Healthy Sight Counseling:

Diabetes and the Eye

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HEALTHY SIGHT COUNSELING

TRANSITIONS PARTNERS IN EDUCATION




BACKGROUND

The Healthy Sight Counseling (HSC) initiative was launched by Transitions Optical Inc. in 2006 as part of an ongoing educational outreach program directed to both professional and lay audiences. The purpose of HSC is to provide eye care professionals with a blueprint to encourage Healthy Sight (HS) in their patients.

Healthy Sight is defined as the enhancement of both quantity and quality of vision and the preservation of good vision through maintenance and preventive eye care. Healthy Sight Counseling extends beyond the usual boundaries of vision care in 4 important ways:

1) By emphasizing the relevance of quality as well as quantity of vision

2) By removing the artificial distinction between refractive (vision) care and medical (eye) care

3) By recognizing the integral relationship between ocular and systemic health

4) By advocating the use of spectacle lens enhancements to maximize vision today and preserve the health and well being of the eyes for tomorrow

Healthy Sight Counseling emphasizes the intimate relationship between ocular health and ocular function, erasing the often artificial distinction that has sometimes been made between vision and eye care, and stressing the importance of maintenance and preventive eye care to achieve Healthy Sight.

If Healthy Sight Counseling is to achieve the goal of fostering Healthy Sight now and for the future, the interrelationships between ocular and systemic health cannot be overlooked. In fact, these relationships must be central.

There are a number of reasons why Healthy Sight Counseling is important for the patient with diabetes:

- There has been an alarming increase in the incidence of diabetes worldwide over the past decade, with the disease reaching what has been described as epidemic proportions
- The eye is one of the most frequent and most important target organs for diabetes-related disease
- A better understanding of the pathophysiology of diabetes and exciting new therapies being developed for the treatment of diabetes and diabetic retinopathy make the early diagnosis and treatment of diabetes and its ocular complications crucial in minimizing both ocular and systemic morbidity from this disease
- Diabetes-related eye disease is one of the major causes of ocular disability and blindness worldwide. Such disability includes both direct ocular sequelae of diabetes (eg, diabetic retinopathy) and indirect sequelae (eg, increased incidence of such vision-threatening ocular diseases as cataract, glaucoma, and age-related macular degeneration)
- The ocular protective aspects of Healthy Sight Counseling are especially relevant for the diabetic eye because of its increased susceptibility to such common vision-threatening diseases as cataract and age-related macular degeneration, in which UV radiation exposure is considered a significant risk factor
- Quality-of-vision issues, such as decreased contrast sensitivity and increased glare sensitivity, may be more relevant in patients with diabetes, so the spectacle lens enhancements recommended as a component of Healthy Sight Counseling may be of particular benefit to diabetics

In an effort to reinforce the integral relationship between the ocular and the systemic aspects of diabetes, this monograph provides a comprehensive approach to diabetes in the eye. It discusses the epidemiology of the disease; its pathophysiology, diagnosis and treatment; characteristics of diabetes-related ocular disease; and the use of modern spectacle lens enhancements to improve, protect, and preserve Healthy Sight in the patient with diabetes.

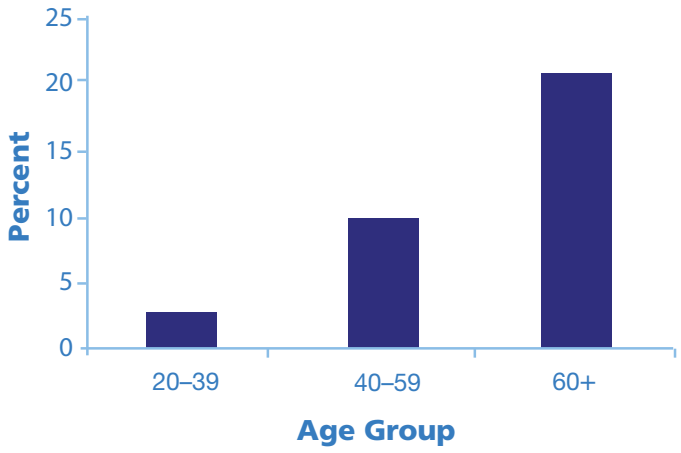
As the individual on the front line for vision care, the eye care professional is in the unique position not only to provide vision correction but also to counsel patients—and particularly those with sight-threatening diseases—about how best to optimize their vision and to protect and preserve it for a lifetime of Healthy Sight. With Healthy Sight Counseling, the role of the eye care professional does not stop at prescribing or dispensing eyeglasses; preventive eye care and ocular health concerns are also addressed. The task of the eye care professional extends one step further by working with the patient and other healthcare professionals to promote good ocular and systemic health.

DIABETES:
The Epidemic of the 21st Century

Many public health experts consider diabetes to be the major health epidemic of the 21st century. The current prevalence of diabetes in the United States has been estimated at approximately 20.8 million people, meaning that 7% of Americans are affected. Compare these figures to earlier data (1996) when there were only 8.5 million cases of diabetes, which represented 3.2% of the US population. Diabetes is widely recognized as one of the leading causes of morbidity, mortality, and disability in the United States.[1]

Diabetes is not just a health care crisis in the United States (FIGURE 1); it is a burgeoning global epidemic. It is projected that for every 1% increase in the population worldwide between 1995 and 2025, there will be a 3% increase in the number of cases of diabetes.[1] An estimated 189 million people worldwide had diabetes in 2003; by 2005 it is estimated that the figure will grow to 324 million. And while countries in the developing world currently have lower rates of diabetes than the United States and Europe, increases in diabetes prevalence of more than 90% are expected in Africa, and in much of Asia and the Middle East (FIGURE 2).

There are 2 types of diabetes: Type 1 and Type 2. Approximately 90% of cases of diabetes are Type 2. While Type 2 diabetes has long been considered a disease of the elderly or middle-aged, the demographics of the disease are rapidly shifting, so that currently approximately 50% of patients with Type 2 diabetes are below age 60.[2]



*1999-2002 National Health and Nutrition Examination Survey estimates of total prevalence (both diagnosed and undiagnosed) projected to year 2005.

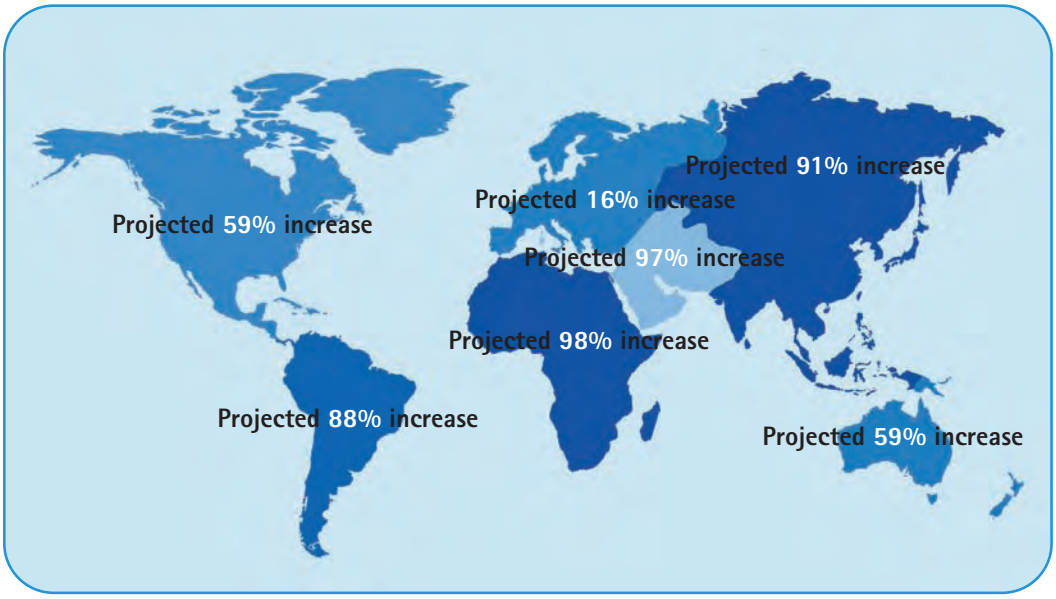
FIGURE 1. Estimated* total prevalence of diabetes in people aged 20 years or older in the United States, by age group

Source: Centers for Disease Control and Prevention. *National Diabetes Fact Sheet: National Estimates on Diabetes.* Available at: http://www.cdc.gov/diabetes/pubs/estimates05.htm. Accessed April 24, 2008.

