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PREVENTION AND MANAGEMENT OF Diabetes-Related Eye Disease

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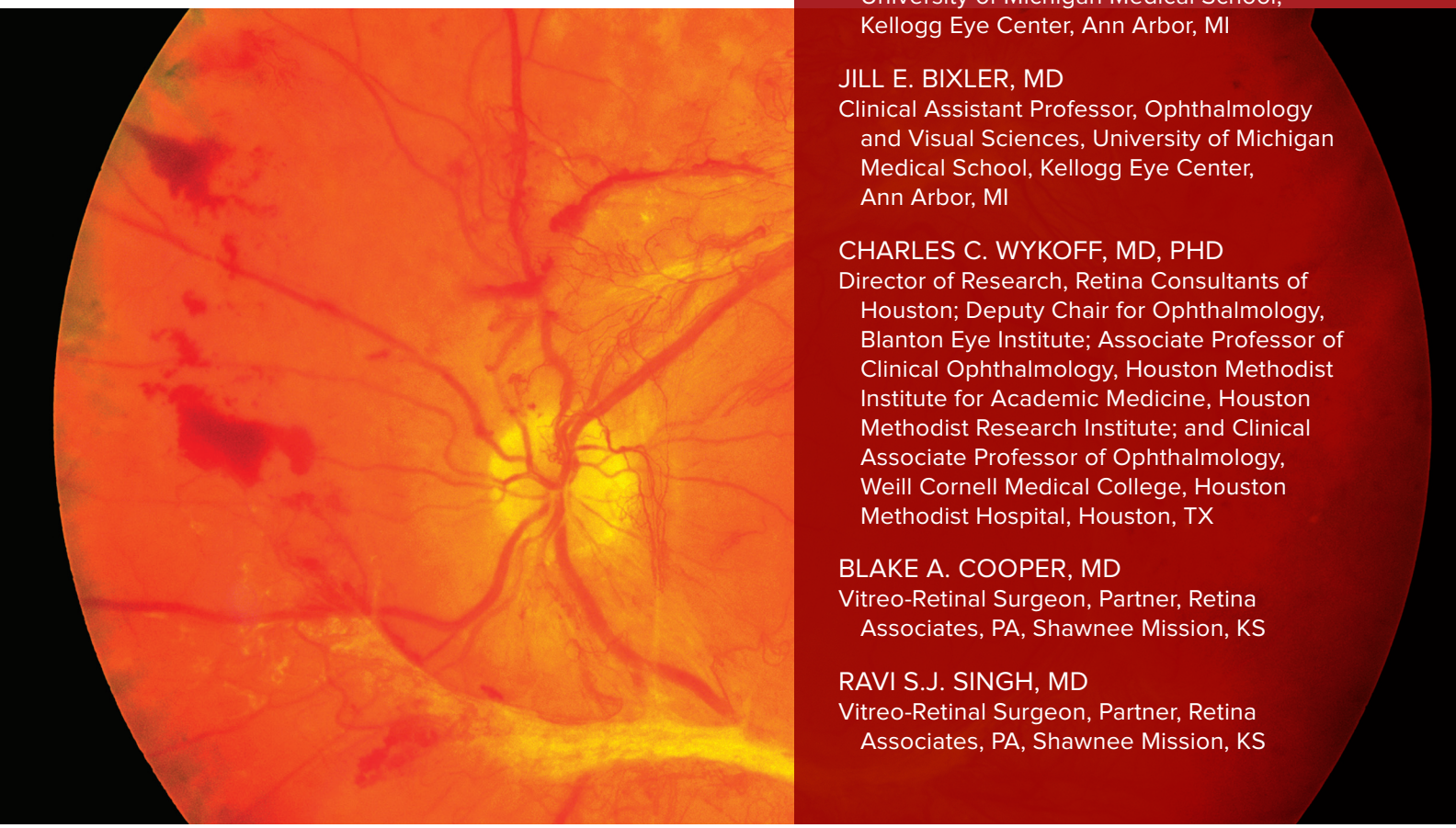

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About the Cover

Proliferative diabetic retinopathy showing neovascularization and scar tissue, a condition that needs immediate surgery. Credit: Visuals Unlimited, Inc. / Chris Barry / Getty Images

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Introduction

Thomas W. Gardner, MD, MS, *University of Michigan Medical School, Kellogg Eye Center, Ann Arbor, MI*

This compendium is intended as a guide to diabetes-related eye disease for primary care providers (PCPs), who treat the vast majority of people with diabetes in the United States. Its goal is to provide the information PCPs need to understand the eye complications of diabetes and effectively counsel patients about them. The chapters included offer discussions of *1*) diabetes-related risk factors for vision impairment; *2*) cataracts and cataract surgery in people with diabetes; *3*) diabetes-related retinopathy (DR), including its pathogenesis, classification, diagnosis, and treatment; and *4*) the emotional aspects of diabetes-induced vision impairment. The underlying premise is that PCPs and ophthalmologists share common goals in collaborating to care for people with diabetes.

Diabetes affects the eyes as part of its systemic effects on all organs, ranging from the kidneys, peripheral nerves, and retinas, to the heart, adipose tissue, liver, and muscle, and even to skin and the brain. Diabetes is a leading cause of vision loss and blindness in working-age adults, with 245 million people affected worldwide (1). Fortunately, rates of vision impairment in the United States and Europe have declined dramatically over the past three decades due to improved systematic management of diabetes, the development of standardized DR screening programs in several European counties (2,3), and the advent of anti-vascular endothelial growth factor (VEGF) therapy (4). However, worldwide, approximately 35% of people with diabetes develop some form of DR, although not all patients lose vision, just as not all patients with nephropathy will require dialysis for end-stage renal disease. Vision-threatening DR, that which requires treatment, develops in about 10% of people with diabetes (1). The expanding population of people with diabetes worldwide thus yields millions of people with DR. The burdens of diabetes and DR are enormous, with total costs of $327 billion—that is, one in seven health care dollars attributable to diabetes—in the United States (5). Clearly, the emphasis must increasingly be to prevent or minimize the chronic complications of diabetes. DR and other complications are eminently preventable, but the tools and medications remain imperfect, and the resources required to achieve a life free of complications are daunting.

The primary ocular manifestations of diabetes are cataracts and DR. Cataracts are twice as common in people with diabetes than in those without diabetes (6) and are a common cause for the need for intraocular surgery. Fortunately, intensive metabolic control reduces the risks of cataract and intraocular surgery (6), at least for people with type 1 diabetes. Cataract surgery is one of the most common operations performed in the United States, and it has become much easier and safer and carries better outcomes now than 30 years ago. Still, cataracts remain a major cause of morbidity in people with diabetes.

DR is now understood to be a neurovascular degeneration or sensory neuropathy akin to other peripheral sensory neuropathies (4), and impairment of the invisible retinal neurons is the ultimate cause of vision impairment. Nonetheless, the primary clinical manifestations of DR are the visible vascular features of microaneurysms, hemorrhages, "cotton wool spots" (small yellowish-white deposits in the retina), and, in a minority of patients, eventual neovascularization (i.e., the formation of new blood vessels).

The ocular manifestations of diabetes develop in parallel with renal and neuropathic complications; they can present as manifestations of diabetes or of glucose intolerance (7), or they can develop in the late stages of the disease (8). The presence of DR, and particularly advanced DR, is associated with a greater risk of other systemic manifestations of diabetes, including stroke, heart attack, and renal insufficiency (9,10). Likewise, advancing renal disease, in particular, is likely to accelerate DR due to hypertension, anemia, and inflammation (11). Thus, the care of patients with DR is best managed as part of a coordinated systematic effort involving PCPs and ophthalmologists.

This compendium focuses on the vision-threatening aspects of diabetes. However, diabetes also affects the motor component of the visual system via cranial nerve palsies. The trigeminal nerve provides sensation to the face and cornea, and corneal sensory neuropathy is a common feature of long-standing diabetes (12,13). This feature is revealed by shortened corneal nerve fibers and reduced fiber density, but is usually asymptomatic. However, in severe cases, corneal neuropathy can increase the susceptibility to corneal abrasions, recurrent epithelial erosions, and infections.

Ocular motility is mediated primarily by the third and sixth cranial nerves, and ischemic insults to these nerves can present with double vision (third and sixth) or inability to close the eyelids (seventh). None of these palsies causes blurred vision. Third cranial nerve palsies associated with diabetes typically cause ptosis and paralysis of gaze toward the nose and inferiorly and ptosis of the upper lid, but do not cause pupil dilation. The finding of a dilated pupil strongly suggests intracranial compression of the oculomotor nerve and warrants prompt neuroimaging to rule out an aneurysm of the posterior communicating artery or a tumor (14). By contrast, a unilateral sixth-nerve palsy causes horizontal diplopia and a lateral out-turning of the affected eye. Seventh-nerve palsies from diabetes cause weakness of the entire half of the facial muscles without double vision. Diabetes-related third-, sixth-, and seventh-nerve palsies usually resolve spontaneously in 6–12 weeks.

Diabetes generally does not increase the risk of open-angle glaucoma, but neovascular glaucoma can develop in people with proliferative DR (PDR). This condition manifests with pain, tearing, and redness, with elevated intraocular pressure, and warrants urgent treatment.

Topics covered in this compendium were selected specifically to meet the information needs of PCPs. The first chapter was written by Dr. Jennifer A. Wyckoff, an endocrinologist, and Dr. Anjali R. Shah, an ophthalmologist and retina specialist. The chapter reflects their ongoing collaborative quality assurance/quality improvement work that recently identified hypertension as a previously unrecognized risk factor for the need to receive intravitreal anti-VEGF injections for DR (15). This finding arose from the ability to gather and analyze data from the electronic medical record (EMR) system at the University of Michigan to seek risk factors for DR progression that are not routinely monitored in ophthalmology-based clinical trials. Moreover, their work epitomizes the systemic nature of DR and the crucial collaboration between PCPs and ophthalmologists. That is, PCPs and other specialists must treat the hyperglycemia, dyslipidemia, hypertension, renal insufficiency, and anemia of chronic diabetes, and data related to these parameters should be readily available for ophthalmologists to interpret the status of their patients' eye disease more effectively than with A1C data alone. Ophthalmologists, in turn, should communicate their findings, treatment plans, and information about prognosis to PCPs so they can act on their patients' most pressing problems. Despite their challenges, EMRs can facilitate these communications.

Key points from this first chapter include:

- The degree of hyperglycemia is important in the long-term risk of DR and other complications; reducing A1C by one percentage point can substantially reduce the risk of DR.
- The degree of control of hyperglycemia and hypertension are more important than the specific agents used to achieve that control. Thus, treatment plans can be optimized for each patient.
- Lifestyle interventions, notably diet and exercise, reduce the risk of complications and all-cause mortality in people with type 2 diabetes.

Our second chapter focuses on the complication of cataracts and their treatment. Dr. Jill E. Bixler, an experienced cataract surgeon, describes the transition from a clear crystalline lens to a cloudy cataract. Cataracts occur in various forms, with the posterior subcapsular and "snowflake" varieties being closely related to diabetes. Many factors are considered when determining the timing and type of surgery and the refractive goals for each patient.

