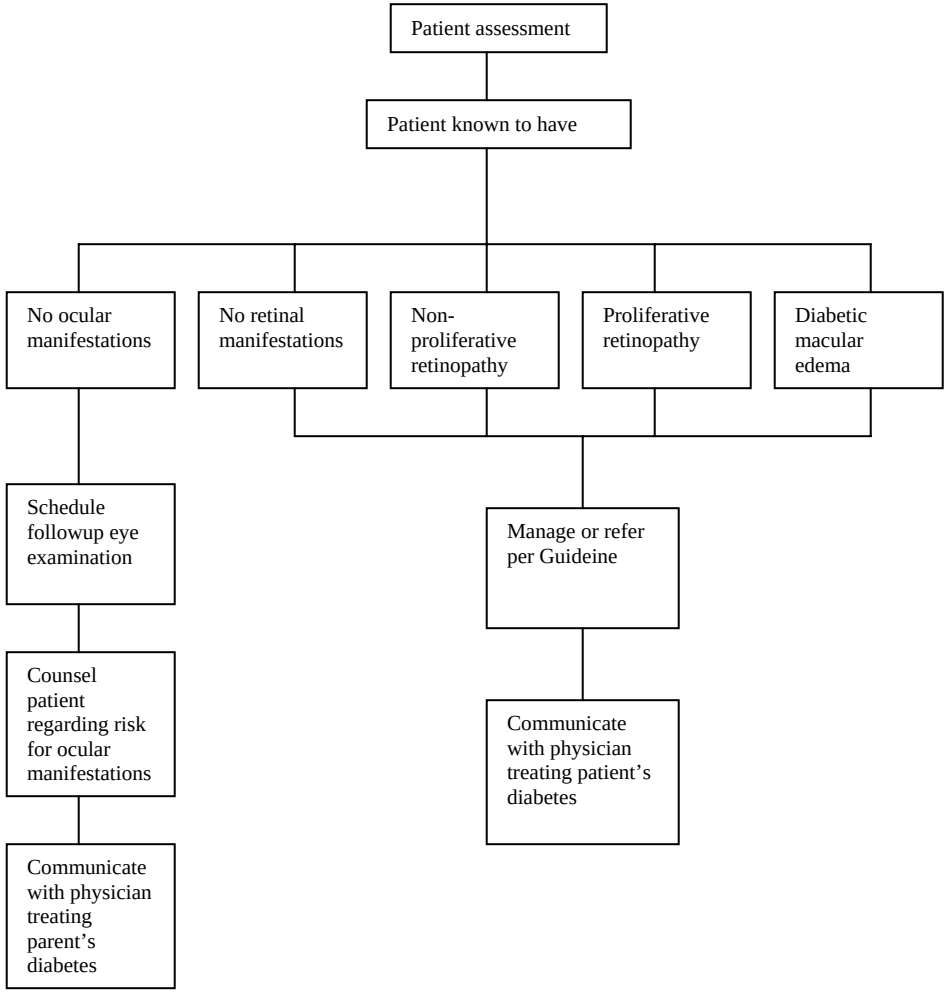

Figure 3
Frequency and Composition of Evaluation and Management Visits for Retinal Complications of Diabetes Mellitus

Severity of Condition	Natural Course Rate of Progression to: PDR (1 year)	Natural Course Rate of Progression to: HRC (5 years)	Frequency of Followup	Composition of Follow-up Evaluations: Fundus Photography	Composition of Follow-up Evaluations: Fluorescein Angiography
Mild NPDR	5%	15%			
No macular edema			12 mos	No	No
Macular edema			4-6 mos	Yes	Occ.
CSME			2-4 mos	Yes	Yes
Moderate NPDR	12-27%	33%			
No macular edema			6-8 mos	Yes	No
Macular edema (not CSME)			4-6 mos	Yes	Occ.
CSME			2-4 mos	Yes	Yes
Severe NPDR	52%	60-75%			
No macular edema			3-4 mos	Yes	No
Macular edema (not CSME)			2-3 mos	Yes	Occ.
CSME			2-3 mos	Yes	Yes
Non-high-risk PDR		75%			
No macular edema			2-3 mos	Yes	No
Macular edema			2-3 mos	Yes	Occ.
CSME			2-3 mos	Yes	Yes
High-risk PDR					
No macular edema			2-3 mos	Yes	No
Macular edema			1-2 mos	Yes	Yes
CSME			1-2 mos	Yes	Yes

* Patient education and written communication with patient's primary care physician are integral to management of DR.

** Consider scatter laser treatment (PRP), especially if every severe NPDR (see levels of DR), significant medical complication, or type 2 DM.

