

DIABETES INSIGHTS & OUTCOMES

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DIABETIC RETINOPATHY

Current Approaches to Screening and Treatment

Blindness is the diabetes complication most feared by patients, and with good reason. Up to 30 percent of people with type 2 diabetes have retinopathy at diagnosis, and more than 60 percent develop it within 20 years. Nearly everyone with type 1 diabetes shows signs of retinopathy within 20 years. Diabetic retinopathy brings with it a 25 times higher risk for blindness.

DEVELOPMENT OF RETINOPATHY

It takes about five years after the onset of hyperglycemia for retinopathy to develop. Vascular permeability is one of the earliest stages. This leads to retinal hemorrhage and, in non-proliferative diabetic retinopathy (NPDR), the accumulation of hard exudates of lipid and protein (left behind after fluid has leaked and been reabsorbed). Other features of NPDR include microaneurysms, cotton-wool spots, venous tortuosity and microvascular abnormalities. NPDR also manifests as macular edema, due to capillary leakage and accumulation of fluid in the retina. Proliferative diabetic retinopathy (PDR) develops when vascular permeability and altered blood flow cause ischemia. Ischemia in turn stimulates angiogenesis and neovascularization. The new blood vessels are fragile and hemorrhage easily, which can impair vision. Retinal detachment can also develop, causing scarring and blindness.

It's crucial to identify retinopathy early, while the disease is most treatable. Because PDR and macular edema can be asymptomatic, regular screening is important. The 2008 American Diabetes Association Standards of Medical Care in Diabetes include the following:

SCREENING

- Type 1 diabetes patients should have an initial dilated and comprehensive eye exam within five years of diagnosis, followed by annual exams.
- Type 2 diabetes patients should have an initial dilated and comprehensive eye exam shortly after diagnosis, followed by annual exams.
- More frequent exams are needed if retinopathy is progressing.
- Reducing exam frequency to every two to three years may be considered for patients with one or more normal exams.
- Women with diabetes who are pregnant or planning to become

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Intensive Insulin Therapy and Hypertension

Hyperglycemia is a risk factor for hypertension in type 1 diabetes, according to a report in the *Archives of Internal Medicine* (September 22, 2008).

In a long-term observational study, researchers followed 1,441 patients with type 1 diabetes for a median of 15.8 years. The patients had originally participated in the multicenter Diabetes Control and Complications Trial (DCCT), which took place from 1983 to 1993.

In the DCCT, patients were randomized to conventional insulin therapy or intensive therapy (three or more insulin shots daily or use of an insulin pump). In the follow-up study, researchers continued to observe the DCCT patients through 2005. During that time, 630 patients developed hypertension. However, despite some weight gain, patients who had been assigned to intensive therapy during the DCCT had a 24 percent lower risk for hypertension. A higher hemoglobin A1c at baseline or during follow-up was also associated with increased risk.

According to the researchers, hyperglycemia has well-known effects on the vascular wall, and the study identified “long-term prevention of hypertension as an additional benefit of intensive insulin therapy.”

PATIENT EDUCATION

A1c vs. Estimated Average Glucose

Estimated average glucose, or eAG, is a new term you can expect to run into—and that’s a good thing. It can help you better educate and talk about glycemic control with your patients.

UNDERSTANDING eAG

The recent A1c-Derived Average Glucose (ADAG) study published in *Diabetes Care* affirmed that a linear relationship exists between A1c and average blood glucose levels. This linear relationship is described by a formula, $28.7 \times A1c - 46.7 = eAG$.

The ADAG study involved 507 subjects with and without diabetes at 10 international sites. It involved the collection of about 2,700 glucose values from each participant over three months. A1c measurements were then compared to average glucose levels. The two values were highly correlated. The linear regression equations were not affected by age, sex, diabetes type, race/ethnicity, or smoking status.

HOW eAG CAN HELP

Although we assess glycemic control by measuring hemoglobin A1c, this value is not an easy concept to explain

to patients, who manage their diabetes on a day-to-day basis using blood glucose levels. It’s difficult for patients to intuitively relate an A1c percentage to glucose measurements. The eAG, however, can help patients understand the link between their day-to-day glucose readings and their long-term glycemic control. The elucidation of the linear relationship between A1c and average glucose levels makes it possible to report A1c results to patients using the same units they see when they check their blood glucose at home or have a lab test for glucose. This means you can both focus on a single set of values for both daily and long-term glycemic control.