Key points from this chapter include:

- Intensive metabolic control reduces the risk of cataract formation and the need for cataract surgery.
- Cataract surgery involves removal of the cloudy lens and replacement with a clear acrylic intraocular lens implant via two small incisions.
- People with diabetes have very high success rates with cataract surgery despite a slightly higher risk of intraocular infection (endophthalmitis) compared to people without diabetes.

The third chapter provides a detailed discussion of DR—the most serious ocular complication of diabetes. Author Dr. Charles C. Wykoff is an expert in the care of people with DR and has led multiple clinical trials of new pharmacologic agents for its treatment. He clearly describes the processes through which DR develops and evolves, and when and how diagnostic and treatment strategies are formulated.

Key points from his chapter include:

- Multiple retinal imaging tests are integral to the care of people with DR.
- Intensive control of diabetes and related risk factors is the core of systemic therapy to optimize outcomes in people with DR.
- Diabetes-related macular edema (DME) is the most common cause of reduced vision in people with DR and is usually treated with intravitreal injections of VEGF-blocking agents and/or corticosteroids, although laser treatment is useful in specific cases.
- PDR can be successfully treated with either laser surgery or anti-VEGF agents.
- Anti-VEGF agents may reduce the progression of moderate to severe nonproliferative DR (NPDR). Panretinal photocoagulation remains a common and important treatment for severe NPDR and PDR. In contrast to the accepted approaches to DME and PDR, standard clinical practices are still emerging for patients with NPDR.

Our final chapter was co-written by Dr. Blake A. Cooper and Dr. Ravi S.J. Singh, vitreo-retinal surgeons whose practice includes a large number of patients with DR. Their discussion of emotional support for people with DR is based on their insights into treating the whole person with diabetes. They emphasize a "3D view" of the distress, depression, and diabetes that often coexist in patients with diabetes and can lead to a sense of despair when an additional diagnosis of DR, often accompanied by neuropathies and/or nephropathy, is made.

Key points from Drs. Cooper and Singh include:

- Self-care is a central feature of diabetes, in contrast to cancer or other serious diseases.
- The language physicians use in communicating with people with diabetes is crucial, and empowering language should be employed.
- Ophthalmologists can assure the vast majority of their patients that they will not become blind.
- Physicians must help patients set realistic goals for the outcomes of ocular and systemic treatment of diabetes.

Optimizing Medical Management for Patients with Diabetes-Related Retinopathy

Jennifer A. Wyckoff, MD, and **Anjali R. Shah, MD,** *University of Michigan Medical School, Kellogg Eye Center, Ann Arbor, MI*

Optimizing the medical treatment of both type 1 and type 2 diabetes is essential to preventing vision loss by delaying the onset and progression of diabetes-related retinopathy (DR) and diabetes-related macular edema (DME; the build-up of fluid in the macula, an area in the center of the retina). Table 1 outlines the key components of comprehensive diabetes treatment for patients with retinopathy.

Treatment of Hyperglycemia

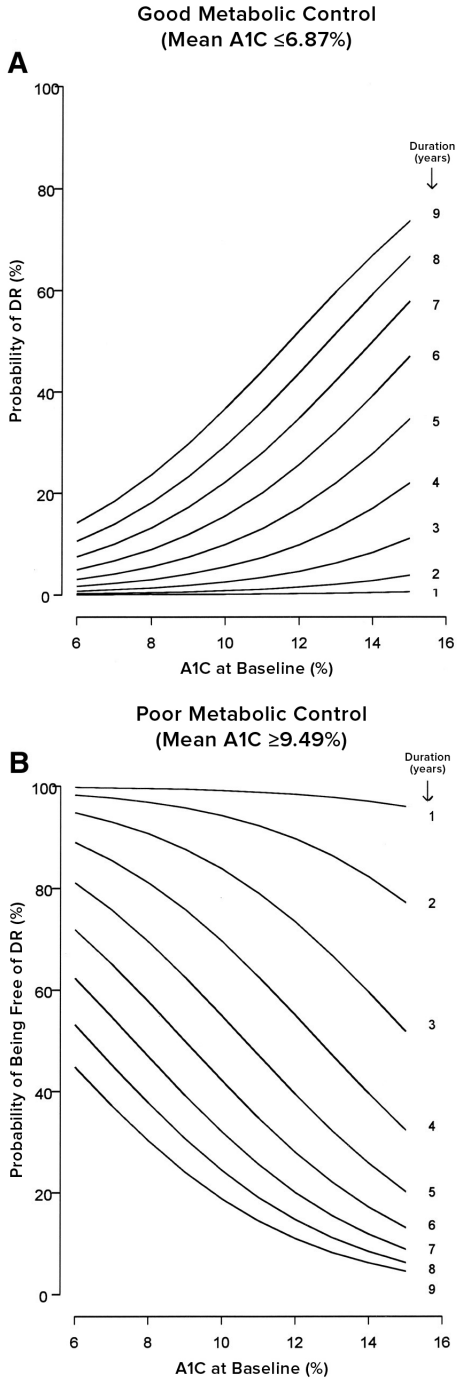
DR occurs exclusively with exposure to hyperglycemia. The degree of hyperglycemia and its duration are two major risk factors for the development of retinopathy. (Figure 1) (16). Therefore, the cornerstone of medical management is to prevent hyperglycemia.

Lowering A1C reduces the development and progression of DR (17–20). The more intensive the control of hyperglycemia is, the greater the benefits will be. The ACCORD (Action to Control Cardiovascular Risk in

TABLE 1 Key Components of Comprehensive Diabetes Treatment for Patients with Retinopathy

Component of Care	Considerations
Glycemic control	▸ Personalize A1C targets. ▸ DR progression is slowed by achieving glycemic targets. ▸ Consider increased surveillance in the setting of rapid glycemic improvement.
Blood pressure control	▸ Personalize blood pressure targets. ▸ DR progression is slowed by a target of systolic blood pressure <130 mmHg.
Lipid control	▸ Consider statins or fenofibrate, when appropriate.
Renal insufficiency	▸ Initiation of dialysis may improve DME.
DSMES	▸ Comprehensive DSMES is recommended at diagnosis, annually, and as needed for complications and transitions of care.
Sleep	▸ Consider screening for sleep apnea, when appropriate.
Exercise	▸ Patients should avoid heavy lifting in cases of acute vitreous hemorrhage.
Substance abuse	▸ Screen for and treat substance abuse.
Aspirin	▸ There are no restrictions on aspirin use in patients with DR.
Pregnancy	▸ Increase surveillance with eye exams each trimester and postpartum.

FIGURE 1 *A*) Probability of developing retinopathy in patients with type 1 diabetes as a function of A1C level (%) at baseline and duration (years) of good metabolic control (A1C ≤6.87%). *B*) Probability of not developing retinopathy in patients with type 1 diabetes as a function of A1C level (%) at baseline and duration (years) of poor metabolic control (A1C ≥9.49%). In both cases, BMI is assumed to be equal to 22 kg/m^2. Adapted from ref. 16.



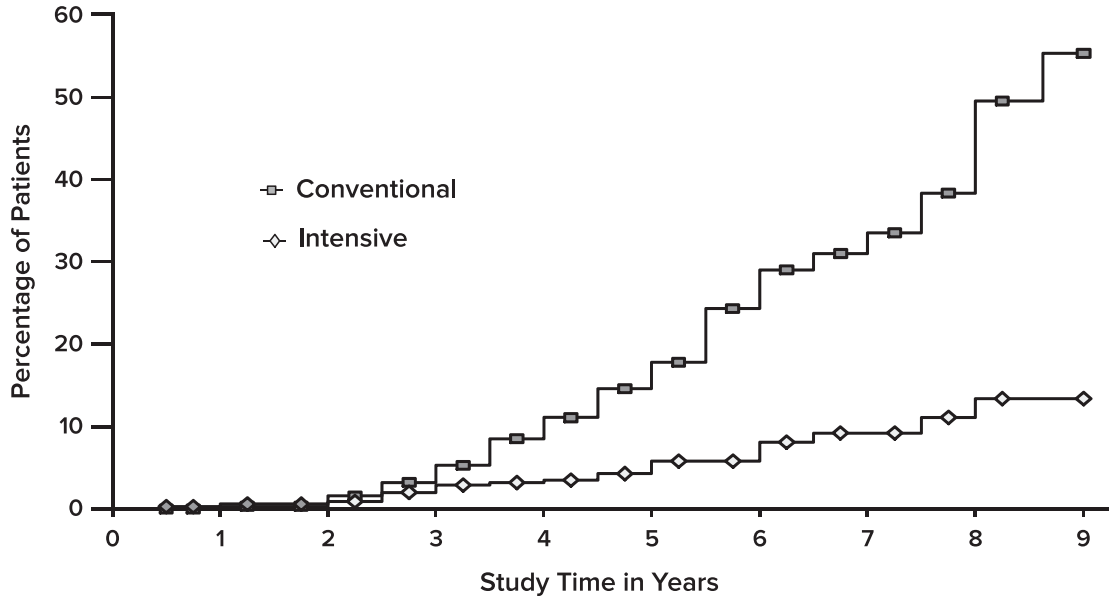
Diabetes) trial showed a reduction in the development and progression of all stages of retinopathy in the intensive control group (mean A1C 6.4%) compared to the standard care group (mean A1C 7.5%), with the greatest effect noted in patients with mild retinopathy at baseline (17). Even a small decrease in A1C can be beneficial. Lowering A1C by 1 percentage point can reduce the risk of DR development by 35% and the risk of its progression by 15–25% (21). Intensive control has also been shown to have persistent benefits in both type 1 and type 2 diabetes (a so-called "legacy effect") after the conclusion of study intervention, despite similar A1C values between the study and control groups at extended follow-up (22–24). These findings suggest that glycemic control has long-term benefits even if not consistently maintained over time (22–24).

The American Diabetes Association's *Standards of Medical Care in Diabetes—2019* recommend a personalized approach to setting target A1C levels for individual patients (25). An A1C <7% is considered an ideal target for many individuals; however, complications such as retinopathy can still occur at that level, so lowering the target should be considered in specific situations where either the risk of a complication is high (e.g., during pregnancy or in young adults) or the risk of treatment is very low (e.g., in patients treated with medications such as metformin that do not confer a risk of hypoglycemia). Similarly, it may be appropriate to increase the target to <8% in individuals who are at high risk of hypoglycemia (e.g., those with hypoglycemia unawareness or dementia) or in those for whom the risk of developing complications from diabetes is low (e.g., individuals with a limited life expectancy) (25).

The rapid correction of a long-standing elevation in A1C is associated with a transient worsening of retinopathy and DME (26–28), although the optimal rate at which A1C should be decreased is not clear. As illustrated in Figure 2, although there are similar rates of progression of DR in the short term after initiating intensive glycemic control, there is a significant reduction in progression in the long term (26,29,30). One large clinical trial did not find evidence that a slower rate of achieving targets was beneficial (28), but strong data are lacking. Increased frequency of eye exams may be considered in patients with long-term poor glycemic control who experience an acute dramatic improvement in A1C (27).

