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

<table>
<thead>
<tr>
<th>Severity of Condition</th>
<th>Natural Course Rate of Progression to PDR (1 year)</th>
<th>HRC (5 years)</th>
<th>Frequency of Followup</th>
<th>Composition of Follow-up Evaluations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fundus Photography</td>
</tr>
<tr>
<td>Mild NPDR</td>
<td>5%</td>
<td>15%</td>
<td>12 mos</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>No macular edema</td>
<td></td>
<td>4-6 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Macular edema</td>
<td></td>
<td>2-4 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>CSME</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>12-27%</td>
<td>33%</td>
<td>6-8 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No macular edema</td>
<td></td>
<td>4-6 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Macular edema (not CSME)</td>
<td></td>
<td>2-4 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>CSME</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe NPDR</td>
<td>52%</td>
<td>60-75%</td>
<td>3-4 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No macular edema</td>
<td></td>
<td>2-3 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Macular edema (not CSME)</td>
<td></td>
<td>2-3 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>CSME</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-high-risk PDR</td>
<td>75%</td>
<td></td>
<td>2-3 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No macular edema</td>
<td></td>
<td>2-3 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Macular edema</td>
<td></td>
<td>2-3 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>CSME</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-risk PDR</td>
<td></td>
<td></td>
<td>2-3 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No macular edema</td>
<td></td>
<td>1-2 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Macular edema</td>
<td></td>
<td>1-2 mos</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>CSME</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 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)

<table>
<thead>
<tr>
<th>Management Plan*</th>
<th>Scatter Laser Treatment</th>
<th>Focal Laser Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Referral for Consultation and/or Treatment</strong></td>
<td><strong>No</strong></td>
<td><strong>No</strong></td>
</tr>
<tr>
<td>Communicate with patient's physician</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Communicate with patient's physician</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>Rarely**</td>
<td>No</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>Occ. after focal**</td>
<td>Occ.</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>Occ. after focal**</td>
<td>Yes</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>Occ.***</td>
<td>No</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>Occ. after focal***</td>
<td>Occ.</td>
</tr>
<tr>
<td>Obtain retinal consult in 2-4 wks.</td>
<td>Occ. after focal***</td>
<td>Yes</td>
</tr>
<tr>
<td>Obtain retinal consult in 24-48 hrs.</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Obtain retinal consult in 24-48 hrs.</td>
<td>Yes</td>
<td>Usually</td>
</tr>
<tr>
<td>Obtain retinal consult in 24-48 hrs.</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*** 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

Table copyright L.M. Aiello, M.D. Used with permission
Figure 4

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

Diabetes mellitus

*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

*Fifth-digit 1 is for use for type 1, insulin dependent, diabetic patients, even if the patient requires insulin*

3 type I [insulin dependent type][IDDM][juvenile type], uncontrolled

Diabetes with ophthalmic manifestations

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

*Code first diabetes (250.5)*
54 Diabetes Mellitus

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

Proliferative diabetic retinopathy

Retinal microaneurysms NOS

Retinal telangiectasia

Retinal neovascularization NOS
  Neovascularization
    choroidal
    subretinal

Other intraretinal microvascular abnormalities
  Retinal varices

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

Retinal exudates and deposits

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

Retinal ischemia

Rubeosis iridis
  Neovascularization of iris or ciliary body
Glaucoma associated with systemic syndromes 365.44
*Code first associated disease*

Glaucoma associated with vascular disorders 365.63
Use additional code for associated disorder