Use of the eAG is being promoted by the American Diabetes Association, European Association for the Study of Diabetes, and International Diabetes Federation. Although A1c remains an invaluable tool for setting treatment goals and predicting risk in patients with diabetes, the eAG can simplify discussions of glycemic control between you and your patients with diabetes.

For an online calculator that translates A1c to eAG, go to <http://professional.diabetes.org/GlucoseCalculator.aspx>.



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American Dental Association

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The Link Between Periodontal Disease and Diabetes

Periodontal disease, once thought to be confined to the mouth, is now understood to have systemic health effects that increase the risk for myocardial infarction and stroke. Diabetes and periodontal disease interact in a particularly vicious cycle: Diabetes makes it easier for periodontal disease to develop, and, once established, periodontitis worsens glycemic control. Periodontal disease also significantly increases the risk for diabetes complications, including cardiovascular, cerebrovascular, and peripheral vascular events and nephropathy.

BEYOND THE MOUTH

Periodontal disease is more prevalent and severe in diabetes patients because chronic hyperglycemia leads to:

- **Increased inflammation.** This is triggered by the formation of glycated proteins and lipids and by an exaggerated response of macrophages and monocytes to bacterial antigens. The result is higher levels of proinflammatory cytokines, including within the gingival crevicular fluid adjacent to teeth.
- **Impaired immunity, including impaired phagocytosis, chemotaxis, and neutrophil adhesion.** This makes it easier for bacteria to thrive in gum pockets and destroy periodontal tissue.

In turn, periodontal disease worsens diabetes. In fact, diabetes patients with periodontal disease have a six times higher risk for worsening glycemic control. This is primarily due to the systemic inflammatory response to the bacteria and bacterial products released as periodontal tissue breaks down. Inflammatory and thrombotic mediators worsen insulin resistance.

OPTIMAL CARE

Treatment of periodontal disease in diabetes patients has been shown to reduce serum inflammatory markers and lower hemoglobin A1c. To improve patients’ glycemic control and reduce the risks associated with periodontal disease, consider taking the following steps:

- Ask patients about their oral health and whether they’ve noticed any signs of infection, such as bad breath or a bad taste in the mouth.
- Ask when they had their last dental exam. For patients without a dental provider, make a referral for preventive care.
- Perform an oral examination.
- Encourage patients to practice good dental hygiene and see their dentist at least every six months for preventive care.
- Discuss the need to seek care promptly for swollen or bleeding gums, pain or soreness, loose teeth, mouth sores, or other signs of infection.



Diabetic Retinopathy: Current Approaches to Screening and Treatment

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pregnant should be counseled about the risk for the development and/or progression of diabetic retinopathy and have a comprehensive eye exam in the first trimester, with close follow-up throughout pregnancy and for one year postpartum.

TREATMENT

- Patients with macular edema, severe NPDR, or PDR should be referred to an ophthalmologist experienced in treating diabetic retinopathy.
- Laser photocoagulation therapy is indicated for clinically significant macular edema, high-risk PDR, and some cases of severe NPDR. Although surgery doesn't reverse existing diminished acuity, it reduces the risk for further visual loss.
- Aspirin therapy for cardioprotection doesn't add to retinal hemorrhage risk and isn't contraindicated in retinopathy.

Several drugs that target the biochemical pathways by which hyperglycemia causes microvascular damage are under investigation as potential retinopathy treatments. Although promising, much additional research is needed.



PREVENTION

To lower the risk for retinopathy and slow the progression of existing disease, management goals should include avoiding smoking, managing dyslipidemia, and controlling hyperglycemia and blood pressure. An Australian study (R.J. Tapp et al., *Diabetes Care*, 2003) found that beginning four years after diagnosis, hemoglobin A1c higher than

7.5 percent and systolic blood pressure higher than 132 mm Hg were associated with increases in the prevalence of retinopathy. Conversely, the Diabetes Control and Complication Trial found that intensive insulin therapy reduced retinopathy risk by 76 percent (in type 1 diabetes without retinopathy at the start of the study) and slowed existing disease progression by 54 percent.

Managing risk factors for retinopathy takes effort. It should be easier to ensure that patients receive screenings. A study at the University Medical Center at Stony Brook found that about two-thirds of 2,308 patients interviewed did not have an eye exam, and about one-third had received an eye exam that didn't include dilation. We can help diabetes patients keep their vision by educating them about eye disease and making timely referrals for dilated and comprehensive eye exams.