Metformin (31), sulfonylureas (18), and insulin therapy (in both type 1 [19] and type 2 diabetes [17]) have all been shown to reduce the rate of retinopathy. There is some evidence that metformin is more beneficial than other treatments in reducing the risk of DME (32). Glucagon like-peptide 1 receptor agonists do not appear to have specific retinopathy-related benefits over other antidiabetic medications, and one—semaglutide—may cause worsening of retinopathy, although these effects are still being studied (33). There are limited data on the effect of treatment with sodium–glucose cotransporter 2 inhibitors on retinopathy risk, although existing data seem favorable, especially with

FIGURE 2 Cumulative incidence of DR progression (three-step or greater progression by Early Treatment Diabetic Retinopathy Study criteria [30]) in the Diabetes Control and Complications Trial primary prevention cohort. There was little difference in percentage of patients with retinopathy progression between the intensive and conventional treatment groups during the first 3 years. However, there was a 76% reduction in risk of DR progression evident at the conclusion of the trial, after a mean follow-up of 6.5 years. Reprinted with permission from ref. 29.



regard to DME (34,35). Thiazolidinediones have been reported to increase the risk of DME (32,36), but not all studies have supported this finding (37). Therefore, the choice of drugs for individual patients should be made based on efficacy and tolerance, rather than on the basis of eye-specific considerations.

Treatment of Hypertension

Hypertension is also a risk factor for DR, and treatment of hypertension reduces the risk of retinopathy progression (38,39). ACE inhibitors, angiotensin receptor blockers, calcium channel blockers, and diuretics all appear to be equally beneficial in reducing the risk of progression of DR. Certain diuretics may be of benefit in DME; however, conclusive data are lacking (40). Thus, ocular status does not dictate the choice of drugs for hypertension in people with diabetes.

In addition to hypertension, the presence of other microvascular complications such as diabetes-related nephropathy and neuropathy are known risk factors for DR (41).

Treatment of Lipids

Statin therapy has been shown to reduce the risk of DME (42), but the impact of statins on the development and progression of retinopathy is unclear.

Hypertriglyceridemia has also been associated with DME (42), and treatment with fenofibrate reduced retinopathy in both the ACCORD and the FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) trials (17,43). Lipid therapy in people with diabetes should be based on established guidelines.

Treatment of Renal Insufficiency

Initiation of either hemodialysis or peritoneal dialysis for renal insufficiency may be associated with improvement in DME, likely due to reduction in fluid volume and systemic uremia (44–46). Similarly, administration of furosemide in a patient with nephrotic syndrome has been reported to cause partial resolution of DME, although conclusive data on the use of diuretics are lacking (47).

Lifestyle Interventions

Comprehensive diabetes self-management education and support (DSMES) has been shown to lower A1C, improve rates of screening for complications, and reduce all-cause mortality (48). DSMES is recommended at diagnosis, annually, and as needed for complications and transitions of care (48).

Data are mixed on the impact of bariatric surgery on the development and progression of retinopathy (49). This is understandable given that obesity is not a direct cause of retinopathy, but rather an indirect cause in some, but not all, cases. Also, the rapid improvement in hyperglycemia that occurs in some instances immediately after bariatric surgery may have short-term detrimental effects on retinopathy, and more frequent eye screening exams may be considered (50).

Regular exercise and increased physical activity have many health benefits, which may include a reduction in retinopathy (51,52). Any activity resulting in a Valsalva maneuver (e.g., heavy lifting) may precipitate a vitreous hemorrhage in patients with unstable proliferative retinopathy, although the benefits of exercise are likely to outweigh the low potential risk (53,54). Thus, consultation with an ophthalmologist may be warranted prior to starting vigorous exercise.

Obstructive sleep apnea is associated with retinopathy, and its treatment may reduce the risk of retinopathy development and progression (55,56).

Smoking increases the risk of retinopathy and proliferative retinopathy in people with type 1 diabetes, although this finding was not confirmed in people with type 2 diabetes (57). Smoking has also been associated with a reduced risk of DME, whereas alcohol intake seems to be associated with an increased risk of DME (58).

Several studies have shown no association between the use of aspirin and the risk of progression of DR (59,60). Little is known regarding the effects of other anticoagulants, but restricting the use of anticoagulants in patients with DR is not typically recommended.

Pregnancy can transiently but rapidly exacerbate DR (61–63), so increased surveillance is recommended, with eye exams in each trimester and postpartum (64).

Association of Diabetes-Related Eye Disease with Vascular Disease

The presence of DME and proliferative retinopathy is associated with increased risk of fatal and incident cardiovascular disease events (10). Nonproliferative and proliferative retinopathy are also associated with peripheral arterial disease (65), suggesting that patients with DR and DME may need more vigilant surveillance for vascular disease.

Conclusion

Optimizing medical management of both type 1 and type 2 diabetes is essential in preventing the development and progression of DR. Lifestyle interventions and improved control of hyperglycemia, hypertension, hyperlipidemia, and renal insufficiency can all positively affect retinopathy outcomes. In addition, it is important to remember that the presence of DR is associated with an increased risk of cardiovascular disease events, and frequent surveillance for vascular disease may be warranted.

Cataracts and Their Treatment in People with Diabetes

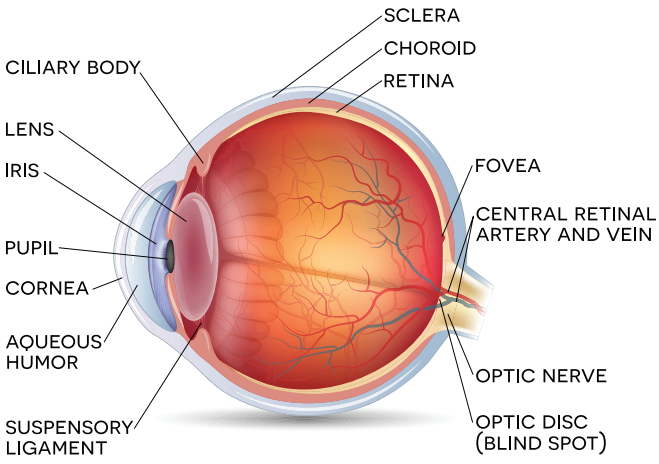
Jill E. Bixler, MD, *University of Michigan Medical School, Kellogg Eye Center, Ann Arbor, MI*

Nearly 90% of Americans surveyed in a 2014 nationwide poll said they considered eye health crucial to overall health, and almost 50% reported viewing a loss of vision as the worst possible health outcome they might experience in their lifetime (66). Two of the diseases that can profoundly affect vision are diabetes and cataracts. The National Institute of Diabetes and Digestive and Kidney Diseases estimates that 30.3 million people in the United States have diabetes (67), and the National Eye Institute projects that, by 2030, there will be almost 40 million people in the United States with cataracts (68). These statistics highlight how common both of these diseases are, yet only 65% of Americans surveyed knew what cataracts were, and just 37% were aware of some of the ways in which diabetes can affect the eye (66). Thus, it is very important for physicians and other primary care providers to know about these common diagnoses and how they affect each other, so they can counsel and educate patients appropriately to help preserve their vision.

From Crystalline Lens to Cataract

The eye is like a camera; light is focused by the cornea and crystalline lens (the "camera lenses") in the front of the eye onto the retina (the "film") in the back of the eye. The portion of the retina that sees the central part of vision is called the macula, and even small amounts of edema or other pathology in the macula can cause significant visual compromise. The information that the retina collects is then sent by the optic nerve to the brain for processing and interpretation (Figure 3). Any irregularities and opacities in the cornea or crystalline lens interfere with the ultimate perception of a clear image in the brain, the way a smudge on a camera lens will create a blurred picture. The role of the retina will be discussed in the next chapter of this compendium.

FIGURE 3 Cross section of the eye. Note that the course of light travels through the cornea, pupil, and crystalline lens (becomes the cataract) to the retina and then to the brain through the optic nerve.



The crystalline lens is one of the major structures that focuses light as it enters the eye. In the absence of congenital abnormalities, the crystalline lens is colorless when we are young. It becomes a cataract when it begins to acquire colored changes. Common causes of cataracts are age, trauma, iatrogenic factors (e.g., medications, radiation, or other intraocular surgeries), and disease (e.g., diabetes). Typically, the lens will become white, yellow, or a combination of the two. Cataracts are progressive and can be present for many years before they start to affect a person's vision and cause symptoms.

There are multiple types of cataract, and the different types are often associated with specific causes and can cause variable symptoms. The type of cataract most associated with aging is called a nuclear sclerotic cataract (NSC) and is diagnosed when the crystalline lens starts to turn yellow. The color of an NSC will usually progress slowly over years from yellow to amber to dark brown in very advanced cases. This type of cataract will appear to affect all layers of the crystalline lens (69).

A posterior subcapsular cataract (PSC) is one of the most common types of cataracts seen in diabetes (70) and occurs when the most posterior layers of the crystalline lens develop areas that look grainy and white. These opacities occur in discrete patches. If the PSC changes are in a peripheral portion of the crystalline lens, the cataract is asymptomatic; when the PSC opacities are in the central part of the crystalline lens, they can quickly become symptomatic. PSCs tend to be more rapidly progressive than NSCs, and their symptoms can develop over weeks or months.

Cortical cataracts are the other type of cataract that is often seen in people with diabetes (70). This type of cataract causes the middle and outer layers of the crystalline lens to become white. These changes can occur in triangular formations (called spokes) or in a more sheet-like arrangement. These cataracts are similar to PSCs in that they are typically symptomatic only when the changes affect the central portion of the crystalline lens, and their symptoms can progress rapidly.

Snowflake cataracts have sometimes been called "diabetic cataracts." Despite their name, they are much less common than the other types of cataracts that are associated with diabetes and can even occur rarely in people without diabetes. These cataracts have an abrupt onset of scattered opacities in a formation that can look like a snowflake beneath the capsule that surrounds the cataract. This type of cataract usually develops in young people with uncontrolled diabetes and may be the initial presentation of diabetes (70).

Vision Changes in Diabetes

Diabetes may affect the eye in multiple ways, and it is important to be able to distinguish the possible causes of vision deficits in people with diabetes. Changes to the crystalline lens that are induced by diabetes can cause short- or long-term effects on the vision (70).

Aqueous humor is the fluid that fills the front of the eye and provides nourishment to the crystalline lens (Figure 3). Increased glucose levels in the aqueous humor lead to increased glucose levels in the crystalline lens. This development causes temporary swelling of the lens that can result in short-term fluctuations in vision (70). People with large fluctuations in their blood glucose levels often report vision fluctuations that mirror their glycemic control. If people with diabetes notice blurred vision across their entire visual field that only lasts for a few hours, short-term osmotic fluctuations in the crystalline lens structure are the likely cause and can be resolved by achieving more consistent blood glucose control (70).

The crystalline lens can enzymatically convert glucose to sorbitol, which is one of the many mechanisms that will eventually result in cataract formation (71). Vision that is consistently blurred over days to months and has no apparent relation to glycemic control is likely the result of a cataract or diabetes-related retinopathy (DR).

The symptoms of cataracts and DR are similar but can sometimes be distinguished by a careful history. A cataract likely causes glare, halos, or starbursts from bright sunlight or headlights at night. Decreased contrast vision, often manifesting as trouble distinguishing dark colors or needing brighter lights to read, is also a typical cataract symptom. Cataracts can also cause a change in the refractive error. A refractive error occurs when the shape and structure of the eye does not allow for light to be well focused on the retina. This lack of sharp focus results in a blurred image and needs an optical correction (usually eyeglasses or contact lenses) to allow the eye to see a sharp, clear image. A person who can obtain clear vision with a new eyeglasses prescription but finds the prescription gradually changing every few months to annually may have a cataract. Of note, in some cases, the presenting symptom of diabetes is a sudden, large change in refractive error that is stable over days to weeks. Diabetes should be considered in the differential diagnosis of patients with a sudden worsening of their refractive error, and eyeglasses should not be prescribed until a work-up is complete and their diabetes is controlled.