Of particular concern is the escalating incidence in children and adolescents of what has been traditionally called "adult onset diabetes" (ie, Type 2). An increasingly sedentary lifestyle and the rising rate of childhood obesity are considered primary contributing factors, setting the stage for a lifetime of diabetes-related health issues. (See *Diabetes and Children: Facts* on page 11).[3,4]

Diabetes also tends to occur more commonly in certain ethnic populations, particularly in African Americans; in Native Americans and Alaskan natives, in some groups of Asian Americans, in Native Hawaiians and other Pacific Islander Americans; and in Hispanics and Latinos. On average, African Americans are 1.8 times as likely to have diabetes as non-Hispanic whites of the same age. Mexican Americans are 1.7 times as likely to have diabetes as non-Hispanic whites of similar age.[1]

FIGURE 2. An estimated 189 million people worldwide had diabetes in 2003. By 2025, it is estimated that 324 million people will have diabetes



Source: Adapted from Zimmet P et al. *Diabet Med.* 2003;20:693-702.

The overall rise in the prevalence of diabetes and the appearance of the disease at increasingly earlier ages can be expected to increase the number and the severity of diabetic complications in the eye as well as in the body, with diabetic retinopathy being of particular concern (FIGURE 3). Diabetes is already the leading cause of new cases of blindness among adults aged 20 to 74 years, with diabetic retinopathy being responsible for between 12,000 and 24,000 new cases of blindness each year in the United States.[2]

According to the Centers for Disease Control and Prevention, the age-adjusted prevalence of visual impairment in 2002 among persons ≥50 years of age with diabetes was 23.5%.[5] In the same age cohort without diabetes, the age-adjusted prevalence of visual impairment was 12.4%. The age-adjusted prevalence of diabetic retinopathy among persons ≥50 years of age with diabetes was 10.2%, and the age-adjusted prevalence of cataracts among persons ≥50 years of age with diabetes was 32% compared to 21% in the same age group without diabetes.[5]

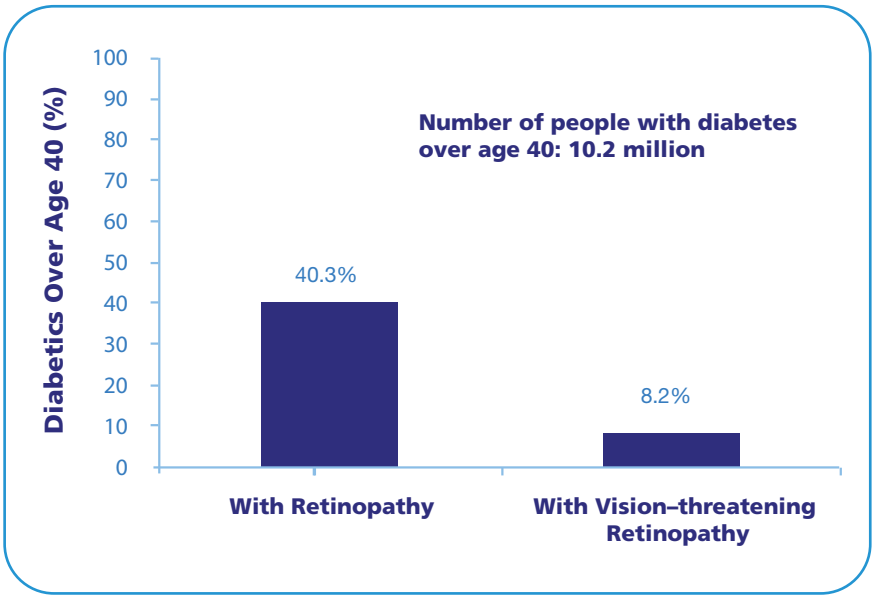


FIGURE 3.
Prevalence of diabetic retinopathy in the United States

Source: The Eye Diseases Prevalence Research Group. *Arch Ophthalmol.* 2004;122:552-563.

DIABETES:
Pathophysiology and Current Concepts

Diabetes is a metabolic disorder characterized by hyperglycemia, insulin resistance, hyper- or hypoinsulinemia, and progressive pancreatic β-cell failure. As mentioned previously, there are 2 principal types of diabetes:

- **Type 1 diabetes** is caused by a decrease in or absence of insulin production, and so its therapy centers on insulin replacement. Genetic, autoimmune, toxic, and infectious mechanisms have been implicated in its etiology

- **Type 2 diabetes** is the more common of the 2 types, representing about 90% of all cases. Here the problem is with insulin resistance and a relative deficiency of insulin, resulting in chronic hyperglycemia. Therapy is multidirectional, often including weight loss, dietary restriction (particularly of carbohydrates), increased activity and exercise, and medications to reduce insulin resistance, address insulin deficiency, or delay intestinal absorption of carbohydrates

Metobolic studies helpful in differentiating Type 1 from Type 2 diabetes include the C-peptide assay and the glucose tolerance test. With both types of diabetes, successful therapy is routinely monitored through fasting and postprandial blood glucoses and hemoglobin A1C levels.

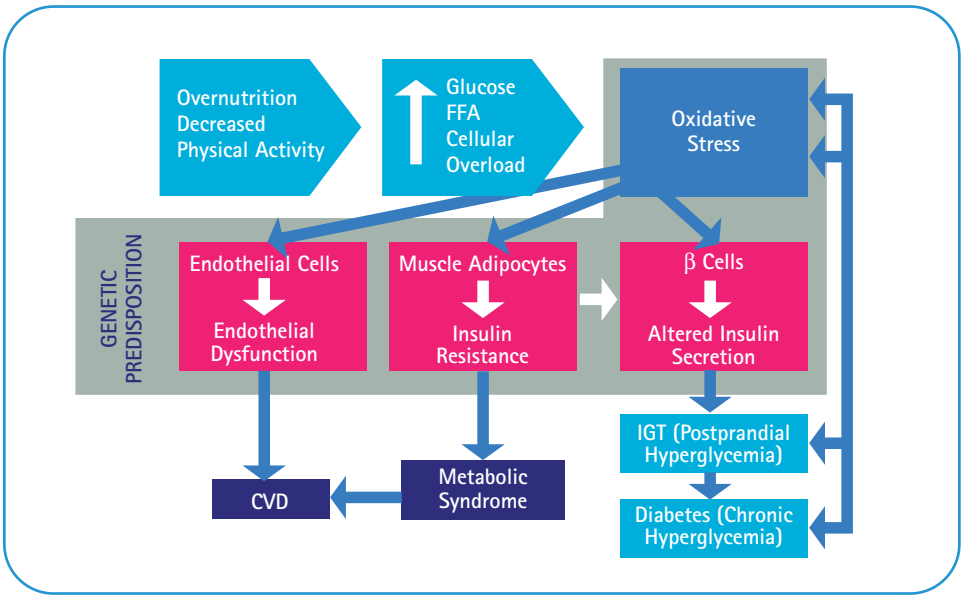
There remains a popular misconception characterizing Type 1 as the "bad" diabetes and Type 2 as the more innocuous variety. But when it comes to diabetic retinopathy, this characterization is not true.