Figure 3 (Continued)

Management Plan*: Referral for Consultation and/or Treatment	Scatter Laser Treatment	Focal Laser Treatment
Communicate with patient's physician	No	No
Obtain retinal consult in 2-4 wks.	No	No
Obtain retinal consult in 2-4 wks.	No	Yes
Communicate with patient's physician	No	No
Obtain retinal consult in 2-4 wks.	No	No
Obtain retinal consult in 2-4 wks.	No	Yes
Obtain retinal consult in 2-4 wks.	Rarely**	No
Obtain retinal consult in 2-4 wks.	Occ. after focal**	Occ.
Obtain retinal consult in 2-4 wks.	Occ. after focal**	Yes
Obtain retinal consult in 2-4 wks.	Occ.***	No
Obtain retinal consult in 2-4 wks.	Occ. after focal***	Occ.
Obtain retinal consult in 2-4 wks.	Occ. after focal***	Yes
Obtain retinal consult in 24-48 hrs..	Yes	No
Obtain retinal consult in 24-48 hrs.	Yes	Usually
Obtain retinal consult in 24-48 hrs.	Yes	Yes

*** Consider scatter laser treatment (PRP), especially if moderate PDR (see levels of DR), significant medical complication, or type 2 DM.

HRC = High risk category; Occ. = Occasionally

[redacted]

[redacted]

Figure 4

ICD-9-CM Classification of Ocular Complications of Diabetes Mellitus

Diabetes mellitus 250
Excludes: gestational diabetes (648.8)
hyperglycemia NOS (790.6)
neonatal diabetes mellitus (775.1)
nonclinical diabetes (790.2)
The following fifth-digit subclassification is for use with category 250:
0 type II [non-insulin dependent type][NIDDM type][adult-onset type] or unspecified type, not stated as uncontrolled
Fifth-digit 0 is for use for type 2, adult-onset, diabetic patients, even if the patient requires insulin
1 type I [insulin dependent type][IDDM type][juvenile type], not stated as uncontrolled
2 type II, [non-insulin dependent type][NIDDM type][adult–onset type] or unspecified type, uncontrolled
Fifth-digit 2 is for use for type II, adult-onset, diabetic patients, even if the patient requires insulin
3 type I [insulin dependent type][IDDM][juvenile type], uncontrolled

Diabetes with ophthalmic manifestations 250.5
Use additional code, if desired, to identify manifestation, as:
diabetic:
blindness (369.00-369.9)
cataract (366.41)
glaucoma (365.44)
retinal edema (362.83)
retinopathy (362.01-362.02)

Diabetic retinopathy 362.0
Code first diabetes (250.5)

Background diabetic retinopathy 362.01
Diabetic macular edema
Diabetic retinal edema
Diabetic retinal microaneurysms
Diabetic retinopathy NOS

Proliferative diabetic retinopathy 362.02

Retinal microaneurysms NOS 362.14

Retinal telangiectasia

Retinal neovascularization NOS 362.16
Neovascularization
choroidal
subretinal

Other intraretinal microvascular abnormalities 362.17
Retinal varices

Retinal hemorrhage 362.81
Hemorrhage:
preretinal
retinal (deep) (superficial)
subretinal

Retinal exudates and deposits 362.82

Retinal edema 362.83
Retinal:
cotton wool spots
edema (localized) (macular) (peripheral)

Retinal ischemia 362.84

Rubeosis iridis 364.42
Neovascularization of iris or ciliary body

Glaucoma associated with systemic syndromes *Code first associated disease*	365.44
Glaucoma associated with vascular disorders Use additional code for associated disorder	365.63
Diabetic cataract *Code first diabetes (250.5)*	366.41
Transient refractive change	367.81
Diplopia Double vision	368.2
Visual field defect, unspecified	368.40
Tritan defect Tritanomaly Tritanopia	368.53
Recurrent erosion of cornea	371.42
Tear film insufficiency, unspecified Dry eye syndrome	375.15
Ischemic optic neuropathy	377.41
Vitreous hemorrhage	379.23