Diabetic cataract 366.41
*Code first diabetes (250.5)*

Transient refractive change 367.81

Diplopia 368.2
  Double vision

Visual field defect, unspecified 368.40

Tritan defect 368.53
  Tritanomaly
  Tritanopia

Recurrent erosion of cornea 371.42

Tear film insufficiency, unspecified 375.15
  Dry eye syndrome

Ischemic optic neuropathy 377.41

Vitreous hemorrhage 379.23
### Table 1

**Standards for Glucose Control**

<table>
<thead>
<tr>
<th>Biochemical index</th>
<th>Nondiabetic</th>
<th>Diabetic goals</th>
<th>Intervention indicated in diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preprandial glucose (mg/dl)</td>
<td>&lt;110</td>
<td>80-120</td>
<td>&lt;80 or &gt;140</td>
</tr>
<tr>
<td>Bedtime glucose (mg/dl)</td>
<td>&lt;120</td>
<td>100-140</td>
<td>&lt;100 or &gt;160</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (HbA1c)</td>
<td>&lt;6</td>
<td>&lt;7</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Duration of disease</td>
<td>Type 1 Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td>Possible ocular manifestations.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>60% have some retinopathy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;15 years</td>
<td>Virtually all patients have some degree of retinopathy. 25% progress to proliferative diabetic retinopathy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;20 years</td>
<td>50% progress to proliferative retinopathy.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of disease</th>
<th>Type 2 Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>At diagnosis</td>
<td>20% have retinopathy.</td>
</tr>
<tr>
<td>&gt;4 years</td>
<td>4% progress to proliferative retinopathy.</td>
</tr>
<tr>
<td>&gt;15 years</td>
<td>60-80% have some retinopathy. Up to 20% progress to proliferative retinopathy.</td>
</tr>
</tbody>
</table>
Table 3
Ocular and Visual Complications of Diabetes Mellitus

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional</td>
<td>Tritan color vision deficiencies</td>
</tr>
<tr>
<td></td>
<td>Refractive error changes</td>
</tr>
<tr>
<td></td>
<td>Accommodative dysfunction</td>
</tr>
<tr>
<td></td>
<td>Visual field defects</td>
</tr>
<tr>
<td>Extraocular muscle anomalies</td>
<td>Mononeuropathies involving third, fourth, or sixth cranial nerves</td>
</tr>
<tr>
<td>Pupillary reflexes</td>
<td>Sluggish pupillary reflexes</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>Bulbar conjunctival microaneurysms</td>
</tr>
<tr>
<td>Tear film</td>
<td>Tear film deficiencies resulting in dry eye syndrome</td>
</tr>
<tr>
<td>Cornea</td>
<td>Reduced corneal sensitivity</td>
</tr>
<tr>
<td></td>
<td>Reduced corneal wound-healing ability</td>
</tr>
<tr>
<td></td>
<td>Basement membrane abnormalities resulting in increased frequency of abrasions or recurrent erosion syndrome</td>
</tr>
<tr>
<td></td>
<td>Descemet's membrane wrinkling</td>
</tr>
<tr>
<td></td>
<td>Endothelial cell morphology changes, often resulting in increased corneal thickness</td>
</tr>
<tr>
<td>Iris</td>
<td>Depigmentation</td>
</tr>
<tr>
<td></td>
<td>Rubeosis iridis, possibly with associated ectropion uvea and peripheral anterior synechiae</td>
</tr>
<tr>
<td></td>
<td>Neovascular glaucoma</td>
</tr>
<tr>
<td>Lens</td>
<td>Higher prevalence of cataracts</td>
</tr>
</tbody>
</table>
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
<table>
<thead>
<tr>
<th>Duration of Type 1 Diabetes</th>
<th>Incidence of Diabetic Retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 years</td>
<td>27%</td>
</tr>
<tr>
<td>5-9 years</td>
<td>71%</td>
</tr>
<tr>
<td>10-14 years</td>
<td>54%</td>
</tr>
<tr>
<td>15+ years</td>
<td>38%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of Type 2 Diabetes</th>
<th>Incidence of Diabetic Retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 years</td>
<td>31%</td>
</tr>
<tr>
<td>5-9 years</td>
<td>32%</td>
</tr>
<tr>
<td>10-14 years</td>
<td>38%</td>
</tr>
<tr>
<td>15+ years</td>
<td>51%</td>
</tr>
<tr>
<td>Category</td>
<td>Ocular Complications</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Functional</td>
<td>Tritan color vision loss</td>
</tr>
<tr>
<td>Extraocular muscle anomalies</td>
<td>Refractive error changes</td>
</tr>
<tr>
<td></td>
<td>Accommodative dysfunction</td>
</tr>
<tr>
<td></td>
<td>Visual field defects</td>
</tr>
<tr>
<td>Extraocular muscle anomalies</td>
<td>Mononeuropathies</td>
</tr>
<tr>
<td>Pupils</td>
<td>Sluggish pupillary reflexes</td>
</tr>
<tr>
<td></td>
<td>Afferent pupillary defects</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>Bulbar microaneurysms</td>
</tr>
<tr>
<td>Tear film</td>
<td>Dry eye syndrome</td>
</tr>
<tr>
<td>-----------</td>
<td>------------------</td>
</tr>
<tr>
<td>Cornea</td>
<td>Reduced corneal sensitivity</td>
</tr>
<tr>
<td></td>
<td>Basement membrane anomalies, recurrent corneal erosions</td>
</tr>
<tr>
<td>Cornea (continued)</td>
<td>Descemet's membrane wrinkling</td>
</tr>
<tr>
<td></td>
<td>Endothelial cell changes</td>
</tr>
<tr>
<td></td>
<td>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.</td>
</tr>
<tr>
<td>Iris</td>
<td>Depigmentation</td>
</tr>
<tr>
<td></td>
<td>Rubeosis iridis (neovascularization on the iris)</td>
</tr>
<tr>
<td>Lens</td>
<td>Cataracts</td>
</tr>
<tr>
<td>----------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Vitreous</td>
<td>Hemorrhage</td>
</tr>
</tbody>
</table>