The occurrence rate for proliferative retinopathy, the most severe form of diabetic retinopathy, is similar in long-standing diabetes Type 1 and 2; proliferative diabetic retinopathy is reported in 25% of people with Type 1 diabetes after 15 years, and in 25% of people with Type 2 diabetes after 25 years. Even milder forms of nonproliferative retinopathy affect both types of diabetics with similar frequency: 80% of Type 1 and 84% of insulin- dependent Type 2 diabetics are affected after 15 years, and 53% of noninsulin-dependent Type 2 diabetics are affected after 19 years of disease.[6]

Diabetes is associated with a wide range of macrovascular and microvascular complications leading to such disorders as atherosclerosis, cardiovascular disease, diabetic nephropathy, peripheral neuropathy, erectile dysfunction, impaired wound healing, peripheral circulatory insufficiency, and diabetic retinopathy.[7,8]

Environmental factors (excessive caloric intake combined with inadequate exercise) as well as genetic factors are frequently involved in the pathogenesis of diabetes, and these factors can eventually lead to plasma glucose and free fatty acid disregulation as well as cellular oxidative stress. These same factors may be involved in a number of pathologies linked to diabetes, such as hypertension and atherosclerosis.[9,10]

FIGURE 4. Pathophysiologic mechanisms leading to diabetes, hypertension, and atherosclerosis

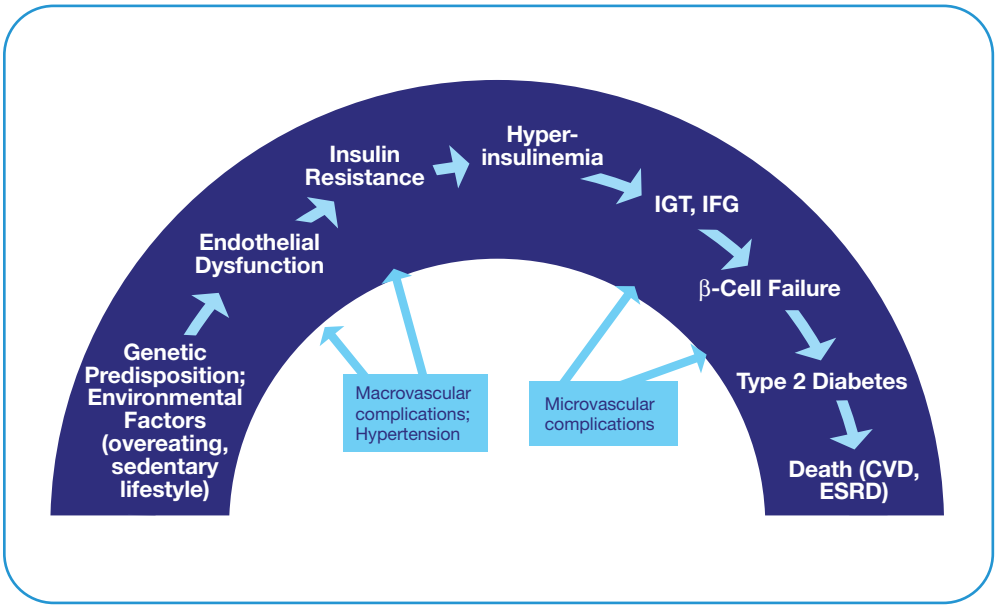


Source: Ceriello A, Motz E. *Arterioscler Thromb Vasc Biol.* 2004;24:816-823.

FIGURE 4 depicts some of the cellular and vascular mechanisms leading to such precursors of diabetes as insulin resistance and β-cell dysfunction.[9] Excessive caloric intake and decreased physical activity promote excess glucose and free fatty acids, which lead to oxidative stress and impact negatively on a variety of cells, including smooth muscle cells, endothelial cells, adipocytes—and retinal cells. Long-term consequences include insulin resistance, hypertension, β-cell dysfunction, atherosclerosis, diabetes (including such microvascular complications of diabetes as diabetic retinopathy), and cardiovascular disease.[10]

The metabolic, glycemic, and vascular dysfunctions that may lead to the development of diabetes can begin years, and even decades, prior to diagnosis. Of interest is the fact that of the estimated 20.8 million people in the United States at this time with diabetes, an estimated 6.2 million (or 30%) remain undiagnosed.[11]

FIGURE 5. The glycemic continuum in Type 2 diabetes



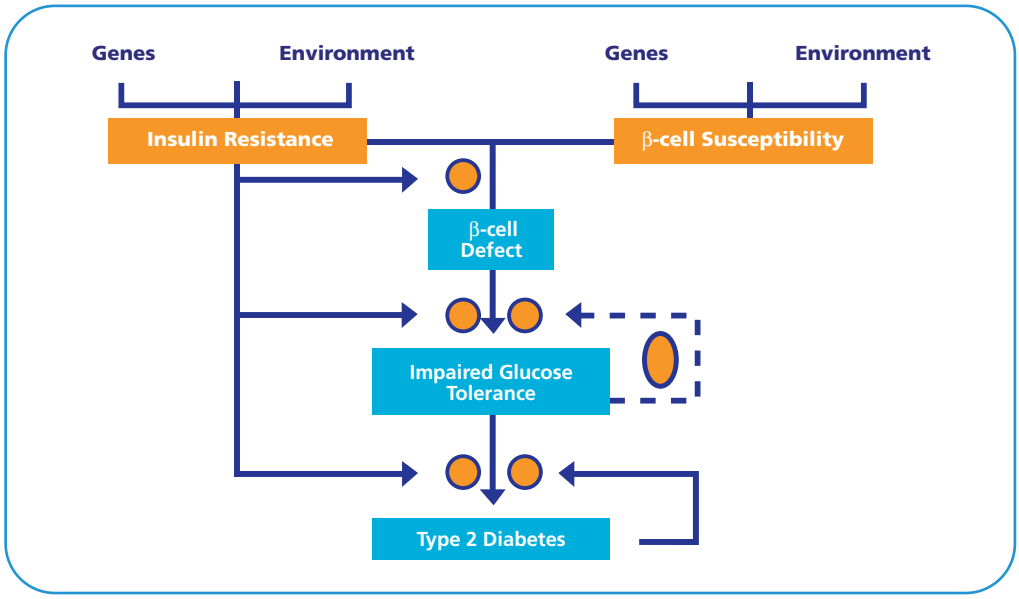
Source: Adapted from Dzau V, Braunwald E. *Am Heart J.* 1991;121(4 part 1):1244-1263.

Progression from normal blood glucose levels and glucose tolerance to Type 2 diabetes may be tied to such environmental factors as poor diet, overeating leading to obesity, and lack of exercise, eventually producing what has been called "insulin resistance." Insulin resistance occurs when the normal amount of insulin secreted by the β-cells in the pancreas is unable to transport glucose from the bloodstream to fat and muscle cells where glucose is stored or converted into energy.