DR is discussed more fully in the next chapter of this compendium. Briefly, visual symptoms that are more typical of DR include a sudden onset of many new floaters (specks or "cobwebs" that float about in the field of vision) that can sometimes cause a sudden, profound decrease in vision, central vision distortion or focal blurring, and loss of a portion of the visual field. But symptoms can overlap, and cataracts and DR can coexist. Whenever patients with diabetes note a significant change in their vision, it is prudent to have them examined by an eye care specialist because most ocular conditions associated with diabetes require an examination by an ophthalmologist for diagnosis and treatment (64).

Cataracts and Diabetes

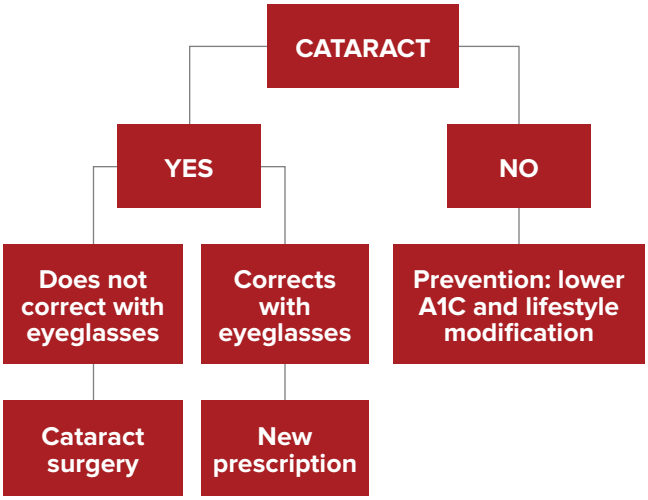
It is well established that both type 1 and type 2 diabetes are risk factors for cataract development (70). The risk factors more specifically associated with cataract formation in people with diabetes are a younger age, increasing duration of diabetes, presence of DME, and insulin use in people with type 2 diabetes (72); the latter two risk factors may be associated with poor glycemic control. The risk of developing cataracts that are specifically associated with diabetes is highest in younger people with diabetes (72). These patients' symptoms can progress more rapidly due to the types of cataracts that are more commonly associated with diabetes (i.e., PSC and cortical cataracts).

Treatment of Cataracts

The definitive treatment for cataracts is surgical, but there are other options to consider before cataract surgery is necessary (Figure 4). Prevention of disease is preferred but ultimately not possible as an enduring solution because nearly everyone will get cataracts if they live long enough. The goal is to prevent the development of the early-onset cataracts that are associated with diabetes. The development of cataracts in younger people with diabetes is linked to hyperglycemia, so achieving tight glycemic control can help to slow the progression of cataracts. Exposure to ultraviolet light, smoking, advancing age, and steroid use are also linked to cataract development (70), and some of these risk factors can be avoided through lifestyle change.

If a cataract causes a shift in a person's refractive error, then a new eyeglasses prescription can help to improve his or her vision. Eventually, new eyeglasses will no longer correct the vision well enough to avoid surgery, but they can often delay the need for surgical treatment of cataracts.

FIGURE 4 Decision tree for how to correct blurred vision in patients with diabetes.



Cataract Surgery

As mentioned above, surgery is the ultimate treatment for cataracts. Cataract surgery is the most commonly performed surgery in the United States, and approximately 3.6 million cataract extractions were performed in 2015 (73). Cataract surgery is rarely an emergency and so is undertaken when patients' vision does not allow them to see well enough to perform visual activities they need or want to do in daily life. Another reason to pursue cataract surgery in people with diabetes might be to improve the view into the back of their eye. A clear view to the retina is required for the surveillance and possible treatment of DR.

Cataract surgery replaces a cloudy lens (the cataract) with a clear lens (the intraocular lens [IOL] implant), thus allowing light to enter the eye and be focused into a sharp image on the retina. Modern cataract surgery is almost always performed on an outpatient basis and often takes only about 10 minutes, although patients are typically at the surgery center or hospital for a few hours for their procedure.

Most patients receive light systemic sedation, along with local anesthesia in or around the eye; patients rarely require general anesthesia for cataract surgery. Patients often are prescribed steroid or antibiotic eye drops to use for about 1 month after getting cataract surgery. Some surgeons inject medications into the eye at the end of surgery, which obviates the need for eye drops during the postoperative period.

Most surgeons ask patients to follow light restrictions on physical activity for a short time, but patients are able to resume almost all of their normal activities immediately. Some types of local anesthesia allow patients to see during and just after cataract surgery, whereas other anesthesia techniques require patients to have their eye closed and patched overnight. Recovery of full vision after surgery can take weeks to achieve, and this interval may be longer for people with diabetes.

The most common approach to cataract surgery in the United States is through two small corneal incisions ranging in size from 1 to 3 mm (74). The cataract is broken up into very small pieces using ultrasound power in a process called "phacoemulsification." The small pieces are then aspirated out of the eye until the cataract is removed completely. The tissue capsule that used to house the cataract is then used to hold the new IOL implant in place. Barring extraordinary circumstances, the IOL should stay in place for the rest of the patient's life, and the cataract will not recur. Modern cataract extraction uses smaller incisions, has a shorter surgical time, and usually results in less inflammation than older techniques of cataract extraction (74).

There are two basic categories of IOLs that can be used during cataract surgery. The lenses have refractive or focusing power as part of their design. Measurements taken in the clinic before surgery can predict what patients' postoperative refractive error will be. Monofocal IOL implants will focus the eye in one location (e.g., for distance or near vision). Patients with a monofocal IOL will need eyeglasses to see clearly at distances other than the one location on which the IOL focuses their eye (e.g., they will need reading eyeglasses if their IOL is focused at far distance). Some people opt to have monofocal IOL used in such a way that will reduce their need for eyeglasses postoperatively, a result known as "monovision." In monovision, one eye is set to be near-sighted for reading vision, and the other eye is focused for distance vision.

Another option to reduce dependence on eyeglasses after cataract surgery is a different type of IOL. These IOLs try to focus the eye for both near and distance vision. There are many types of lens designs that try to achieve this goal. These lenses are usually not covered by medical insurance and cannot be implanted in every eye due to ocular contraindications. Patients' ophthalmologist will discuss their refractive goals before surgery so the lens selected to be implanted will have the best chance of fulfilling patients' vision preferences. It is important to note that, for multiple reasons, many people will still need a small vision correction from eyeglasses to achieve their best vision even at the distance at which their IOL is set to focus.

Considerations for Cataract Surgery in Patients with Diabetes

Up to 20% of cataract surgeries are performed in people with diabetes (70), and there are some special considerations when planning cataract surgery for people with diabetes. These considerations encompass the preoperative through

postoperative time period. The advances in surgical technique and pre- and postoperative pharmacological management of DR have made cataract surgery safer for people with diabetes (75).

Preoperative Considerations

As mentioned earlier, cataracts occur at a younger age in people with diabetes. This means that, at the time of cataract surgery, these younger patients still have a significant portion of their accommodation (ability to adjust the focus of the crystalline lens from near to distant objects).

Presbyopia is the gradual loss of accommodation that occurs as we age. Most older cataract surgery patients have already lost their accommodation and are thus used to relying on reading eyeglasses or bifocals for their near vision. In contrast, younger cataract patients with diabetes may not be using reading eyeglasses or bifocals for their vision preoperatively.

As noted above, the most common type of IOL used during cataract surgery is the monofocal IOL. If a monofocal IOL implant is well focused for distance, the patient will need eyeglasses for near-vision activities such as computer work, tablet use, and reading. This can be quite an adjustment for younger individuals who have had no experience with bifocals or reading eyeglasses. As such, it should be discussed in detail with patients before their cataract surgery so they will have appropriate expectations.

It may seem that younger patients with diabetes who are not used to reading eyeglasses would be ideal candidates for the type of IOL that focuses at both near and distance. Unfortunately, this type of IOL is not recommended in people with macular pathology such as DME. Thus, the presence of preoperative DME would rule out the use of this type of IOL. The lifetime risk of DME also needs to be considered in young patients who have diabetes but do not have DME preoperatively. IOL implants are considered permanent, so patients who choose an IOL contraindicated for macular pathology but then later develop macular disease such as DME may have late vision compromise.

The choice of an IOL is limited in another way by diabetes. IOLs that are made with silicone should not be used in people with diabetes. At some point, a retina surgeon may use silicone oil for surgical management of severe DR. Silicone oil may condense on silicone IOLs. Hydrophobic acrylic is typically the preferred material for IOLs in people with diabetes because it should retain its clarity if future retinal intervention is necessary.

Intraoperative Considerations

The pigment epithelium of the iris can accumulate glycogen or develop neovascularization (the formation of new blood vessels) and a resultant fibrous membrane from diabetes. Both of these conditions cause the pupil to dilate poorly. The pupil needs to dilate well during cataract surgery to ensure adequate access to the cataract that sits directly behind the iris (Figure 3). Poor pupillary dilation can make cataract surgery more complicated.

There are surgical maneuvers during cataract surgery to expand pupillary dilation pharmacologically or mechanically. The more effective mechanical techniques can result in abnormally shaped pupils, iris pigment dispersion with subsequent intraocular pressure elevation, and iris depigmentation. Although these effects are typically very mild with modern approaches, they can increase the risk of complications during and after surgery (70).

Postoperative Considerations

Corneal hypoesthesia (decreased corneal sensitivity) is common in people with diabetes. The two small corneal incisions needed for cataract surgery often will have small corneal epithelial defects overlying them at the end of surgery, similar to small corneal abrasions. Diabetes can slow the recovery of the epithelium after cataract surgery and prolong discomfort from the abrasions or result in recurrent corneal erosions (70).

A posterior capsular opacity (PCO) is a loss of clarity to the posterior surface of the tissue capsule that holds the IOL in place. This opacity can scatter light and cause blurry vision and glare similar to the effects of a cataract. A film of lens epithelial cells can grow behind the IOL implanted during cataract surgery, or the capsule can develop fibrosis and wrinkle.

Approximately 30% of people who have cataract surgery will develop a PCO in the months or years after their procedure (76). Younger people have a higher rate of PCOs (76). There are conflicting reports of whether PCOs are more common in patients with diabetes (76). However, we know that many patients with diabetes are younger at the time of their cataract surgery, so many of them will end up with a PCO sometime after surgery.

PCOs are treated in the clinic with a straightforward laser procedure that lasts a few minutes. Most of these are very routine, but there are some rare, yet serious, risks associated with the laser treatment of PCOs.

Endophthalmitis is an intraocular infection that can occur after cataract surgery. Many such infections can be treated successfully, but they do sometimes result in permanent loss of vision or loss of the eye completely. The rate of endophthalmitis is extremely low, at 0.044% with the modern use of intracameral antibiotics at the time of cataract surgery (77). People with diabetes have a 31% increase in the rate of endophthalmitis after cataract surgery (77). This increased risk of developing a devastating infection is

concerning, even though the overall number of endophthalmitis cases is very small even in patients with diabetes.