* Patient education is an integral part of management for all conditions.
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 ≥ standard photo 2A in all four quadrants
  - VB definitely present in at least two quadrants (see standard photo 6B)
  - IRMA ≥ 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)

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 ≥ 1/4 to 1/3 DA (standard photo 10A)
    - NVD and VH/PRH
    - NVE ≥ 1/2 DA and VH/PRH

III. Clinically Significant Macular Edema (CSME)
  • One or more of the following:
    - Thickening of the retina ≤500 microns (1/3 DD) from the center of the macula
    - Hard exudates ≤ 500 microns (1/3 DD) from the center of the macula with thickening of the adjacent retina
    - A zone or zones of retinal thickening ≥1 DA in size, any portion of which is ≤1 DD from the center of the macula
***All figures and tables above are from:
Values for Glucose Testing

Fasting plasma glucose

Normal range: 65 to 99mg/dL
Pre-Diabetes: 100 to 125mg/dL *
Diabetes: >126mg/dL *

Random plasma glucose

Normal range: 65 to 200mg/dL
Diabetes: > 200mg/dL *

Oral glucose tolerance test after 100g glucose load
Fasting: <105mg/dL
1 hour: < 190mg/dL
2 hours: < 165mg/dL
3 hours: <145mg/dL

Glycosylated hemoglobin (HbA1c or A1c)

Normal: 4% to 6%
Good control: <7%
Fair control: 7% to 9%
Poor control: >9%

Serum Lipid Profile Normal Values
Total cholesterol
100 to 199mg/dL
Triglycerides
0-149mg/dL
High-density lipoproteins
40-59mg/dL
Low-density lipoproteins
0-99mg/dL
Very-low density lipoproteins
5-40mg/dL

Complete Blood Count Normal Values

Hematologic Test
Red blood cell
Normal Adult Value
4.6million to 6.2 million cells/uL (males)
4.2million to 5.4 million cells/uL (females)

Hemoglobin
12 to 18g/dL

Hematocrit
40% to 54% (males); 37% to 47% (females)

Mean corpuscular volume
80 to 100fL

Platelets
140,000 to 450,000/mm

Mean platelet volume
7 to 11fL

White blood cell
4000 to 10,000/mm
Normal Values for Differential White Blood Cells

Neutrophils 3,150 to 6,200/uL; 36% to 68%
Lymphocytes 1,500 to 3,000/uL; 22% to 50%
Monocytes 300 to 500/uL; 5% to 11%
Eosinophils 50 to 250/uL; 1% to 5%
Basophils 15 to 50/uL; <1%

Renal Function Tests Normal Values

Blood urea nitrogen 10 to 20mg/dL
Serum creatinine 0.3 to 1.5mg/dL

Thyroid Function Testing Normal Values

Triiodothyronine (T3) 80 to 180ng/dL
Thyroxine (T4) 4.5 to 12ug/dL
Thyroid stimulating hormone 0.3 to 3.04mU/L

***Data above referenced from the following article:

Standards of Care

- Supplemental Reference – 2005 Diabetic Fact Sheet
- American Optometric Association
- American Diabetes Association
National Diabetes Fact Sheet, 2005

General Information

What is diabetes?

Diabetes is a group of diseases marked by high levels of blood glucose resulting from defects in insulin production, insulin action, or both. Diabetes can lead to serious complications and premature death, but people with diabetes can take steps to control the disease and lower the risk of complications.