The body's response to insulin resistance is the production of increasing amounts of insulin. Eventually, this chronic demand for increased insulin as a result of glucose loads produced by meals or by glucose production in the liver can lead to the death of β-cells. β-cell death or dysfunction results in an absolute reduction in available insulin, leading to a chronic hyperglycemic state and diabetes. These pathophysiological processes may lead to the development of microvascular disorders such as retinopathy and macrovascular disorders such as atherosclerosis and heart disease (FIGURE 5).[12,13]

Clinicians speak of a dual-defect hypothesis in the pathophysiology of Type 2 diabetes—insulin resistance leading to β-cell dysfunction and death (FIGURE 6). Diabetes has been described as a chronic hyperglycemic state occurring as a result of a relentless progression of β-cell dysfunction and β-cell death, with a backdrop of chronic insulin resistance and initial increase in insulin production, followed by eventual insulin deficiency.[14-16]

FIGURE 6. Pathogenesis of Type 2 diabetes: β–cell failure resulting from insulin resistance



Source: Weyer C, et al. *J Clin Invest.* 1999;104:787-794.

DIABETES AND CHILDREN:
Facts

- Diabetes is one of the most common chronic diseases in school-aged children
- In the United States, about 176,500 people under the age of 20 years have diabetes. About 1 in every 400 to 600 children has Type 1 diabetes
- Each year, more than 13,000 children are diagnosed with Type 1 diabetes. The incidence of Type 1 diabetes is about 7 per 100,000 per year in children ages 4 and younger; 15 per 100,000 per year in children 5 to 9 years old, and about 22 per 100,000 per year in those 10 to 14 years of age
- About 75% of all newly diagnosed cases of Type 1 diabetes occur in individuals younger than 18 years of age
- Currently, because 10% to 15% of children and teens are overweight—about double the number 2 decades ago—increasing numbers of young people have Type 2 diabetes. Most children diagnosed with Type 2 diabetes are overweight or obese
- Of children newly diagnosed with diabetes, only 5% were classified as Type 2 before 1994, whereas 30% to 50% have been classified as Type 2 in recent years
- Although no ethnic group is untouched by the problem, the disease disproportionately affects Native American, African American, Mexican American, and Pacific Islander youth. An example of this over-representation is the Pima Indians, among whom the prevalence of Type 2 diabetes in 15- to 19-year-olds is 5%

Source: National Institutes of Health. *National Diabetes Education Program Fact Sheet.* Available at: http://www.ndep.nih.gov/diabetes/youth/youth_FS.htm#Statistics. Accessed August 28, 2007.

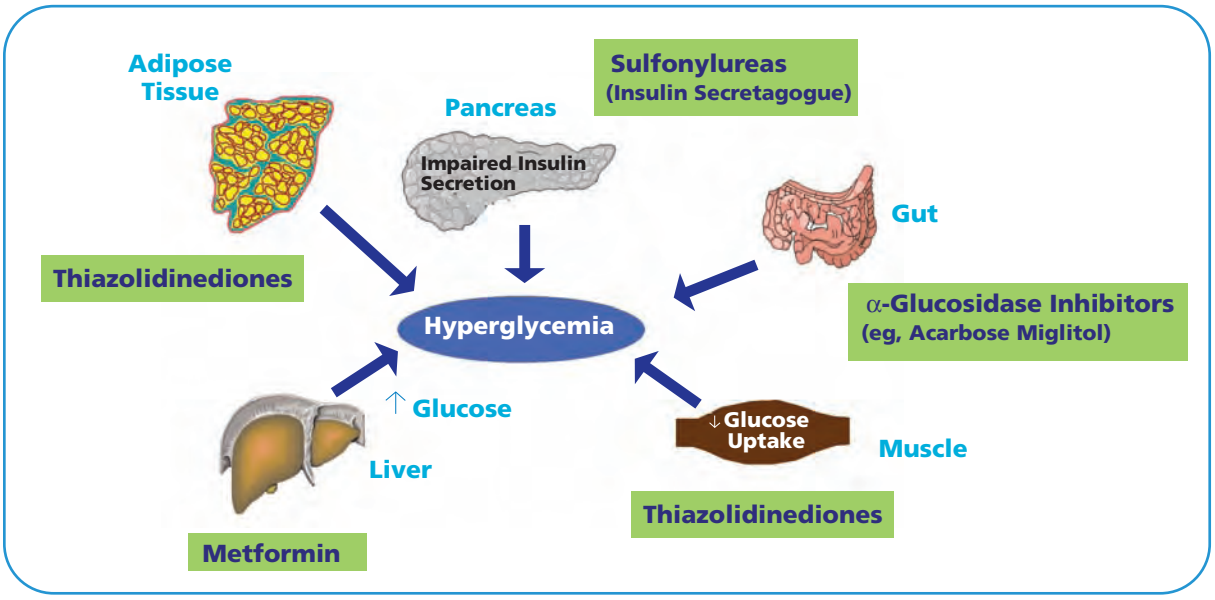
Treatments for Diabetes

Since the hallmark of diabetes is hyperglycemia, the hallmark of its treatment is glycemic control (FIGURE 7). A wide range of agents exist to achieve this goal, including:

- **Sulfonylureas**
  - — Insulin secretagogues
- **Metformin**
  - — Suppresses hepatic glucose production
  - — Insulin sensitizer
- **Thiazolidinediones**
  - — Insulin sensitizer
  - — β-cell protection
- **α–Glucosidase Inhibitors**
  - — Inhibit GI absorption
- **Insulin Analogs**
  - — Supplement inadequate physiologic insulin supply
- **GLP–1 Mimetics**
  - — Enhance glucose-dependent insulin secretion, reduce inappropriate elevations of glucagon secretion
- **DPP–IV Inhibitors**
  - — Reduce blood glucose, reduce glucose excursions

Active research continues in new modalities to treat diabetes more effectively. One exciting example is a newly described surgical technique (AHST) wherein autologous nonmyeloablative hematopoietic stem cells are transplanted in an effort to decrease insulin dependence.[17]

FIGURE 7. Organ targets for oral anti-diabetic agents



In considering the treatment of diabetes, it is important to identify specific management goals. Guidelines have been suggested by both the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists (AACE). These guidelines address what have been called modifiable risk factors in diabetes—specifically blood glucose levels, hemoglobin A1C, blood pressure, and lipid profiles (LDL, or low-density lipoprotein; HDL, or high-density lipoprotein; and TC, or total cholesterol). TABLE 1 summarizes the management goals put forth by the ADA and the AACE.

Of the potentially modifiable risk factors, probably the most important to monitor in diabetic retinopathy is glycosylated hemoglobin A1C. It has been estimated that the risk of developing diabetic retinopathy decreases by 21%, and the risk of progression of this condition decreases by 43%, with every 1% decrease in A1C. One important additional risk factor in the modifiable category is smoking, which is associated with poorer glycemic control and may accentuate circulatory problems in diabetics.

While therapy based on modifiable risk factors can help limit the occurrence and severity of diabetic retinopathy, there remain a number of nonmodifiable risk factors for which little can be done. These include the age of onset of diabetes and the duration of the disease. The only strategy that offers any hope in modifying such risk factors is preventive medicine, especially in Type 2 diabetes, because diet and weight control, along with lifestyle changes (eg, increased physical activity and a regular program of exercise) can prevent the development of diabetes or at least delay its onset. Recent studies, including the Finnish Diabetes Prevention Study and, in the United States, the Diabetes Prevention Program Study, have shown that intensive lifestyle intervention is associated with reduced incidence of new diabetes in those at risk. In the Finnish Study, body weight reduction, reduced dietary saturated fat, increased physical activity, and increased dietary fiber were associated with a diabetes risk reduction of 58%.