Other vision-threatening complications after cataract surgery in patients with diabetes involve the retina. Older studies reported an increase in DR and DME and a predisposition to anterior segment neovascularization after cataract surgery (75). These serious risks led to the recommendation that cataract surgery be delayed in patients with diabetes. The modern approach to cataract surgery has reduced the worst of the risks in uncomplicated surgeries, and thus must ophthalmologists use the same preoperative criteria in recommending cataract surgery for patients with or without diabetes. Still, there are some risks to the diabetic retina with the current approach to cataract surgery, and certain measures should be taken to ensure the best outcome for patients with diabetes (75).

The main postoperative concern about the retina of a patient with diabetes is the development or worsening of DME, which can lead to poor vision. In patients without DME preoperatively, the risk of postoperative visual compromise from the development of DME is greatest in people with preexisting DR, and there should be special consideration given to using eye drop nonsteroidal anti-inflammatory drugs (NSAIDs) in this group at the time of cataract surgery (75). In fact, regardless of the presence of DR, patients with diabetes who do not have DME have a lower relative risk of developing DME with the prophylactic use of NSAIDs in the perioperative period (75). This treatment is not without concerns, however. The course of treatment can last beyond the usual time course for postoperative eye drops, which may decrease compliance. This longer time period also results in increased cost to patients for drug copayments and exposes them to potential side effects from an additional medication.

Patients with diabetes who have pre-existing DME also need special treatment in the perioperative period. There are multiple treatment options for these patients at the time of cataract surgery that will help to prevent the worsening of their DME. These options include macular laser therapy, intravitreal anti–vascular endothelial growth factor medications, and intravitreal steroids (both injections and implants). Each of these options has risks, and a clear best choice for the treatment of preoperative DME has not yet emerged (75).

Conclusion

The aging population and increasing prevalence of diabetes together ensure that the number of people with cataracts will continue to increase. Vision is one of the most important contributors to quality of life and is the sense people most fear losing (77). People with diabetes can decrease their risk of cataract formation by improving their glycemic control and controlling for other lifestyle factors that increase cataract risk. The many advances in cataract surgery technique and procedural and pharmacological management of DR have made cataract surgery a safe and effective procedure for people with diabetes in the vast majority of cases.

Management of Diabetes-Related Retinopathy

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Diabetes-Related Retinopathy: Pathogenesis, Terminology, and Mechanisms of Visual Impairment

The retina is a highly metabolically active tissue and has the highest oxygen consumption per gram of tissue of all the organs of the human body. To supply this oxygen and nutrient demand, the retinal neurons that provide vision are heavily dependent on an adequate blood supply. Breakdown of this blood supply is the hallmark of a multitude of retinal vascular diseases that occur concurrently with damage to retinal neurons (78). Poor metabolic control over extended periods of time can lead to microvascular damage to the retinal circulation mediated by pericyte loss, basement membrane thickening, and endothelial cell dysfunction, along with nerve cell dysfunction and damage. These pathologic processes lead to capillary occlusion and progressive retinal nonperfusion, with subsequent local ischemia and disruption of the neurovascular unit as a whole (4). Vision impairment ultimately results from damage to the neurons, particularly the ganglion cells and their axons. Thus, diabetes-related retinopathy (DR) can be considered a form of diabetes-related sensory neuropathy, analogous to the diabetes-related peripheral sensory neuropathies (79).

There are many directly visible, ophthalmic examination findings associated with DR. The most common retinal findings include microaneurysms, intra-retinal hemorrhages, hard exudates, edema or thickening of the retina, venous beading, "cotton wool spots" (i.e., small yellowish-white deposits in the retina), intra-retina microvascular abnormalities, and pre-retinal neovascular tissue (Figures 5–7). By contrast, retinal nerve cells are transparent and not visible by ophthalmic or photographic examinations. Layers of retinal neurons and their synapses can be seen by optical coherence tomography (OCT) and reveal atrophy and disorganization of the retinal layers in early stages of DR (80,81).

At present, DR severity is quantified using feature-based, structured grading of color images of the retina, referred to as fundus images, and allows the designation of an eye to a category on the Early Treatment Diabetic Retinopathy Study (ETDRS) DR severity scale (DRSS), which was defined and refined through the 1970s and 1980s and is still widely used today (30). From a clinical perspective, the DRSS is complicated and not intuitive; there are at least 12 distinct steps, each with discrete sub-levels. Simplified, however, the DRSS can be used to classify eyes into one of two clinically relevant DR categories: eyes with nonproliferative DR (NPDR; Figure 5) and those with proliferative DR (PDR; Figure 6).

FIGURE 5 Fundus photograph of a right eye with severe NPDR. Microaneurysms, intraretinal hemorrhages, hard exudates, cotton wool spots, and intraretinal microvascular abnormalities are visible.

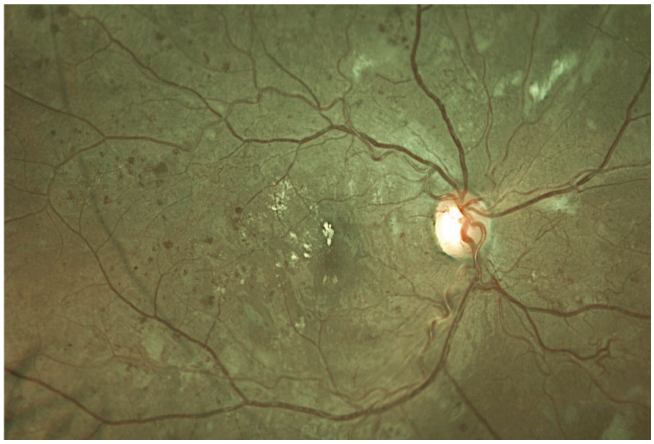
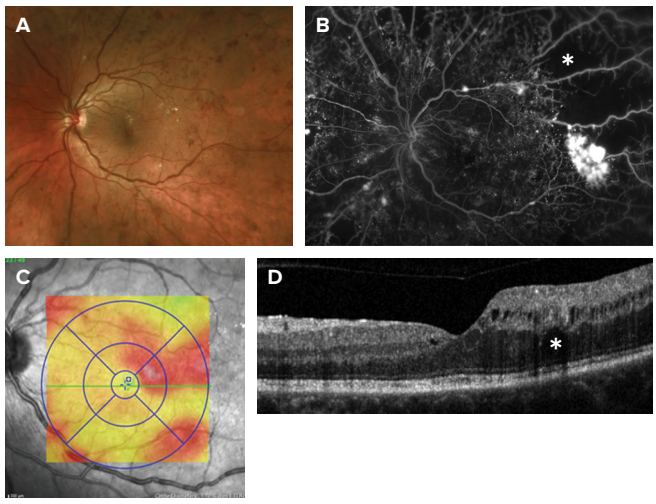
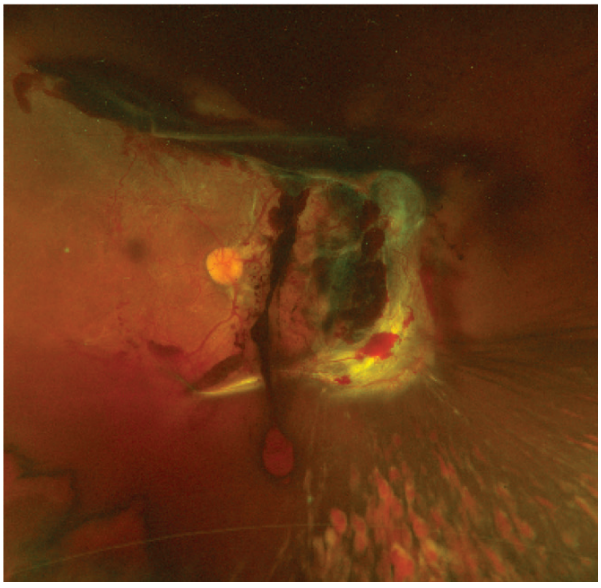


FIGURE 6 *A*) Fundus photograph of a left eye with PDR and DME. Microaneurysms, intraretinal hemorrhages, and hard exudates are visible. *B*) Wide-field fluorescein angiogram illustrating zones of retinal nonperfusion (*), diffuse microvascular leakage consistent with breakdown of the blood-retinal barrier, and prominent leakage temporally associated with pathologic neovascularization. *C*) OCT map showing multifocal zones of retinal thickening (highlighted red) consistent with DME. *D*) OCT line scan through the center of the macula showing central involvement of the DME with multiple intraretinal cysts (*).



The pathologic changes underlying DR lead to visual impairment through three inter-related mechanisms. First, retinal nonperfusion (Figure 6) leading to ischemia can directly impair retinal function. In response to local ischemia and breakdown of the blood-retinal barrier, a local inflammatory response is mounted that includes upregulation of multiple cytokines, including vascular endothelial growth factor-A (VEGF). Elevated levels of VEGF then directly contribute to visual impairment through two additional pathologic processes related to an aberrant wound-healing response. First, pathologic levels of VEGF further impair normal retinal vascular integrity, leading to breakdown of the blood-retinal barrier and exudation into the retina of fluid, lipids, and proteins that are normally contained intravascularly. This process leads to retinal thickening, referred to as diabetes-related macular edema (DME) (Figure 6), and dysfunction of the neuronal signaling needed for optimal visual function. Second, pathologic levels of VEGF can drive abnormal angiogenesis (the development of new blood vessels), a process termed PDR. These pathologic new vessels classically sprout from retinal veins and extend into the vitreous cavity along the collagen network composing the optically clear vitreous gel. At first, these vessels are isolated, but over time they recruit fibrotic components. These friable vessels can bleed into the vitreous cavity causing vitreous hemorrhage, and the fibrotic components can contract and cause retinal detachment (Figure 7).

FIGURE 7 Fundus photograph of a right eye with PDR and tractional retinal detachment, a common end-stage manifestation of untreated PDR. Extensive vitreous hemorrhage, pathologic vessels (neovascularization of the optic disc and neovascularization elsewhere), and a tractional retinal detachment predominately involving the superior and nasal retina with sparing of the macula are visible.



Imaging in the Management of DR

Although the retina can be visualized directly using specific lenses in combination with an appropriate light source, management decisions often rely heavily on the use of exceptionally sensitive imaging techniques, so DR management often employs multimodal imaging.

Noninvasive OCT is a cornerstone of DME management and is used to confirm the presence of DME, quantify retinal thickness, and evaluate the effectiveness of intervention. Patients with any DR typically undergo OCT imaging at most, if not all, clinic encounters. In addition, OCT can be used to visualize individual retinal layers, which can be a helpful prognostic tool.

Color fundus photography, fluorescein angiography (FA), ultrawide-field (UW) imaging, and OCT angiography (OCTA) are adjunct modalities that can also provide valuable information. Physicians can compare images longitudinally to look for DR progression and use images as a tool for patient education. Angiography can be used to evaluate retinal perfusion and vascular leakage. Beyond the macula and posterior pole, physicians often use UW imaging to more completely understand the severity of retinopathy across the entire retina and to guide treatment. For example, UW FA may demonstrate neovascularization and nonperfusion in the periphery that are not otherwise apparent (Figure 6), and this finding may alter classification and prognostication compared to clinical exam or more limited posterior pole fundus photography alone. OCTA provides high-resolution noninvasive images of the retinal vasculature without the use of the intravascular dye injection needed for traditional FA and is being used with increasing frequency in both clinical trials and daily practice.