Types of diabetes

Type 1 diabetes was previously called insulin-dependent diabetes mellitus (IDDM) or juvenile-onset diabetes. Type 1 diabetes develops when the body's immune system destroys pancreatic beta cells, the only cells in the body that make the hormone insulin that regulates blood glucose. To survive, people with type 1 diabetes must have insulin delivered by injection or a pump. This form of diabetes usually strikes children and young adults, although disease onset can occur at any age. Type 1 diabetes accounts for 5% to 10% of all diagnosed cases of diabetes. Risk factors for type 1 diabetes may be autoimmune, genetic, or environmental. There is no known way to prevent type 1 diabetes. Several clinical trials of methods of the prevention of type 1 diabetes are currently in progress or are being planned.

Type 2 diabetes was previously called non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes. Type 2 diabetes accounts for about 90% to 95% of all diagnosed cases of diabetes. It usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to produce it. Type 2 diabetes is associated with older age, obesity, family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity. African Americans, Hispanic/Latino Americans, American Indians, and some Asian Americans and Native Hawaiians or Other Pacific Islanders are at particularly high risk for type 2 diabetes and its complications. Clinically-based reports and regional studies suggest that type 2 diabetes in children and adolescents, although still rare, is being diagnosed more frequently, particularly in American Indians, African Americans, and Hispanic/Latino Americans.

Gestational diabetes is a form of glucose intolerance diagnosed in some women during pregnancy. Gestational diabetes occurs more frequently among African Americans, Hispanic/Latino Americans, and American Indians. It is also more common among obese women and women with a family history of diabetes. During pregnancy, gestational diabetes requires treatment to normalize maternal blood glucose levels to avoid complications in the infant. After pregnancy, 5% to 10% of women with gestational diabetes are found to have type 2 diabetes. Women who have had gestational diabetes have a 20% to 50% chance of developing diabetes in the next 5–10 years.

Other types of diabetes result from specific genetic conditions (such as maturity-onset diabetes of youth), surgery, drugs, malnutrition, infections, and other illnesses. Such types of diabetes account for 1% to 5% of all diagnosed cases.
Treating diabetes

- To survive, people with type 1 diabetes must have insulin delivered by injection or a pump.
- Many people with type 2 diabetes can control their blood glucose by following a healthy meal plan and exercise program, losing excess weight, and taking oral medication.
- Many people with diabetes also need to take medications to control their cholesterol and blood pressure.
- Diabetes self-management education (DMSE) is an integral component of medical care.
- Among adults with diagnosed diabetes, 16% take insulin only, 12% take both insulin and oral medication, 57% take oral medication only, and 15% do not take either insulin or oral medications.

Treatment with insulin or oral medications among adults with diagnosed diabetes—United States, 2001–2003

![Pie chart showing treatment with insulin or oral medications](chart)

Source: 2001–2003 National Health Interview Survey

Prediabetes: Impaired glucose tolerance and impaired fasting glucose

- Prediabetes is a condition that raises the risk of developing type 2 diabetes, heart disease, and stroke. People with prediabetes have blood glucose levels higher than normal but not high enough to be classified as diabetes.
- People with prediabetes have impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). Some people have both IFG and IGT.
- IFG is a condition in which the fasting blood sugar level is 100 to 125 milligrams per deciliter (mg/dL) after an overnight fast. The level is higher than normal but not high enough to be classified as diabetes.
- IGT is a condition in which the blood sugar level is 140 to 199 mg/dL after a 2-hour oral glucose tolerance test. This level is higher than normal but not high enough to be classified as diabetes.
- In a cross-section sample of U.S. adults aged 40–74 years tested from 1988 to 1994, 33.8% had IFG, 15.4% had IGT, and 40.1% had prediabetes (IGT or IFG or both). Applying these percentages to the entire U.S. population in 2000, an estimated 35 million adults aged 40–74 had IFG, 16 million had IGT, and 41 million had prediabetes.
• Progression to diabetes among those with prediabetes is not inevitable. Studies have shown that people with prediabetes who lose weight and increase their physical activity can prevent or delay diabetes and even return their blood glucose levels to normal.