Table 1. Diabetes treatment guide

	ADA Guidelines	AACE Guidelines
Hemoglobin A1C	<7.0%	≤6.5%
Fasting blood sugar	70-130 mg/dL	<110 mg/dL
Postprandial blood sugar	<180 mg/dL	<180 mg/dL
Blood pressure	<130/90 mm Hg	<135/85 mm Hg
LDL	<100 mg/dL	<100 mg/dL
HDL (men/women)	>40/>50 mg/dL	>40/>50 mg/dL
Triglycerides	<150 mg/dL	<150-200 mg/dL
Total cholesterol	<200 mg/dL	<170-200 mg/dL

Sources: American Diabetes Association. *Diabetes Care.* 2008;31(suppl):S1-S110. Lebovitz HE et al. *Endocr Pract.* 2006;12(1):6-12. AACE Diabetes Mellitus Clinical Practice Guidelines Task Force. *Endocr Pract.* 2007;13(suppl 1):3-68.

DIABETIC RETINOPATHY

One of the major complications of diabetes, both Type 1 and Type 2, is the development of diabetic retinopathy, which occurs in an estimated 40% of diabetics overall. In 20% of patients, this retinopathy eventually becomes vision threatening. The longer the duration of the disease, the more likely the occurrence of diabetic retinopathy. In persons with Type 1 diabetes, diabetic retinopathy is nearly universal 20 years post diagnosis; in persons with Type 2 diabetes incidence of retinopathy exceeds 60% 20 years post diagnosis (FIGURE 8).[6] It has been observed that nearly every person diagnosed with diabetes before age 30 will develop retinopathy within 20 years of diagnosis. Retinopathic damage will already have occurred in approximately 5% of patients diagnosed with diabetes by age 30.[18]

It is worth emphasizing that many individuals will have experienced visual loss secondary to diabetic retinopathy before their systemic disease is diagnosed and treated. An estimated 20% of those newly diagnosed with Type 2 diabetes already have diabetic retinopathy at the time of diagnosis. In these patients, it may actually be the retinopathy that leads to the diagnosis of diabetes. This is of particular importance to the eye care professional practicing Healthy Sight Counseling, in view of the fact that there are more than 6 million currently undiagnosed diabetics in the United States; in some of these cases, it may be the eye care professional who is the first to identify the diabetes.[11,19]

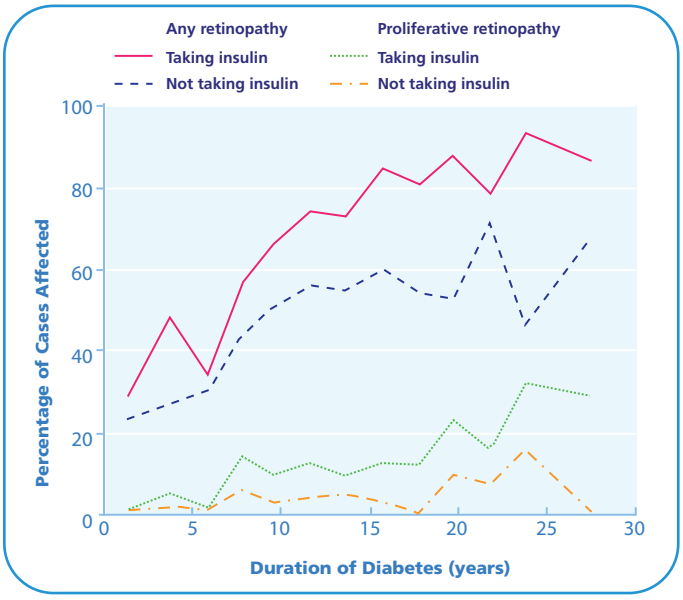


FIGURE 8. Frequency of retinopathy (any degree) and proliferative retinopathy by duration of diabetes in people with diabetes diagnosed at age 30 or under, according to insulin treatment

Source: Watkins PJ. *BMJ*. 2003;326:924-926.

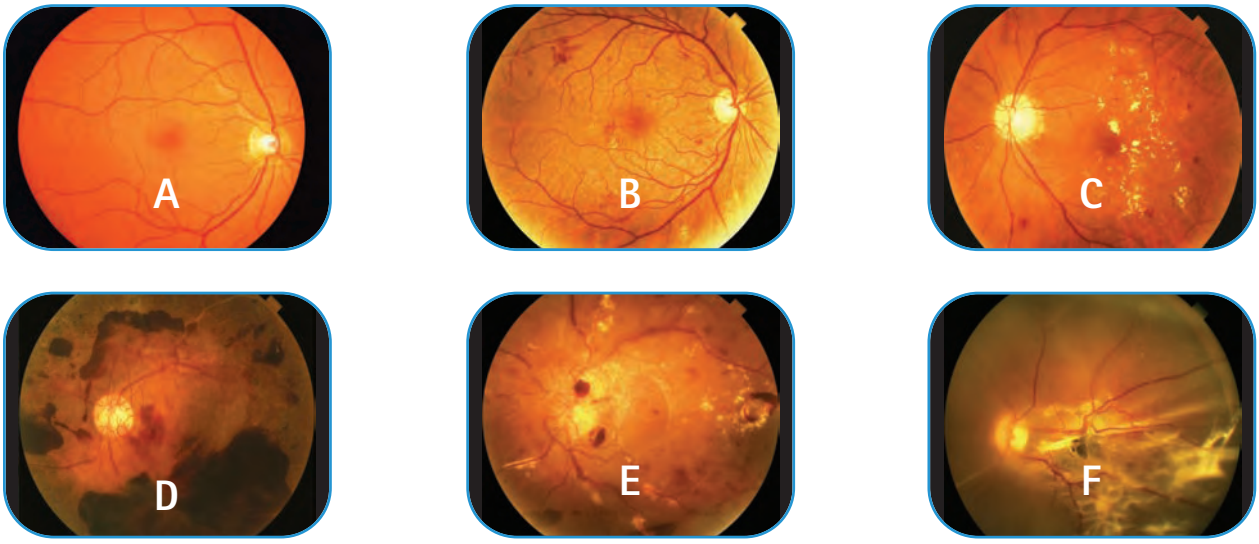
Several distinct stages of diabetic retinopathy have been identified (FIGURES 9–11):

- **Nonproliferative, or background, retinopathy with or without maculopathy:** development of microaneurysms in capillary walls; occasional hemorrhages; hard exudates often coalescing in the macula; and retinal edema. Nonproliferative retinopathy may have no overt signs or symptoms; however, the development of maculopathy can result in reading difficulties and central vision loss

- **Preproliferative retinopathy:** increased retinal ischemia due to capillary occlusion; larger, more frequent hemorrhages; microinfarcts in the nerve fiber layer. The condition can result in cotton-wool spots; and more extensive hemorrhage. Overt signs or symptoms may be absent

- **Proliferative retinopathy, advanced diabetic eye disease:** persistent retinal ischemia leading to neovascularization of the retina or optic disk in an attempt to keep tissues supplied with blood, oxygen, and nutrients; occurrence of retinal and vitreous hemorrhage; traction retinal detachment. Signs or symptoms include visual "floaters," distorted vision, and severe vision loss[6]

FIGURE 9. Normal retina (A), nonproliferative diabetic retinopathy (B), diabetic macular edema (C), neovascularization of optic nerve and retinal/vitreous hemorrhage (D), proliferative diabetic retinopathy(E), and traction retinal detachment (F)



Images courtesy of Raphael Castillo, MD and Maria Pei.