Management of DME

Diabetes is the most common chronic systemic disease seen by ophthalmologists and is unique in that patients assume primary responsibility for their care, in contrast to cancer or infectious diseases. Therefore, the fundamental treatment of all forms of DR centers on the treatment of the underlying systemic risk factors, as detailed in the first chapter of this compendium. Factors such as diabetes duration, sex, and genetic susceptibility obviously cannot be altered. However, metabolic control, blood pressure, renal function, lipid levels, and nonhealing ulcers are modifiable and should be addressed in a comprehensive manner coordinated with patients, their physicians, and ophthalmologists (82). This intensive care is vital because DR severity can improve in 18% of patients with type 1 diabetes whose A1C declines by 1 percentage point (83). Moreover, the outcome of treatment with panretinal

photocoagulation (PRP) for PDR is significantly better in patients with a baseline A1C <8% compared to those with an A1C ≥8% (84).

Three Clinically Relevant DME Sub-Categories

Historically, the threshold for treating DME with laser photocoagulation was set by the ETDRS in the 1980s as clinically significant macular edema. However, this definition has become outdated. More clinically relevant is classification of DME as either central-involved DME (CIDME) or non-CIDME.

In the setting of non-CIDME, the results of the ETDRS trial remain relevant to current practice, and laser photocoagulation appropriately applied to the macula remains a validated option for treatment. Specifically, laser photocoagulation significantly reduces the risk of moderate visual loss by approximately 50%, a protective effect that is independent of baseline visual acuity (85). Despite its potential value in slowing the progressive visual loss from DME, however, laser photocoagulation has limitations and possible untoward effects. For example, photocoagulation for DME has shown limited effectiveness in improving visual acuity and can rarely cause blind spots in the central visual field.

CIDME is most accurately determined by OCT and is defined by thickening that affects the 1-mm-diameter central sub-field of the macula. In the setting of CIDME, pharmacological management of DME is now first-line therapy in most clinical situations. Seven pharmaceutical agents encompassing two mechanistic classes are used for the treatment of DME. All are given by direct injection into the eye in an in-office procedure called an intravitreal (or intravitreous) injection. Engineered proteins, including the U.S. Food and Drug Administration (FDA)-approved ranibizumab (86) and aflibercept (87), as well as the non–FDA-approved bevacizumab (88), block the activity of VEGF. Alternatively, the FDA-approved dexamethasone (89) and fluocinolone acetonide (90) implants, as well as two formulations of triamcinolone acetonide—an FDA-approved preservative-free version and a non–FDA-approved preserved version—are corticosteroid agents.

In cases of CIDME, there are two clinically relevant sub-categories: those with preserved visual function and those with associated visual loss. Although there are limited prospective data to guide treatment of CIDME with preserved visual function, the field continues to move toward earlier intervention. Supporting earlier pharmacologic treatment, better visual function at the time of initiation of intravitreal pharmaceutical therapy for DME is associated with better long-term visual outcomes, a correlation that has demonstrated remarkable consistency across many exudative retinal diseases, including neovascular age-related macular degeneration and retinal venous occlusive disease (86,91,92).

In eyes with CIDME and visual loss, intravitreal pharmaceutical agent delivery is usually first-line therapy. Numerous well-designed, phase 3 clinical trials have demonstrated significant benefit with intravitreal pharmaceutical treatment compared to observation or macular laser therapy (93,94). Most of these trials enrolled patients with 20/40 or worse visual acuity in a randomized, double-blinded manner (meaning that neither the patients nor the treating physicians knew which treatment specific patients were receiving). In these trials, patients treated with fixed dosing regimens of ranibizumab or aflibercept through 3 years gained an average of 10 or more ETDRS letters, also referred to as two lines of visual acuity (since five letters represent one line), or the equivalent of an eye improving from 20/60 to 20/40 visual acuity. In comparison, patients treated with macular laser therapy or observation gained little or no visual acuity over the same time period.

A single phase 3 trial, primarily sponsored by the National Institutes of Health and known as the Diabetic Retinopathy Clinical Research Network Protocol T (DRCR.Network Protocol T), compared the three available anti-VEGF agents through 2 years of DME management (95). Among better-seeing eyes, all three agents (bevacizumab, ranibizumab, and aflibercept) achieved similar visual benefit, whereas anatomic benefit was superior with both aflibercept and ranibizumab compared to bevacizumab. Among worse-seeing eyes (baseline vision of 20/50 or worse), although all three medications achieved robust visual acuity gains, aflibercept achieved the greatest visual and anatomic gains compared to bevacizumab, with similar ultimate visual and anatomic outcomes compared to ranibizumab at the 2-year endpoint.

In clinical practice, treatment of DME in most patients is initiated with monthly anti-VEGF intravitreal injections. When optimal visual and anatomic outcomes are achieved, the anti-VEGF dosing frequency is often then reduced. Such a reduction in treatment frequency is often achieved in one of two ways. First, patients may continue to receive treatments separated by increasing time intervals, a process known as "treat and extend." Alternatively, treatment may be stopped and only reinitiated when recurrence of DME is observed, a management approach known as "pro re nata" (PRN).

Although anti-VEGF pharmacotherapy is typically considered to be first-line treatment for DME, corticosteroids can play an important role in management. Some eyes treated with anti-VEGF monotherapy will have an incomplete response to adequate anti-VEGF dosing. In

prospective studies, this proportion of patients ranges from approximately 30 to 68% (96). In these cases, incorporation of an intravitreal steroid agent can lead to better DME control (97). Mechanistically, this is likely related to the observation that numerous inflammatory pathways are active in DR and DME that are not influenced by anti-VEGF monotherapies. In comparison, corticosteroids are capable of modulating a multitude of inflammatory pathways, including blockade of VEGF.

Despite their potential extended durability compared to anti-VEGF monotherapies, corticosteroids are typically not used as first-line therapy because of the risks inherent to intravitreal steroid delivery, including cataract acceleration and increased intraocular pressure (IOP). Although cataract is a readily treatable pathology and the IOP elevation observed in approximately one-third of eyes treated with intravitreal steroids is generally manageable and reversible, these factors often place corticosteroids as a second-line option.

Long-Term Dosing Requirements in DME Management

The management burden for patients with CIDME through 2 years is substantial and should be directly communicated with patients and their caregivers. For example, regardless of treatment, through 2 years of the DRCR.Network Protocol T trial, patients underwent a mean of 23 clinical visits and received a mean of 15–16 intravitreal injections (95).

Fortunately, after initially intensive anti-VEGF therapy for CIDME, several analyses have suggested that less-frequent-than-monthly anti-VEGF dosing may be effective in maintaining visual and anatomic gains in most patients and that a clinically meaningful proportion of patients can maintain quiescent disease without ongoing treatment through at least 2 additional years of follow-up. For example, after fixed dosing through 3 years in three phase 3 trials, approximately one-fourth of patients received no additional anti-VEGF dosing, with no DME recurrence, whereas an average of 3–4 intravitreal injections were given annually to the entire population for DME control through the fourth and fifth years of management (98,99).

Management of PDR

Diseases relatively confined to the macula, including most cases of DME and age-related macular degeneration, may cause substantial visual impairment, with loss of the capacity to perform visual activities requiring detailed vision such as reading, driving, and recognizing faces. However, even in their severe form, such diseases often allow affected individuals to retain the gross visual function to recognize large objects and ambulate. In comparison, the natural history of diseases that routinely affect both the macula and the peripheral retina, such as PDR, can and often do lead to more complete loss of vision, with more profound impairment in performance of activities of daily living.

PDR can be treated with either PRP or intravitreally delivered pharmaceuticals that inhibit VEGF. Each of these treatments has unique benefits and challenges. PRP is analogous to radiation therapy for cancers, whereas intravitreal anti-VEGF or corticosteroid administration is analogous to chemotherapy. The two approaches are often used in combination. The advantages and disadvantages of each approach must be weighed carefully by patients, their families, and their physicians.

In the 1970s, the pivotal Diabetic Retinopathy Study defined PRP as the cornerstone of treatment for PDR by demonstrating a dramatic reduction in blindness with treatment compared to observation (100). Although PRP remains a mainstay of PDR management today, it is an inherently destructive treatment. Retinal tissue is selectively ablated, and a scar is created. Although this process often stops the progression of the proliferative process inherent to PDR, it has limitations and can lead to untoward effects. First, PRP is not a cure in many eyes. For example, a 5-year study comparing PRP to anti-VEGF pharmacotherapy (the DRCR.Network Protocol S) found that slightly greater than half of eyes treated with PRP at baseline required additional PRP through 5 years of follow-up (101). Second, PRP can lead to peripheral visual field defects, night vision loss, and loss of contrast sensitivity. The key benefit of PRP is that the treatment is permanent. PRP creates a lasting scar where laser energy is applied. Thus, some eyes can be adequately managed with one or at least a limited number of PRP applications. In the DRCR.Network Protocol S, just 15% of eyes randomized to PRP received additional laser application cumulatively in years 3, 4, and 5.

The main benefit of anti-VEGF pharmacotherapy is that it avoids the destructive nature of PRP. This translates into less severe, even though progressive, visual field loss with anti-VEGF pharmacotherapy compared to PRP. The downside to anti-VEGF pharmacotherapy is the transient biological effect related to the medication pharmacokinetics, which translates into an increased visit and treatment burden. Through 5 years of the DRCR.Network Protocol S, eyes randomized to anti-VEGF treatment required a median of 43 clinical visits, compared to 21 clinical visits among the patients randomized to PRP. Furthermore, although the treatment burden from anti-VEGF therapy decreased after the first year, a majority (63–75%) of eyes still required repeated dosing annually through year 5, with 43% still requiring four or more injections in the fifth year of management (101).

Management of NPDR

For the past four decades, treatment of DR has been reactionary, typically initiated only once the potentially blinding pathologies of PDR and DME are manifest. However, accumulating data indicate that there may be tremendous value in initiating ocular-specific pharmacological treatment for DR at earlier stages. Specifically, prevention of progression to PDR and development of DME may represent a tremendous public health opportunity. The clinical rationale for doing so is twofold. First, worsening NPDR severity carries prognostic information indicating an increased risk of disease progression and visual loss. Second, as NPDR severity worsens even in the absence of DME, health-related quality of life related to vision-dependent functions such as driving ability progressively decline.

Improving DR Severity with Pharmacotherapy

Historically, DR as assessed by the DRSS was generally accepted clinically as a one-way track, with progressive accumulation of retina damage associated with DR over time. More recently, the field has realized that position on this scale can be modified with pharmaceutical treatment. Although the phase 3 trials leading to FDA approval of aflibercept and ranibizumab for DME treatment revealed remarkable efficacy at improving retinal anatomy and function, they also demonstrated that VEGF blockade can affect far more than just macular edema.

First, just as PRP of eyes with severe NPDR can delay progression to PDR, pharmacotherapy can significantly blunt progression from NPDR to PDR (102,103). Second, anti-VEGF therapy not only slows progression of DR, but also has the added benefit of improving DR severity in a substantial proportion of eyes. In phase 3 trials focused on DME management, approximately one-third of anti-VEGF–treated eyes experienced a clinically meaningful improvement in DR severity, defined as a two-step or greater DRSS improvement, compared to 5–16% of sham-treated eyes (86,87). Anti-VEGF treatments can also reduce the development of PDR in eyes with moderately severe and severe NPDR. Within this high-risk population, a much larger proportion of eyes with DME, more than 75%, experienced a clinically meaningful DRSS improvement with ranibizumab treatment (104). Third, VEGF blockade appears to have a significant impact on the underlying retinal vasculature itself, slowing progressive capillary loss (105), suggesting that pharmacotherapy may be able to achieve fundamental disease modification.