National Estimates on Diabetes

The estimates on diabetes in this fact sheet were derived from various data systems of the Centers for Disease Control and Prevention, the outpatient database of the Indian Health Service (IHS), the U.S. Renal Data System of the National Institutes of Health, the U.S. Census Bureau, and published studies. Estimates of the total number of persons with diabetes and the prevalence of diabetes in 2005 were derived using 1999–2002 National Health and Nutrition Examination Survey (NHANES), 1999-2003 National Health Interview Survey (NHIS), 2003 IHS data, and 2005 resident population estimates. Many of the estimated numbers and percentages of people with diabetes were derived by applying diabetes prevalence estimates from health surveys of the civilian, noninstitutionalized population to the most recent 2005 resident population estimates. These estimates have some variability due to the limits of the measurements and estimation procedures. The procedures assumed that age-race-sex–specific percentages of adults with diabetes (diagnosed and undiagnosed) in 2005 are the same as they were in earlier time periods (e.g., 1999–2002) and that the age-race-sex percentages of adults with diabetes in resident population is identical to that in the civilian, noninstitutionalized population. Deviations from these assumptions may result in over- or under-estimated numbers and percentages. For further information on the methods for deriving total, diagnosed, and undiagnosed prevalence of diabetes from NHANES data, see http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5235a1.htm. More detail on the data sources, references, and methods are available at http://www.cdc.gov/diabetes/pubs/references.htm.

Diabetes Prevalence

Total prevalence of diabetes in the United States, all ages, 2005

Total: 20.8 million people—7.0% of the population—have diabetes.

Diagnosed: 14.6 million people

Undiagnosed: 6.2 million people

Prevalence of diagnosed diabetes in people under 20 years of age, United States, 2005

About 176,500 people under 20 years of age have diabetes. This represents 0.22% of all people in this age group.

About one in every 400 to 600 children and adolescents has type 1 diabetes.
Although type 2 diabetes can occur in youth, the nationally representative data that would be needed to monitor diabetes trends in youth by type are not available. Clinically-based reports and regional studies suggest that type 2 diabetes, although still rare, is being diagnosed more frequently in children and adolescents, particularly in American Indians, African Americans, and Hispanic/Latino Americans.

Total prevalence of diabetes among people aged 20 years or older, United States, 2005

**Age 20 years or older**: 20.6 million, or 9.6% of all people in this age group have diabetes.

**Age 60 years or older**: 10.3 million, or 20.9% of all people in this age group have diabetes.

**Men**: 10.9 million, or 10.5% of all men aged 20 years or older have diabetes.

**Women**: 9.7 million, or 8.8% of all women aged 20 years or older have diabetes.

Total prevalence of diabetes by race/ethnicity among people aged 20 years or older, United States, 2005

**Non-Hispanic whites**: 13.1 million, or 8.7% of all non-Hispanic whites aged 20 years or older have diabetes.

**Non-Hispanic blacks**: 3.2 million, or 13.3% of all non-Hispanic blacks aged 20 years or older have diabetes. After adjusting for population age differences, non-Hispanic blacks are 1.8 times as likely to have diabetes as non-Hispanic whites.
Hispanic/Latino Americans: After adjusting for population age differences, Mexican Americans, the largest Hispanic/Latino subgroup, are 1.7 times as likely to have diabetes as non-Hispanic whites. If the prevalence of diabetes among Mexican Americans was applied to the total Hispanic/Latino population, about 2.5 million (9.5%) Hispanic/Latino Americans aged 20 years or older would have diabetes. Sufficient data are not available to derive estimates of the total prevalence of diabetes (both diagnosed and undiagnosed diabetes) for other Hispanic/Latino groups. However, residents of Puerto Rico are 1.8 times as likely to have diagnosed diabetes as U.S. non-Hispanic whites.

American Indians and Alaska Natives: 99,500, or 12.8% of American Indians and Alaska Natives aged 20 years or older who received care from IHS in 2003 had diagnosed diabetes. Applying the rate of undiagnosed diabetes in the total U.S. population to the American Indians and Alaska Natives who receive care from IHS gives an estimate of 118,000 (15.1%) American Indians and Alaska Natives aged 20 years or older with diabetes (both diagnosed and undiagnosed diabetes). After adjusting for population age differences, the total prevalence of diabetes in this group is lowest among Alaska Natives (8.1%) and highest among American Indians in the southern United States (26.7%) and in southern Arizona (27.6%). Taking into account population age differences, American Indians and Alaska Natives are 2.2 times as likely to have diabetes as non-Hispanic whites.