Microvascular leakage and microvascular occlusion are characteristic of diabetic retinopathy.[20] These processes lead to capillary dropout (the vessels are so blocked they can no longer transport blood and oxygen), development of microaneurysms, vascular occlusion and/or hyperpermeability, and neovascularization.[21-23]

Even slight changes in blood flow and the resulting ischemia can be critical to retinal photoreceptor cells, which are avascular and have little reserve capacity of oxygen.[21-23] The vision loss and blindness resulting from diabetic retinopathy are usually due to vascular leakage or ischemia.[20] More recent data suggest that even prior to obvious retinal microvascularity, diabetes may be causing retinal neuronal dysfunction—retinal cell atrophy and death of retinal neurons—perhaps as a result of a diabetes-induced upregulation of reactive oxygen species (ROS).[18,24]

CELLULAR PATHWAYS OF DIABETIC RETINAL DAMAGE

Another approach to understanding the pathophysiology of diabetic retinopathy is to recognize how chronic hyperglycemia inflicts damage on a cellular level. Three primary cellular mechanisms are believed to contribute[23-27]:

- **Increased flux through the polyol pathway leading to sorbitol accumulation:** Sorbitol is a sugar alcohol that is metabolized relatively slowly. Excessive intracellular sorbitol may cause cell damage. In the eye, intracellular sorbitol has been linked to disruption of osmotic balance, loss of integrity of the retina-blood barrier, and diabetes-related retinal edema
- **Increased formation of advanced glycation end products (AGEs):** AGEs are a class of complex, often unstable, reactive compounds formed in excess during aging and in the presence of diabetes. According to the "glycation hypothesis," accumulation of AGEs alters the structural properties of tissue proteins and reduces their susceptibility to catabolism. AGE formation has been linked to oxidative stress, disruption of retinal hemodynamics, and vascular endothelial cell damage
- **Increased oxidative stress, which has been associated with production of cell–damaging free radicals and ROS:** Intracellular oxidation of fatty acids precipitated by ROS and free radicals may alter the permeability of cell membranes, eventually causing cell death. In diabetic retinopathy, increased oxidative stress is also associated with sorbitol accumulation, pericyte loss, and retinal hemodynamic abnormalities

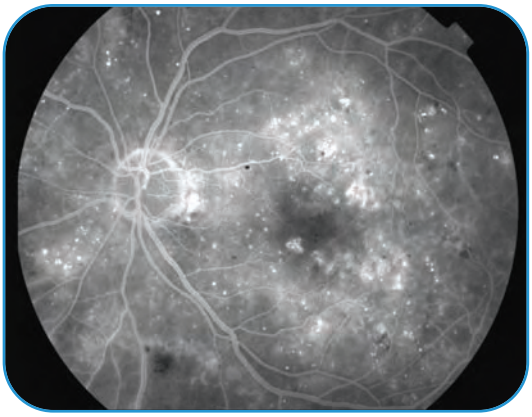


FIGURE 10. Diabetic retinopathy (Fluorescein angiogram)

Image courtesy of Raphael Castillo, MD and Maria Pei.

SCREENING AND MANAGEMENT of Diabetic Retinopathy

Recent data, such as that obtained from the Diabetes Control and Complications Trial (DCCT), indicate that annual dilated eye examinations should be implemented upon diagnosis of either Type 1 or Type 2 diabetes. Various stages of diabetic retinopathy (nonproliferative and proliferative) and diabetic macular edema (DME) can be diagnosed on dilated retinal examination and confirmed with diagnostic testing, including fluorescein angiography and optical coherence tomography (OCT).

Because of the intimate relationship between diabetes and diabetic retinopathy, a partnership between the eye care professional and the internist or endocrinologist treating the patient is crucial to avoid or minimize the ophthalmic and the systemic complications of the disease. In addition to taking an ocular history, the eye care professional should routinely inquire about diabetic control—specifically about hemoglobin A1C levels and pre- and postprandial blood sugars. Healthy Sight Counseling should include reminders to patients with diabetes—particularly those already demonstrating diabetes-related ocular disease—about recommended follow-up.[23]

Of course, with diabetes, as with many other diseases, prevention, when possible, is the best treatment. This is especially true in patients who are at higher risk for Type 2 diabetes—for example, patients with a family history of the disease, the obese, and patients with a sedentary life style.

In those cases where prevention is not possible, effective therapy is the next step. Adequate blood sugar control is essential for minimizing the progression of microvascular and cardiovascular complications. Control of the metabolic abnormalities of diabetes has a major effect on the development of diabetic microvascular complications. Large clinical trials, such as the DCCT and the United Kingdom Prospective Diabetes Study (UKPDS), have demonstrated that good glycemic control (ie, normalizing blood sugar levels) can delay the onset and reduce the progression of a number of diabetes-related complications, including diabetic ocular diseases.[23]

Conversely, poor glycemic control, and especially chronically poor control, has been associated with progression and worsening of diabetic retinopathy in patients with Type 2 diabetes. In their study of a cohort of 1378 patients with Type 2 diabetes 40 years of age and older, Henricsson and colleagues found that poor glycemic control was significantly associated with worsening of retinopathy.[28] Comorbid conditions, such as hypertension, cardiovascular disease, albuminuria, and smoking can also have an impact on the frequency and severity of diabetic ocular complications. Women with diabetes may be more susceptible to ocular complications of their disease during pregnancy.

TREATMENTS
for Diabetic Retinopathy

The most effective way to prevent diabetic retinopathy is to prevent diabetes (specifically Type 2) from developing, whenever possible, and when this it not possible, to treat diabetes promptly and aggressively. When diabetic retinopathy does occur, the most effective way to deal with it and to minimize its potential sight-threatening sequelae is through early diagnosis and management. Regular screening is crucial in this regard. There is an increasing number and variety of available treatments for diabetic retinopathy, including laser photocoagulation and surgery.

Laser photocoagulation uses the heat from a laser to seal or destroy abnormal, leaking blood vessels in the retina. There are 2 basic laser coagulation treatment protocols: focal photo-coagulation and panretinal photocoagulation.[29]

- **Focal photocoagulation** uses a limited number of focal laser burns to seal microvascular leaks. It is used primarily in diabetic macular edema
- **Panretinal (scatter) photocoagulation** uses a much larger number of laser burns to slow the growth of abnormal new blood vessels that have developed over a wide area of the retina. The purpose of this treatment is to reduce the release of chemical factors that stimulate the growth of abnormal vessels (neovascularization) by destroying large areas of the peripheral ischemic retina while preserving central retinal function. The result is to prevent, to slow, or to reverse the growth of new abnormal vascular tissue. The technique is used primarily in proliferative diabetic retinopathy

Surgical treatments for diabetic retinopathy include vitrectomy, membrane peeling, and retinal detachment repair. These are employed in cases of vitreous hemorrhage, retinal scarring, and retinal traction leading to retinal detachment.[29]

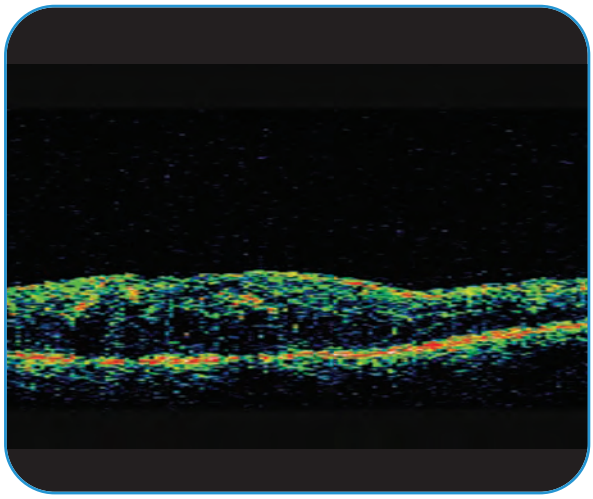


FIGURE 11. Optical coherence tomography (OCT) scan showing diabetic macular edema (DME)

Image courtesy of Raphael Castillo, MD and Maria Pei.