Pharmacological Treatment of DR in Individuals with NPDR But No DME

Although the value of pharmacological therapy for improving DR severity has been documented in multiple prospective studies enrolling individuals with DME or PDR, the value of such therapy in those with NPDR but no DME, representing a larger patient population who currently remain largely untreated, is under active investigation. Intravitreal injections do carry risk, especially when considering the cumulative risk of many years of repeated treatments. These risks include infection (referred to as "endophthalmitis"), retinal tear, retinal detachment, cataract, and potentially even systemic side effects. The costs of treatment also include time off from work for patients and their families. To better define the risk-benefit ratio in high-risk NPDR eyes without DME (DRSS levels of 47 and 53), two independent, large, randomized, phase 3 trials were initiated in 2016 comparing sham injections to VEGF blockade with aflibercept injections.

PANORAMA was a 2-year trial that randomized 402 patients to either sham treatment or anti-VEGF dosing with aflibercept (106). The primary outcome was met, with 55–62% and 65–80% of anti-VEGF–treated patients achieving at least two steps of DR severity improvement at 6 and 12 months compared to 6 and 15% of sham-treated eyes, respectively. More clinically relevant, however, was that 41% of sham-treated eyes had developed either DME or PDR by 12 months, compared to 11% of anti-VEGF–treated eyes. A distinct 4-year trial with a similar sham-controlled design and a 2-year primary endpoint is ongoing (107). At the time of the completion of this compendium, ranibizumab has been approved by the FDA for the treatment of all forms of DR (with or without DME), and aflibercept has been approved for the treatment of DR in patients with DME.

Compliance and Dosing Frequencies in the Real World

In the prospective trials evaluating current-generation anti-VEGF agents for DME and DR management, frequent visits and regular treatments are typically employed. However, recommendations based on clinical trial protocols can be challenging to implement in routine clinical settings. Patients with DR are often in poor health and require complex medical care—so much so that many DR patients have difficulty adhering to frequent office visits, especially given that this disease often manifests within a working-age population. In a recent health care claims database analysis, patients with DME averaged 25.5 heath care visit days annually, of which 4.4 visits were attributed to ophthalmic care (108).

Multiple real-world analyses have concluded that anti-VEGF dosing in the real world appears to be substantially less than that given during registration trials on a population basis (108,109). Because visual gains across

multiple DME trials have been positively correlated with the number of injections, especially in the first year of treatment, overall consistent anti-VEGF dosing until maximal visual and anatomic improvement have been achieved in the setting of DME management is generally recommended.

In the setting of PDR, challenges with patient compliance are especially common. In the prospective DRCR.Network Protocol S, just 66% of living patients completed the 5-year endpoint (101). In most real-world clinical settings, noncompliance can be even more dramatic, with one analysis of more than 2,000 PDR patients followed over a 4-year period reporting that approximately 25% were lost to follow-up for more than 12 months. Age, race, and regional average adjusted gross income were found to be key risk factors associated with loss to follow-up (110).

Conclusion

The core tenet of DR management is that all patients with diabetes need regular ophthalmic examinations over the long term. The primary reason for this is because patients could have substantial DR and yet remain asymptomatic. Highly effective, ocular-specific treatments are widely available and are often used even when patients have no or limited symptoms. Furthermore, accumulating data from many perspectives indicate that earlier intervention leads to better outcomes, likely with less intensive treatment. If patients receive appropriate screening and follow-up care, much of the visual impairment associated with diabetes and DR could be reduced or prevented.

Emotional Support of People with Diabetes-Related Retinopathy

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Emotional support can be defined as the expression of empathy and understanding toward an individual living with a problem. For people living with diabetes, the provision of emotional support may allow them to communicate their health-related fears and anxieties, provide positive feedback from friends and family, and help to sustain their self-care abilities.

Diabetes requires lifelong self-care and discipline, and many people with diabetes self-manage the disease in the absence of any day-to-day positive feedback. However, emotional support and encouragement from health care providers and others is essential to strengthening patients' motivation to perform routine self-care tasks and thereby improving their self-management of diabetes (111).

Research has consistently documented the beneficial effects of social support and supportive relationships on physical and mental well-being, particularly for people living with diabetes (112,113). This chapter provides primary care providers with practical tips for empowering their patients with diabetes by addressing their fears and discussing treatments options with them in a respectful and meaningful manner.

A 3D View: Distress, Depression, and Diabetes

Self-care is the cornerstone of diabetes management. Living with diabetes means managing and coping with the condition every hour of every day. This constant effort can be exhausting and stressful for patients and often leaves them feeling isolated and alone. Thus, it is not surprising that people living with diabetes have a higher risk of developing emotional problems than the general population (114). Despite advances in diabetes care, a significant proportion of people with diabetes still experience diabetes-related distress (44.6%) or clinical depression (13.8%) (115). Distress and depression in people with diabetes can lead to worsening of metabolic control and a higher rate of complications, which may in turn lead to end-organ damage and possibly death. Put simply,

diabetes-related distress and depression can limit a person's functional ability and coping mechanisms and thereby have a negative impact on diabetes self-care.

Receiving a diagnosis of diabetes-related retinopathy (DR) can be the source of significant additional emotional stress for people with diabetes, raising concerns about numerous issues, including:

- **Potential loss of eyesight.** A new diagnosis of DR can be especially distressing because it raises fears about potentially losing vision or going completely blind. This anxiety is heightened by the fact that individuals living for many years with diabetes are 25 times more likely to experience visual impairment than those without diabetes (116). People who have had diabetes for some time without retinopathy may view this new diagnosis as a setback in their efforts to manage diabetes. Patients' distress may be further intensified by a lack of relevant information about appropriate care of DR and its prognosis. Social media posts, blogs, and other unreliable information about DR and its complications on the Internet may further exacerbate patients' anxiety and distress.
- **Potential negative effects on quality of life.** For most of us, the world is what we see through our eyes. When confronted with the possibility of vision loss, patients worry about how it could affect their daily life. Patients express fears about losing their ability to work and thereby maintain their standard of living, ensure their financial security, and support their family. They also worry about the costs of care, rising insurance premiums, and higher copayments that could come with needed specialty care.
- **Loss of independence.** For many people, the prospect of vision loss raises concerns about becoming dependent on friends and family for daily tasks they have thus far routinely handled for themselves. Loss of vision may mean having to give up driving, reading, playing sports, or other activities.

It has been well documented that the psychological well-being of patients plays a pivotal role in day-to-day self-management of diabetes (112,113).

As physicians, it is our job to acknowledge patients concerns regarding DR and to help them control risk factors to ensure the best possible visual outcome. Fortunately, as discussed in the previous chapter of this compendium, the medical management of DR has become easier, with improvements in both systemic and intraocular medications. Coupled with advancements in insulin delivery and glucose monitoring, these improvements now allow us to arrest and often reverse the stages of DR that, if left untreated, can lead to visual loss. However, when discussing these treatment modalities with patients, it is important to deliver this care in a supportive and understanding manner; often, it is not what is said, but rather how it is said that will be remembered.

Throughout this compendium, we have provided information that should ease some common concerns and fears related to the development and management of DR. Here, we wish to stress that, aside from preventing vision loss, we believe the goal from an ophthalmologic point of view should be to help patients improve their self-management skills and reduce the diabetes-related distress that so often hinders the lives of people with diabetes.

Sticks and Stones: The Language of Diabetes

A familiar childhood saying teaches that "sticks and stones will break my bones but words will never hurt me." Sadly, though, words do hurt, and the language we choose to use with patients can often reflect our unspoken opinions. When talking to patients not only about DR and other complications, but also about diabetes in general, it is important to use language that does not judge, but rather informs (117). Try to avoid language that implies a moral judgment about behaviors and blame. Try to respect and accept that patients have the right to make choices, and use language that reflects your understanding that diabetes may not always take priority in a person's life and that patients have accepted responsibility for their condition. Having diabetes is frustrating, challenging, and distressing for many people. When we focus on what is perceived as patients' "nonadherent" behavior, we can dismiss the efforts patients are making. Remember that wellness and health involve more than just gaining "control" or achieving a number on a laboratory test result. We should enable and educate our patients using appropriate and encouraging language (118).

The Most Powerful Drug Used by Mankind

It can be argued that the role of physicians is evolving toward patients being at the center of care and physicians becoming peripheral health advisors. Physicians empower their patients to use available resources, wanting what is best and practicing under the guiding principle to "first, do no harm." Physicians recommend tests or treatments when their benefits outweigh their potential harms. What is often unrecognized and unintentional, however, is that the way these recommendations are delivered can cause harm. Patients will draw meaning not only from the words used, but also from the subtle nonverbal cues, tone, and demeanor used for delivery (119).

The English writer Rudyard Kipling once said, "Words are, of course, the most powerful drug used by mankind." Words can shape how people think and feel about themselves as well as their medical conditions. As physicians, we use words to influence patients to do or feel things that are not normal for them—just as

medications would do. Language can empower people when used in a positive way. Words can link people together, spread knowledge, and improve self-image. However, it is important to realize that language can also be used to disempower people by degrading or harming their self-image. Words can completely wipe out a part of someone's identity and can leave a negative impression, causing their emotions to deflate. Language cannot be separated from thought or experience.

Empowering language should be used to educate and motivate people with diabetes. Careful use of language applies equally to the conduct of health services, health professionals, family, friends, and colleagues of people with diabetes, and the media. When people use language to shame and judge others, it can contribute to diabetes distress and ultimately slow progress and hinder diabetes outcomes. Furthermore, people with diabetes may do themselves a disservice if they also use negative language. There are effective ways of communicating about diabetes. When discussing a medical condition such as diabetes we, as physicians, should use language that encourages positive interactions and positive outcomes (120).

To provide one important example, the word "diabetic" is often used as an adjective or as a noun. When used as an adjective (e.g., "diabetic foot," "diabetic eye," and "diabetic person"), the word places focus on the physiology or pathophysiology. It is better, when possible, to put the person first. Avoid using a disease to describe a person, and avoid describing people as a disease. Suggested replacement language would include "foot ulcer," "infection of the foot," "diabetes-related retinopathy," and "person with diabetes." When "diabetic" is used as a noun, as in, "Are you a diabetic?" this usage labels a person as a disease. There is much more to a person than his or her diabetes. When in doubt, remember that person-first language puts the person first (117), so call people with diabetes by their name. Using mindful language is a simple shift that can have a powerful effect in reducing stigma and negativity.

As health care professionals, we should work toward person-centered care that is based on respectful, inclusive, and empowering interactions (48). We have an opportunity to respect the language used when counseling our patients and should be selecting strength-based, collaborative, and person-centered messages that encourage people to learn about and take action to manage complex diseases.

An Emotionally Supportive Approach to DR Management

Diabetes-related visual loss is a fear that nearly all people with diabetes experience at one time or another. When faced with the thought of blindness, individuals often focus on what they stand to lose along with their vision. Patients often express concern over the potential loss of their employment, independence, and privacy, along with potential strains on relationships with friends and family. These anxieties are normal and to be expected.