Asian Americans and Pacific Islanders: The total prevalence of diabetes (both diagnosed and undiagnosed diabetes) is not available for Asian Americans or Pacific Islanders. However, in Hawaii, Asians, Native Hawaiians, and other Pacific Islanders aged 20 years or older are more than 2 times as likely to have diagnosed diabetes as whites after adjusting for population age differences. Similarly, in California, Asians were 1.5 times as likely to have diagnosed diabetes as non-Hispanic whites. Other groups within these populations also have increased risk for diabetes.

Estimated age-adjusted total prevalence of diabetes in people aged 20 years or older, by race/ethnicity—United States, 2005

Source: For American Indians/Alaska Natives, the estimate of total prevalence was calculated using the estimate of diagnosed diabetes from the 2003 outpatient database of the Indian Health Service and the estimate of undiagnosed diabetes from the 1999-2002 National Health and Nutrition Examination Survey. For the other groups, 1999-2002 NHANES estimates of total prevalence (both diagnosed and undiagnosed diabetes) were projected to year 2005.

Incidence of diabetes, United States, 2005

1.5 million new cases of diabetes were diagnosed in people aged 20 years or older in 2005.
Estimated number of new cases of diagnosed diabetes in people aged 20 years or older, by age group—United States, 2005


Deaths among people with diabetes, United States, 2002

- Diabetes was the sixth leading cause of death listed on U.S. death certificates in 2002. This ranking is based on the 73,249 death certificates in which diabetes was listed as the underlying cause of death. According to death certificate reports, diabetes contributed to a total of 224,092 deaths.
- Diabetes is likely to be underreported as a cause of death. Studies have found that only about 35% to 40% of decedents with diabetes had it listed anywhere on the death certificate and only about 10% to 15% had it listed as the underlying cause of death.
- Overall, the risk for death among people with diabetes is about twice that of people without diabetes of similar age.

Complications of diabetes in the United States

Heart disease and stroke

- Heart disease and stroke account for about 65% of deaths in people with diabetes.
- Adults with diabetes have heart disease death rates about 2 to 4 times higher than adults without diabetes.
- The risk for stroke is 2 to 4 times higher among people with diabetes.

High blood pressure

- About 73% of adults with diabetes have blood pressure greater than or equal to 130/80 millimeters of mercury (mm Hg) or use prescription medications for hypertension.
Blindness

- Diabetes is the leading cause of new cases of blindness among adults aged 20–74 years.
- Diabetic retinopathy causes 12,000 to 24,000 new cases of blindness each year.

Kidney disease

- Diabetes is the leading cause of kidney failure, accounting for 44% of new cases in 2002.
- In 2002, 44,400 people with diabetes began treatment for end-stage kidney disease in the U.S. and Puerto Rico.
- In 2002, a total of 153,730 people with end-stage kidney disease due to diabetes were living on chronic dialysis or with a kidney transplant in the U.S. and Puerto Rico.

Nervous system disease

- About 60% to 70% of people with diabetes have mild to severe forms of nervous system damage. The results of such damage include impaired sensation or pain in the feet or hands, slowed digestion of food in the stomach, carpal tunnel syndrome, and other nerve problems.
- Almost 30% of people with diabetes aged 40 years or older have impaired sensation in the feet (i.e., at least one area that lacks feeling).
- Severe forms of diabetic nerve disease are a major contributing cause of lower-extremity amputations.

Amputations

- More than 60% of nontraumatic lower-limb amputations occur in people with diabetes.
- In 2002, about 82,000 nontraumatic lower-limb amputations were performed in people with diabetes.

Dental disease

- Periodontal (gum) disease is more common in people with diabetes. Among young adults, those with diabetes have about twice the risk of those without diabetes.
- Almost one-third of people with diabetes have severe periodontal disease with loss of attachment of the gums to the teeth measuring 5 millimeters or more.

Complications of pregnancy

- Poorly controlled diabetes before conception and during the first trimester of pregnancy can cause major birth defects in 5% to 10% of pregnancies and spontaneous abortions in 15% to 20% of pregnancies.
- Poorly controlled diabetes during the second and third trimesters of pregnancy can result in excessively large babies, posing a risk to both mother and child.