PHARMACOLOGICAL THERAPIES for Diabetic Retinopathy

There are a number of new pharmaceutical agents currently in use or in developmental stages for the treatment of diabetic retinopathy (DR).[29-31]

- **Protein kinase C inhibitors.** Agents such as ruboxistaurin that inhibit the activity of protein kinase C have been used to treat diabetic retinopathy. Protein kinase C has been implicated in microvascular changes to blood vessels in the retina

- **Corticosteroids.** Intravitreal steroids, including triamcinolone acetonide, fluocinolone acetonide, and dexamethasone, produce an anti-inflammatory effect and can lead to a reduction in microvascular leakage

- **Vascular endothelial growth factor (VEGF) inhibitors.** Vascular endothelial growth factors are important regulators of vascular permeability and angiogenesis. They are upgraded under conditions of hypoxia and may contribute to increased vascular permeability and induce neovascularization. For this reason, intravitreal injections of such VEGF inhibitors as pegaptanib (Macugen®), bevacizumab (Avastin®), and ranibizumab (Lucentis®), currently being used in the therapy of age-related macular degeneration, are being tried in diabetic retinopathy

- **Hyaluronidase.** Studies are underway evaluating the intravitreal injection of purified bovine hyaluronidase (Vitrase®) to facilitate the clearing of vitreous hemorrhages

- **Anti-oxidants.** Therapy with such anti-oxidants as Vitamins C and E could potentially counteract cellular oxidative stress and production of reactive oxygen species associated with the chronic hyperglycemic state

- **Renin-angiotensin-aldosterone system (RAAS) blockers.** Agents that block RAAS activity, including angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), which have long been used to lower blood pressure in hypertension, may play a role in the treatment of diabetic retinopathy. Both ACEIs and ARBs block the activity of angiotensin II (Ang II), which is a potent vasoconstrictor. Ang II has also been implicated in retinal angiogenesis

- **Other experimental agents.** Additional agents being studied in early clinical trials include aldose reductase inhibitors and advanced glycation end product inhibitors

DIABETES
and Other Ocular Disease States

Diabetic retinopathy occurs as a direct result of diabetes. There are a number of serious vision-threatening ocular diseases distinct from diabetic retinopathy that occur more frequently in diabetic patients, and in these diseases the metabolic and microvascular abnormalities characteristic of diabetes may play an important role in etiology.

These include cataract (See FIGURE 12), age-related macular degeneration, and glaucoma.

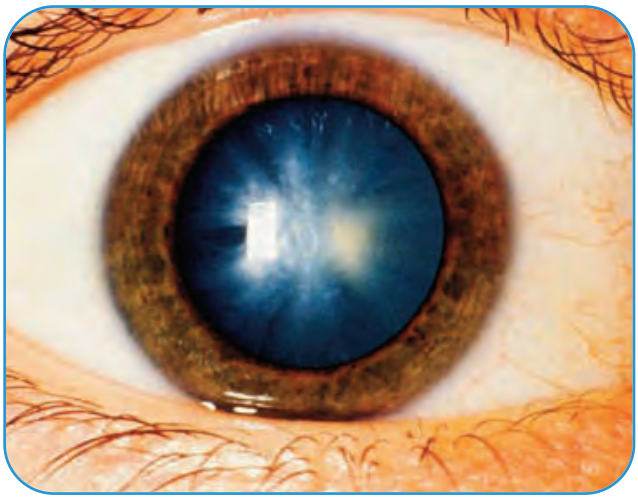
DIABETES AND CATARACT

Data from a wide range of epidemiologic studies, including the Wisconsin Epidemiology Study of Diabetic Retinopathy and the Framingham Eye Study, have demonstrated that diabetes significantly increases the risk of cataract. In diabetic patients under the age of 65 years, the prevalence of cataract increases 3- to 4-fold compared to demographically similar individuals without diabetes. In those patients over age 65 with diabetes, the prevalence of cataract increases 2-fold compared with demographically similar individuals without the disease.[32] The Beaver Dam Eye Study evaluated diabetes, cardiovascular disease, selected cardiovascular disease risk factors, and the 5-year incidence of cataract and progressive lens opacification. The investigators found that diabetes was associated with an increased incidence of cortical and posterior subcapsular cataract and with progression of cortical and posterior subcapsular lens opacities.[33]

DIABETES AND AGE-RELATED MACULAR DEGENERATION

Data suggest a possible correlation between diabetes and age-related macular degeneration (AMD). In the recent Age-Related Eye Disease Study (AREDS), the dietary glycemic index (dGI) was used to measure the risk of diabetes and cardiovascular disease.[34] A positive correlation was found both between dGI and AMD and between dGI and the *severity* of AMD. There was a 49% increase in the risk of advanced AMD in subjects with dGI ratings higher than the median for each sex. The investigators concluded that higher glycemic dietary levels increase the risk not only for diabetes and heart disease, but also for AMD.

FIGURE 12. Diabetic cortical cataract



DIABETES AND GLAUCOMA

Elevated intraocular pressure, a risk factor for glaucoma, appears to increase progressively with chronic hyperglycemia and diabetes.[35] One of the most severe, intractable forms of glaucoma, neovascular glaucoma, is associated with severe proliferative diabetic retinopathy.[36] Certain populations at higher risk for the development of diabetes also show a higher incidence of glaucoma; the African American population in the United States is a prime example of this medical double jeopardy.

PHOTOTOXIC OCULAR TISSUE DAMAGE AND DIABETES–INDUCED OCULAR TISSUE DAMAGE

Intriguing symmetries and linkages exist between diabetic retinopathy, retinal damage, and retinal degeneration associated with exposure to ultraviolet radiation (UVR) and certain spectra of visible light (eg, blue light). For example, sorbitol, whose buildup under chronic hyperglycemic conditions has been associated with microvascular cell disruption and the breakdown of the retinal-blood barrier, may also accumulate in retinal pigment epithelial (RPE) cells, apparently as a result of cumulative exposure to UVR and to certain wave lengths of visible light (eg, blue light). Sorbitol accumulation in RPE cells leads to increased production of advanced glycation end-products, increased oxidative stress, and eventual physiologic impairment and cellular death. Many of those same processes have been identified in diabetic eyes, although in patients with diabetic retinopathy the causative factor appears to be chronic hyperglycemia.[23]

Van Kuijk has proposed that light exposure may be a factor in promoting lipid peroxidation in photoreceptor cells because light of the appropriate wavelength may trigger photo-oxidative reactions.[37,38] Age and disease, particularly diabetic retinopathy, may increase the vulnerability of photoreceptors and RPE cells to phototoxic damage. Retinal damage associated with chronic exposure to UVR and visible light may increase the vulnerability of retinal cells to various pathophysiologic mechanisms associated with diabetic retinopathy.[39]

As Roberts has pointed out, exposure of ocular tissue to sunlight may either cause or exacerbate age-related ocular diseases. These diseases have other major causal contributors—eg, chronic hyperglycemia in the case of diabetic retinopathy and diabetic cataract—but sunlight may play a role in the vision-degrading effects of these diseases by inducing photo-oxidative reactions and ensuing phototoxic damage.[39] Many of the same pathophysiologic processes observed in UVR-related cataract development have also been found to be at work in diabetic eyes, including superoxide formation and lipid peroxidation.[40,41]

All of these findings suggest that sunlight-related retinal degeneration in persons with diabetes, and particularly with diabetic retinopathy, exacerbates the risk of degradation and loss.[42] Similarly, cataract formation may be potentiated by hyperglycemia, UVR, or a combination of both of these risk factors in individuals with diabetes.