As care providers, it is important for us to acknowledge our patients' fears; it is also our responsibility to help our patients move beyond their fears and reclaim a positive outlook about their vision and diabetes management. Patients find it reassuring to hear from their primary care providers that most people with DR are able to keep most of their vision with proper treatment, although they may need ongoing care. It is also important to help patients recognize that visual impairment does not mean they will be unable to manage their diabetes. Patients with diabetes and visual impairment can learn new skill sets that allow them to live independently and remain productive.

Sadly, it is concern about and fear of going blind that will often lead patients to miss appointments and delay care, which can lead to worsening of their DR and vision. It is currently recommended that adult patients with type 1 diabetes undergo an eye exam 5 years after diagnosis, and adults with type 2 diabetes should have an eye exam at the time of their diagnosis. Subsequent exams should occur every 1–2 years if no signs of DR are detected; more frequent examinations will be required if there is evidence of DR (121). Unfortunately, although 90% of diabetes-related visual loss can be avoided with appropriate treatment (122), less than two-thirds of patients in the United States are receiving appropriate screening (123). By educating our patients about the importance of eye screenings and addressing their fears, we have the ability to prevent visual loss from diabetes.

Eye Exams, Timing, and Experience

As covered elsewhere in this compendium, eye examinations are recommended for patients with diabetes, as these patients can remain asymptomatic even in advanced stages of DR. There are several components to an eye exam that is performed by an ophthalmologist (medical doctor) or optometrist, and patients should be told what to expect. The typical eye examination begins with an initial screening during which a technician may take a complete medical history, including a complete list of the patient's medications and allergies. Both near and distance vision is then checked, with and without eyeglasses. After a careful assessment of pupillary reactions, eye drops are placed in each eye to dilate the iris and check the intraocular pressure. Dilation will typically take about 15–20 minutes. Once the eyes are dilated, the doctor will examine them using a microscope called a slit lamp. Further examination

of the retina may be done with a light source worn on the head, called an indirect ophthalmoscope. Both of these devices allow a view of the ocular structures, including the retina. The light from each instrument may appear very intense but will not injure the eyes. The doctor may also decide to take various photographs of the back portion of the eyes. This may or may not include an injection of a dye to better visualize the retinal vessels and ocular circulation.

Images of the retina are often displayed on a monitor to help the doctor explain the ocular findings. This is meant as a tool to help patients understand their diagnosis and not to criticize or frighten patients. If DR has been detected and requires treatment, it may come in the form of an intravitreal injection, laser treatment, or intraocular surgery. The importance of maintaining glycemic control in the target range, coupled with controlling blood pressure and lipid levels and avoiding tobacco, should also be emphasized.

The Reversal of Retinopathy: Setting Expectations

As discussed in other chapters of this compendium, the past decade has seen a dramatic shift in the management of DR. With appropriate care, we are now able to stabilize retinopathy, and ongoing treatment will often lead to improvement in vision (95). The wonderful aspect about treating conditions that can affect vision is that the eye is an organ that is easily accessed. Although the thought of placing medications into the eye can be frightening at first for patients, the reality is that, by treating the eye locally, we can minimize complications that may occur if the medication were given systemically.

Primary care providers (PCPs) have the ability to help set their patients expectations regarding these therapies, and these discussions should focus on hope, rather than fear and punishment. Too often, we tell our patients, "If you don't do this, you will have to do that." "If you don't control your blood sugar, you will have to go on insulin. You don't want a shot, do you?" In using this communication style, we create a relationship through which our patients come to believe that they have failed and may view the necessary treatment as a form of punishment. However, we know that diabetes progresses toward the failure of pancreatic β-cells to produce enough insulin (124). This happens early for people with type 1 diabetes and later for those with type 2 diabetes. We should express to our patients that it is this known progression of diabetes—not their personal failure—that leads to the need to take medications to remain healthy. By presenting a positive outlook on how we are able to treat the damage that diabetes causes, and carefully preparing patients for their eye exams and possible treatments, we have the ability to dramatically reduce the number of patients who lose their sight from DR.

Cross My Heart and Hope to Die . . . (Well, You Know the Rest): What to Expect from Intraocular Injection

As previously mentioned, the eye, unlike most organs in the body, is conveniently located where it can be accessed easily. Thus, ophthalmologists can safely inject medications into the eye that will have a targeted and local effect, while avoiding potential complications that could occur if the same medications were delivered systemically. In the past decade, intraocular injections of various medications have become recognized as safe and effective treatments for many ocular diseases, including DR. By reducing patients' anxiety and increasing their knowledge about a recommended procedure, PCPs can help to reduce patients' emotional and physical discomfort with intravitreal injections. Eye care specialists can also do their part. For example, Chen et al. (125) reported that diversion methods such as playing classical music before and during intravitreal injections significantly decreased patients' anxiety.

Explain to patients that, although there are multiple ways to give an injection, the basic principles are as follows:

- The patient is placed in a comfortable supine position with the head supported.
- Numbing drops or a numbing injection will be placed on the eye.
- Topical povidone-iodine (Betadine) drops will be instilled on the eye.
- A small device may be used to help keep the eyelid open and away from the site of injection.
- The patient will then be asked to look in a given direction, often away from the physician.
- Medicine will then be injected into the eye with a small needle. Patients may experience a pressure sensation, but typically not much pain.
- Afterward, the eye may be rinsed with a sterile eyewash.

The procedure is performed in the physician's office and takes less than 15 minutes. Injections may need to be repeated as often as monthly until DR stabilizes.

General Emotional Support and Information for Patients with Diabetes

Patients living with diabetes should be well educated about the disease, its management, and its consequences. Having a strong knowledge base regarding disease pathophysiology, dietary and lifestyle modifications, treatment regimens, and warning signs of possible complications is prudent for patients and their close family and friends. Patients should also have easy access to information about new treatments and technologies.

The Internet can be a useful resource; however, patients should be educated about reliable websites and information

sources and cautioned about unfiltered and unsubstantiated online perspectives on diabetes, which may provide disinformation and cause additional anxiety and stress.

Following are some trusted information resources.

- American Academy of Ophthalmology's Preferred Practice Pattern for DR. Available from www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp-updated-2017
- American Optometric Association's Evidence-Based Clinical Practice Guideline on Eye Care of the Patient with Diabetes Mellitus. Available from aoa.uberflip.com/i/374890-evidence-based-clinical-practice-guideline-diabetes-mellitus
- American Diabetes Association. Retinopathy: A Position Statement by the American Diabetes Association. Available from care.diabetesjournals.org/content/40/3/412
- American Diabetes Association. *Standards of Medical Care in Diabetes—2019*. Section 11, Microvascular Complications and Foot Care. Available from www.care.diabetesjournals.org/content/42/Supplement_1/S124
- American Association of Diabetes Educators; AADE7 Self-Care Behaviors for Managing Diabetes Effectively. Available from www.diabeteseducator.org/living-with-diabetes/aade7-self-care-behaviors

Patients are also likely to benefit from being involved in a support group. Online support groups through social networking sites provide easy access for patients to share their experiences and learn from the experiences of others. However, patients should be cautioned that information on these platforms is unedited and may not be medically sound. They should be encouraged to confer with their doctors if questions arise. Nonetheless, patients may find solace in the fact that they are not alone and get positive feedback from others in similar situations.

Support for Visual Impairment and Low Vision

"Visual impairment" refers to any reduction in visual acuity that cannot be corrected. In the United States, "legal blindness" is defined as best-corrected vision worse than 20/200 in the best eye or 20 degrees or less of visual field remaining. Fortunately, very few individuals are without sight; even when classified as "blind," most individuals have various levels of vision. With training and the use of low-vision aids, individuals with visual impairment can improve their function and quality of life.

Visual loss and impairment are rare in the early stage of DR, and thus no visual aids or assistance will be needed for patients at this point. As DR worsens, patients may experience visual loss from cataracts, macular edema, macular ischemia, vitreous hemorrhage, tractional retinal detachment, neovascular glaucoma, and ischemic optic neuropathy. With early identification and treatment, many of these blinding complications can be prevented, treated, or reversed. Despite our best efforts, however, some patients may still lose vision and go blind, and there is no such thing as being prepared for this turn of events.

It is important to remember that, regardless of the stage of DR, individuals with diabetes and eye complications should continue to control their risk factors to help preserve their remaining vision and minimize other diabetes-related complications. Fortunately, professional support is available and far more accessible than most people realize. There are adaptive techniques and remarkable, ever-advancing technologies and products to help patients with visual loss continue to maintain visual independence.

People with diabetes have specific visual needs related to their diabetes self-care. These include being able to test their blood glucose, administer appropriate oral medication and insulin doses, read food labels and medicine bottles, perform foot examinations, and treat any wounds or sores. The use of visual aids may allow patients with visual impairment to maximize their remaining vision and live independently while managing their diabetes. Although it is always best to seek the consultation of an eye care professional to determine optimal low-vision tools for a given patient's level of vision and task requirements, following are several simple options that can help patients maximize their vision.

- **Good lighting.** Adequate light can improve contrast and definition in some situations. Often, directing light onto a task will improve the image that is being viewed. Remember, though, that too much light can cause glare and often wash out an image and worsen eyesight. When evaluating a patient's environment, pay attention to the availability of directional lighting for near tasks and lights in dark areas where falls are most likely to occur. Contrast enhancement with the use of filters may help many patients with diabetes who experience color vision loss along the yellow-blue axis.
- **Magnification.** Whereas light and filters can improve contrast, it is often important to increase the size of the image that is being viewed. Reading books, newspapers, mail, or food or medicine labels can be made easier with the use of simple reading eyeglasses, a lighted, handheld magnifier, large-print reading materials, e-readers or computer magnification programs, and closed-circuit television systems.
- **Smart devices.** We often think of phones or watches as smart devices, but for people with diabetes and low vision, this can also include smart insulin pens or other insulin delivery devices, as well as smart glucose meters. Many of these devices are Bluetooth compatible and operate via voice commands.

Following are some trusted resources for additional information about visual impairment support.

- American Academy of Ophthalmology's Initiative in Vision rehabilitation. Available from www.aao.org/low-vision-and-vision-rehab
- American Optometric Association's Care of the Patient with Visual Impairment (Low Vision Rehabilitation). Available from www.aoa.org/documents/optometrists/CPG-14.pdf
- American Association of Diabetes Educators' Diabetes Advanced Network Access, a health care technology resource for diabetes educators. Available from www.danatech.org

Conclusion

DR can be a source of significant anxiety and stress for people with diabetes. This can limit patients' self-care abilities and even prevent some from seeking timely care. PCPs are in a position to identify and address patients' concerns about retinopathy. Providing emotional support begins with the recognition that such support is needed. Patients should be encouraged to voice any concerns and given access to educational information and support. With modern treatment regimens and timely follow-up with a retinal specialist, most patients with DR can expect to keep their vision.

Summary and Conclusion

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The worldwide diabetes epidemic has created an unsustainable financial and personal crisis for health care systems and for patients and their families. At the same time, the ability of patients to maintain useful vision has never been greater. Screening of people who are at risk and timely institution of treatment, combined with coordination of systematic and ophthalmic care, provides the best outlook for people with diabetes.

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