Other complications

- Uncontrolled diabetes often leads to biochemical imbalances that can cause acute life-threatening events, such as diabetic ketoacidosis and hyperosmolar (nonketotic) coma.
• People with diabetes are more susceptible to many other illnesses and, once they acquire these illnesses, often have worse prognoses. For example, they are more likely to die with pneumonia or influenza than people who do not have diabetes.

Preventing diabetes complications

Diabetes can affect many parts of the body and can lead to serious complications such as blindness, kidney damage, and lower-limb amputations. Working together, people with diabetes and their health care providers can reduce the occurrence of these and other diabetes complications by controlling the levels of blood glucose, blood pressure, and blood lipids, and by receiving other preventive care practices in a timely manner.

Glucose control

• Studies in the United States and abroad have found that improved glycemic control benefits people with either type 1 or type 2 diabetes. In general, every percentage point drop in A1C blood test results (e.g., from 8.0% to 7.0%) reduces the risk of microvascular complications (eye, kidney, and nerve diseases) by 40%.

Blood pressure control

• Blood pressure control reduces the risk of cardiovascular disease (heart disease or stroke) among persons with diabetes by 33% to 50%, and the risk of microvascular complications (eye, kidney, and nerve diseases) by approximately 33%.
• In general, for every 10 mm Hg reduction in systolic blood pressure, the risk for any complication related to diabetes is reduced by 12%.

Control of blood lipids

• Improved control of cholesterol or blood lipids (for example, HDL, LDL, and triglycerides) can reduce cardiovascular complications by 20% to 50%.

Preventive care practices for eyes, kidneys, and feet

• Detecting and treating diabetic eye disease with laser therapy can reduce the development of severe vision loss by an estimated 50% to 60%.
• Comprehensive foot care programs can reduce amputation rates by 45% to 85%.
• Detecting and treating early diabetic kidney disease by lowering blood pressure can reduce the decline in kidney function by 30% to 70%. Treatment with ACE inhibitors and angiotensin receptor blockers (ARBs) are more effective in reducing the decline in kidney function than other blood pressure lowering drugs.

Estimated diabetes costs in the United States in 2002

Total (direct and indirect): $132 billion

Direct medical costs: $92 billion

Indirect costs: $40 billion (disability, work loss, premature mortality)
These data are based on a study by the Lewin Group, Inc., for the American Diabetes Association and are 2002 estimates of both the direct (cost of medical care and services) and indirect costs (costs of short-term and permanent disability and of premature death) attributable to diabetes. This study used a specific cost-of-disease methodology to estimate the health care costs due to diabetes.
Acknowledgments

The following organizations collaborated in compiling the information for this fact sheet:

• Agency for Healthcare Research and Quality
  http://www.ahrq.gov/browse/diabetes.htm
• American Association of Diabetes Educators
  http://www.aadenet.org
• American Diabetes Association
  http://www.diabetes.org
• Centers for Disease Control and Prevention
  http://www.cdc.gov/diabetes
  http://www.cdc.gov/nchs
• Centers for Medicare and Medicaid Services
  http://cms.hhs.gov
• Department of Veterans Affairs
  http://www.va.gov/health/diabetes
• Health Resources and Services Administration
  http://www.hrsa.gov
• Indian Health Service
  http://www.ihs.gov/MedicalPrograms/Diabetes/index.asp
• Juvenile Diabetes Research Foundation International
  http://www/jdrf.org
• National Diabetes Education Program, a joint program of NIH and CDC
  http://www.ndep.nih.gov
  http://www.cdc.gov/diabetes/ndep/index.htm
• National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health
  http://www.niddk.nih.gov
• U.S. Department of Health and Human Services, Office of Minority Health
  http://www.omhrc.gov

Note
This publication is not subject to copyright restrictions; please duplicate and distribute copies as desired.

Citation

CDC Division of Diabetes Translation Public Inquiries/Publications
Phone toll free: 1-877-CDC-DIAB (877-232-3422)
Fax: 1-301-562-1050
Internet: www.cdc.gov/diabetes
E-mail: diabetes@cdc.gov
Mail: P.O. Box 8728, Silver Spring, MD 20910
OPTOMETRIC CLINICAL PRACTICE GUIDELINE
CARE OF THE PATIENT WITH DIABETES MELLITUS

Reference Guide for Clinicians

Third Revision
2002

Edited and Revised by:

Jerry Cavallerano, OD, PhD
Ramachandiran Cooppan, MD
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 providers in more than 4,300 communities.