Abbreviations of Commonly Used Terms

ACE	-	Angiotensin converting enzyme
ADA	-	American Diabetes Association
BMI	-	Body mass index
CSME	-	Clinically significant macular edema
DA	-	Disc area
DCCT	-	Diabetes Control and Complications Trial
DD	-	Disc diameter
DM	-	Diabetes mellitus
DNA	-	Deoxribonucleic acid
DR	-	Diabetic retinopathy
DRS	-	Diabetic Retinopathy Study
DRVS	-	Diabetic Retinopathy Vitrectomy Study
ETDRS	-	Early Treatment Diabetic Retinopathy Study
FA	-	Fluorescein angiography
FDA	-	Food and Drug Administration
FPD	-	Fibrous proliferations on or within 1 DD of disc margin
FPE	-	Fibrous proliferations elsewhere, not FPD
FPG	-	Fasting plasma glucose
GAD65	-	Glutamic acid decarboxylase
GDM	-	Gestational diabetes mellitus
HbA_{1c}	-	Glycosylated hemoglobin
HDL	-	High density lipoprotein(s)
HLA	-	Human leukocyte antigen(s)
H/Ma	-	Hemorrhage(s) and/or microaneurysm(s)
IAAs	-	Insulin autoantibodies

ICAs	-	Islet cell antibodies
IDDM	-	Insulin dependent diabetes mellitus
IFG	-	Impaired fasting glucose
IGT	-	Impaired glucose tolerance
IRMA	-	Intraretinal microvascular abnormality
LDL	-	Low density lipoproteins
Ma	-	Microaneurysms
ME	-	Macular edema
MODY	-	Maturity-onset diabetes of the young
NIDDM	-	Non-insulin dependent diabetes mellitus
NPDR	-	Nonproliferative diabetic retinopathy
NVD	-	New vessels on or within 1 DD of disc margin
NVE	-	New vessels elsewhere in the retina outside of disc and 1 DD from disc margin
NVI	-	New vessels on the iris; rubeosis iridis
OGTT	-	Oral glucose tolerance test
PAI-1	-	Plasminogen activator inhibitor
PDR	-	Proliferative diabetic retinopathy
PRH	-	Preretinal hemorrhage
UKPDS	-	United Kingdom Prospective Diabetes Study
VB	-	Venous beading
VH	-	Vitreous hemorrhage
WHO	-	World Health Organization

Glossary

Diabetes mellitus (DM) A group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.

- **Type 1 diabetes** The result of cell-mediated autoimmune destruction of the beta cells of the pancreas, formerly referred to as insulin dependent diabetes mellitus (IDDM).

- **Type 2 diabetes** A disease in which individuals can produce insulin but have cellular resistance to it, formerly referred to as non-insulin dependent diabetes mellitus (NIDDM)

Diabetic cataract A rapidly forming, sometimes reversible, bilateral cataract associated with diabetes mellitus.

Diabetic papillopathy A noninflammatory edema of the optic nerve head associated with diabetes mellitus.

High-risk proliferative diabetic retinopathy New vessels on or within 1 disc diameter of the optic nerve head greater than approximately l/4 to l/3 of the disc, or new vessels on or within 1 disc diameter of the optic nerve head less than l/4 to l/3 the disc area when accompanied by vitreous and/or preretinal hemorrhage, or new vessels elsewhere in the retina greater than l/2 the size of the disc area.

Intraretinal hemorrhage A radially striated hemorrhage in the inner layers of the retina, especially in the nerve fiber layer (flame-shaped hemorrhage).

Intraretinal microvascular abnormality (IRMA) An abnormality that represents either new vessel growth within the retina or pre-existing vessels with endothelial cell proliferation.

Macular edema (ME) Collection of intraretinal fluid in the macular portion of the retina, with or without lipid exudates, and with or without cystoid changes.

Clinically significant macular edema (CSME) The case when there is retinal thickening at or within 500 microns of the center of the macular and/or hard exudates within 500 microns of the center of the macula associated with retinal thickening of the adjacent area of the retina and/or a zone or zones of retinal thickening 1 disc area in size, any part of which is within 1 disc diameter of the center of the macula.

Microaneurysm (Ma) As to the eye, a focal retinal capillary dilation.

Neovascularization Growth of abnormal new blood vessels.

Papilledema Noninflammatory edema of the optic nerve head from various causes, such as increased intracranial pressure, orbital tumor, or blood dyscrasias.

Proliferative diabetic retinopathy (PDR) A type of retinopathy associated with diabetes mellitus, characterized by proliferation of connective tissue and the formation of new blood vessels in the retina, and by hemorrhages into the vitreous.

Retinal hypoxia A deficiency of oxygen supply to the retinal tissue.

Rubeosis iridis Noninflammatory neovascularization of the iris occurring in diabetes mellitus, characterized by numerous, small intertwining blood vessels which anastomose near the sphincter region to give the appearance of a reddish ring near the border of the pupil. The vessels may extend from the root of the iris to the filtration angle to cause peripheral vascular synechiae and secondary glaucoma.

Venous beading (VB) A fragmented appearance of the bloodstream in the retinal veins subsequent to retinal artery occlusion.

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