Although hyperglycemia is the primary patho-physiologic precipitator of diabetic retinopathy and diabetic cataract, oxidative processes induced by exposure to sunlight co-exist in patients with diabetes and may increase the risk of ocular tissue damage already heightened by the diabetes. In any case, hyperglycemia-induced disease processes would appear to make the diabetic eye even more vulnerable than the non-diabetic eye to phototoxic ocular damage associated with exposure to UVR and visible light. Consequently, UVR- and blue light-protection for the eyes is an especially high priority in diabetics.

HEALTHY SIGHT COUNSELING AND DIABETES

Healthy Sight Counseling can be of particular benefit to patients with diabetes because their disease and the medications that many must take to control it may directly affect their quality of vision (including, in particular, reduced contrast sensitivity and increased sensitivity to glare) as well as their long-term visual health.

Eye care professionals can play an important role in ensuring optimal overall health for patients with diabetes by emphasizing the importance of frequent, dilated eye exams, monitoring signs of ocular disease progression, monitoring signs of suboptimal diabetes control, and *communicating* and helping coordinate care with the patient's primary care provider and endocrinologist.

Just as important is providing diabetic patients with advice and education about vision-wear options and enhancements. When providing Healthy Sight Counseling to the patient with diabetes, it's important to take into account both long-term vision protection and vision enhancement that will benefit patients immediately whenever they put on their eyewear.

Patients with diabetes should be made aware of the full range of spectacle lens options and enhancements available to them, and they should be educated about the potential benefits of each. Appropriate optical enhancements to spectacle lenses may include:

- **Tinted lenses, clips, and shields** reduce excessive light and provide UV protection
- **Photochromic lenses**
  - Help protect vulnerable ocular tissue by automatically blocking 100% of UV radiation
  - Promote visual comfort and convenience and reduce eyestrain by titrating light as they adjust the level of tint based upon changing ambient light conditions
  - Preserve and enhance contrast sensitivity and decrease discomforting and disabling glare

- **AR coatings** reduce glare, indoors and at night
- **Polarized lenses** reduce the blinding glare caused by reflected light from water or snow
- **Lens materials** (such as Trivex® or polycarbonate) provide extra safety through impact protection

LONG-TERM VISUAL HEALTH

Normal, healthy eyes benefit from UV-protective lenses; all patients should have lenses that provide 100% blockage of both UV-A and UV-B light. While everyone is at potential risk for UV-mediated ocular damage, patients with diabetes are at increased risk. Hyperglycemia-induced disease processes make the diabetic eye even more vulnerable to damage associated with exposure to UVR and visible light. UV-mediated damage may increase the risk of vision loss in patients with diabetic retinopathy, and cataract formation may be also potentiated by hyperglycemia or by UVR, or by both risk factors, in persons with diabetes.

Even when no overt signs of diabetic eye disease exist, patients should be encouraged to protect their eyes. And patients should also understand strategies to improve the quality of their vision. Healthy Sight Counseling can help patients with diabetes understand their increased risk and can counsel them about making appropriate choices for spectacle lens enhancements.

Lenses, clips, or shields with fixed tints are all possibilities. Photochromic lenses are a particularly convenient means of protecting vulnerable ocular tissue by automatically blocking 100% of UVR; they also maximize visual comfort and visual acuity by reducing glare and enhancing contrast sensitivity.

QUALITY OF VISION TODAY

Long-term protection from UVR is only one aspect of healthy sight for the diabetic patient. Providing healthy sight also entails enhancing the patient's vision today. This enhancement must take into account not only quantity of vision, as measured by Snellen acuity, but also *quality* of vision.

After all, Snellen acuity alone is in many ways an artificial construct, a "doctor's office" kind of vision, a black-and-white version of vision for people who must exist and function in a real world where there are shades of gray and colors. Furthermore, even as new treatments offer hope for people with diabetes, at the present time, some decrease in quantitative acuity must eventually be expected in most patients with diabetes. In view of this, quality of vision becomes increasingly important as a measure of visual function and satisfaction.

Two crucial elements in determining quality of vision are contrast and glare sensitivity. Various systemic diseases, including diabetes, have been associated with reductions in contrast sensitivity and increased susceptibility to glare. Using Pelli-Robson and Bailey-Love charts, Mackie and colleagues measured contrast sensitivity and glare susceptibility in normal subjects and in diabetic patients with a broad range of diabetes-related ocular disease. They found that contrast sensitivity was reduced while glare sensitivity progressively increased in a linear fashion throughout the range from normal to advanced diabetic eye disease.[43] In a small trial examining contrast sensitivity in diabetic patients with no retinopathy or background retinopathy vs normal controls, Trick and colleagues found contrast sensitivity deficits in 24% of the diabetic patients with no detectable retinopathy and in 45% of those with background retinopathy, compared within 3% of the control subjects.[44]

Many diabetic patients, particularly those with diabetes-associated ocular disease, are reported to have poor visual function as a result of glare disability and loss of contrast.[45] There are a variety of other potential signs of visual dysfunction in patients with diabetes including color vision anomalies, visual field defects, and dark adaptation abnormalities, even during the clinically silent phases of the disease. Optical solutions in the form of fixed-tint and photochromic lenses and anti-reflective coatings to address the problems of glare and diminished contrast sensitivity are an important component of Healthy Sight Counseling and allow the eye care professional to offer an enhanced quality of vision to those diabetics whose quantity of vision has been compromised as a result of their disease.

CONCLUSIONS: A LIFE TIME OF HEALTHY SIGHT

Healthy Sight Counseling is particularly relevant to the diabetic patient. Early disease recognition and treatment can have a tremendous influence on both ocular and systemic morbidity (and systemic mortality), and careful monitoring of the diabetic patient with good and consistent glycemic control and regular ophthalmic and medical check-ups can serve to forestall or at least to minimize sequelae of disease in the eyes and elsewhere in the body. Thus there exists a cogent argument for a collaborative approach to dealing with diabetes on the part of eye care professionals and the internists, pediatricians, and endocrinologists involved in the care of patients with diabetes. This is another example of the "It takes a village" approach to encouraging and maintaining ocular and systemic well-being, good vision, and good health.

Furthermore, with the fact that diabetes is rapidly approaching epidemic proportions in the 21st century, greater attention must be directed to prevention by all health care practitioners involved in the care of patients with diabetes. It becomes the responsibility of every eye care professional practicing Healthy Sight Counseling to advise patients of the risk of diabetes and to work with them not only to achieve Healthy Sight but also to encourage a Healthy Life through regular medical and ophthalmic examinations, weight and dietary controls, and alterations in lifestyle such as avoiding sedentary habits and adopting a program of regular exercise.

Modern spectacles have come a long way from the simple correction of refractive errors. With current trends in surgical refractive eye care that serve to decrease and even eliminate the need for the quantitative aspects of spectacle-related vision correction, qualitative aspects of spectacle-related vision correction—such as light modulation, contrast preservation, glare control, and protection against UVR—are becoming increasingly important.

Because of certain unique aspects of diabetes and the diabetic eye—including disease-related decreased quantity of vision, impaired contrast sensitivity, greater susceptibility to glare, and increased risk from UVR—spectacle lens enhancements such as fixed-tint and photochromic lenses, impact-resistant lens materials, and anti-reflective coatings, have the potential to help protect and improve vision and the visual experience for diabetic patients and, in so doing, to improve their quality of life.

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HEALTHY SIGHT COUNSELING

PROVIDED AS A SERVICE TO EYE CARE PROFESSIONALS
THROUGH THE TRANSITIONS PARTNERS IN EDUCATION PROGRAM