The mission of the profession of optometry is to fulfill the vision and eye care needs of the public through clinical care, research, and education, all of which enhance the quality of life.

NOTE: Clinicians should not rely on this 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.
INTRODUCTION

I. STATEMENT OF THE PROBLEM
   A. Description and Classification of Diabetes Mellitus
      1. Diabetes Mellitus
         a. Type 1 Diabetes Mellitus
         b. Type 2 Diabetes Mellitus
         c. Impaired Glucose Tolerance
         d. Gestational Diabetes Mellitus
         e. Other Specific Types of Diabetes
      2. Treatment of Diabetes Mellitus
   B. Epidemiology of Diabetes Mellitus
      1. Prevalence and Incidence
         a. Diabetes Mellitus
         b. Ocular Manifestations
      2. Risk Factors
         a. Screening for Diabetes Mellitus
         b. Examination for Ocular Manifestations of Diabetes Mellitus
   C. Clinical Background of Ocular Manifestations of Diabetes Mellitus
      1. Natural History
      2. Classification and Signs of Diabetic Retinopathy
         a. Nonproliferative Diabetic Retinopathy
         b. Proliferative Diabetic Retinopathy
         c. Macular Edema
      3. Early Detection and Prevention

II. CARE PROCESS
   A. Diagnosis of Ocular Manifestations of Diabetes Mellitus
      1. Patient History
         a. Patients with Undiagnosed Diabetes Mellitus
         b. Patients with Diagnosed Diabetes Mellitus
      2. Ocular Examination
      3. Examination Technique
      4. Supplemental Testing
   B. Management of Ocular Manifestations of Diabetes Mellitus
      1. Basis for Treatment
         a. Patients with Undiagnosed Diabetes Mellitus
         b. Patients with Nonretinal Ocular Complications
         c. Patients with Retinal Complications
      2. Available Treatment Options
         a. Nonproliferative Diabetic Retinopathy
         b. Proliferative Diabetic Retinopathy
         c. Macular Edema
      3. Patient Education
      4. Prognosis and Followup
      5. Management of Patients with Severe, Irreversible Vision Loss
CONCLUSION

REFERENCES

APPENDIX

Figure 1: Optometric Management of the Patient with Undiagnosed Diabetes Mellitus: 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
Figure 4: ICD-9-CM Classification of Ocular Complications of Diabetes Mellitus
Abbreviations of Commonly Used Terms
Glossary
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. The definitions and categories of DM used in this document are based on the most recent classifications reported by the American Diabetes Association. (See Appendix Figure 4 for ICD-9-CM classifications).

The following important changes have been made in the classification of DM:

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.
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).  

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.

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<sub>1c</sub>) 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.

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, thiazolidinedione (troglitazone). 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. 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 (HbA1c) 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 HbA1c 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. A strong relationship between glycemic control and microvascular complications was also noted in the Stockholm Diabetes Intervention Study. 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. 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 HbA1c 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 HbA1c levels following the conclusion of the DCCT. Four years following the DCCT, the mean HbA1c of the patients who were in the control group was 8.2 percent, compared with 7.9 percent for the intensive group. The average HbA1c 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 HbA1c levels. 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, gliargine, 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

Insert Table 1 Here

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 80.66 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. 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.

INSERT TABLE 2 HERE

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. The United Kingdom Prospective Diabetes Study showed similar findings for persons with type 2 diabetes.

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. 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/m²)
- 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
- 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. Patients with positive results should be retested. Screening of urine glucose levels is not recommended, nor should the HbA₁c 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:

- 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.

- 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.

| INSERT TABLE 3 HERE |

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.\textsuperscript{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:

- 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. Diabetic papillopathy is a distinct clinical entity that must be distinguished from papilledema or other etiologies of optic disc swelling. 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.

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. The clinical appearance of early anterior ischemic optic neuropathy is difficult to distinguish from diabetic papillopathy. Diabetic patients are also susceptible to retrobulbar ischemic optic neuropathy, although its occurrence is uncommon in DM.

2. Classification and Signs of Diabetic Retinopathy