

Treat early, treat often

Protect your health and your future by starting blood glucose-lowering medications as soon as you're diagnosed with type 2 diabetes.

BY Hope S. Warshaw, R.D., CDE



It's human nature to delay unwanted tasks—especially when they involve pricey prescription drugs, syringes, and finger pricks. But when people diagnosed with type 2 diabetes put off taking blood glucose-lowering medications, it's a prescription for trouble.

"We now know that type 2 is a progressive disease that requires serious attention from day one," says Virginia Valentine, R.N., CDE, PWD type 2, a nurse specialist and co-owner of Diabetes Network, Inc., in Albuquerque, New Mexico. Mounting evidence shows that early, aggressive management of blood glucose can make type 2 easier to care for and prevent problems down the road.

Too often, however, we're slow to act, particularly when it comes to adding and changing medications.

Delay tactics

The typical wait-and-see approach to treating type 2 can lead to years of living with blood glucose levels that are too high. Both the person with diabetes (PWD) and the health care provider often contribute to the treatment inertia, Valentine says.

She and other providers commonly hear PWDs give misguided reasons for avoiding medications, such as: "If I'm not on medications, then it must not be the serious kind of diabetes," "Metformin will damage my kidneys," and "Insulin will cause me to lose a

foot." There are also valid concerns: drug costs, weight gain, and fear of low blood glucose (hypoglycemia) with some medications.

As PWDs plead for one more chance to lose weight or get more exercise, providers hold off prescribing blood glucose-lowering medications. Blood glucose remains out of control for too long, and organs and tissues from head to toe are damaged.

"It's not the insulin or side effects of oral medicines that cause damage to your body's organs," says Claudia Shwide-Slavin, R.D., CDE, a dietitian and diabetes educator in New York City. "It's the out-of-control blood glucose levels for years at a stretch."

44 percent of adults with diabetes miss the A1C target of 7 percent or less.

—*Diabetes Care*, 2008

Weight loss matters

The treatment for type 2 used to focus on lifestyle changes in eating, regular exercise, and weight loss. But this approach provides inadequate control as diabetes advances.

In the years before type 2 is diagnosed, blood glucose becomes elevated and the body is unable to make good use of its own insulin (this effect is called insulin resistance). The body churns out more insulin in response. Eventually, the insulin-producing beta cells in the pancreas dwindle. By the time most people are diagnosed with diabetes, they have lost 50–80 percent of their beta cells.

Less and less insulin and continued insulin resistance lead to ever-higher

blood glucose levels. In addition, several other damaging health problems, including high blood pressure and abnormal blood lipids (such as cholesterol), are associated with insulin resistance.

There's no doubt that weight loss improves insulin sensitivity. "Losing even 10–20 pounds with a healthy eating and physical activity plan can improve insulin resistance—the centerpiece of the type 2 storm—and results in lower blood glucose, lower blood pressure, and improved blood lipids," says Shwide-Slavin. But for many people, weight loss doesn't happen, and diabetes marches on.

Many factors cause weight loss efforts to fizzle. Our food choices are often high-calorie and nutrient-poor. And insulin resistance makes losing pounds and keeping them off tougher than usual. By the time type 2 is diagnosed or PWDs take action, the high blood glucose has plagued them for years. At this point, weight loss alone is unlikely to improve blood glucose numbers.

Starting meds earlier

The push is on to treat type 2 diabetes aggressively from day one. The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) now recommend that adults diagnosed with type 2 immediately start the medicine metformin, which combats insulin resistance. The goal is to stabilize the beta cells and keep them alive longer to slow the progression of type 2. Mounting evidence shows that aggressive lowering of blood glucose in newly diagnosed diabetes, especially with the use of insulin, can slow the decline of beta cells.

Another reason to get an early start? Research shows that people newly diagnosed with diabetes who target tight control early in the diagnosis can more easily control their blood glucose with less medication for a longer time. People who have years of inadequately controlled blood glucose have more difficulty gaining control and use more medicines.

Multiple medications

Eventually, blood glucose control may need a boost from additional medications. The best mix of blood glucose-lowering meds for you depends on several factors. For starters: your blood glucose levels, your A1C, and how much the medicine is likely to lower blood glucose. Next: your tolerance for the medicine, other health problems, and medical concerns affecting whether you can take

Goals for control: ABCs

Diabetes control for type 1 and type 2 involves three clear goals: managing blood glucose, blood pressure, and blood lipids (cholesterol) to prevent or delay damage to your heart and blood vessels, eyes, nerves, and kidneys. You will likely require medicine, and often more than one type, to achieve your targets.

A IS FOR ...	B IS FOR ...	C IS FOR ...
<p>A1C (blood glucose) <7 percent</p> <p>Blood glucose after fasting and before meals: 70–130 mg/dl</p> <p>Blood glucose 1–2 hours after starting a meal: <180 mg/dl</p>	<p>Blood pressure <130/80 mmHg</p> <p>People without diabetes are diagnosed with hypertension or high blood pressure if >140/80 mmHg</p>	<p>Cholesterol (blood lipids)</p> <p>Total cholesterol: <200 mg/dl</p> <p>LDL (bad) cholesterol: <100 mg/dl (with heart disease: <70 mg/dl)</p> <p>HDL (good) cholesterol: Men: >40 mg/dl Women: >50 mg/dl</p> <p>Triglycerides: <150 mg/dl</p>

Source: American Diabetes Association's 2009 Clinical Practice Recommendations.

If your A1C tops the 7 percent mark, talk to your health care provider about stepping up your therapy to regain control.

certain medicines. Make sure your provider considers whether your schedule fits with the desired regimen and that you can handle the drug costs.

There's no one right answer to which medicines should be prescribed and when. Ditto for when to raise the dose or add a new drug as blood glucose creeps up and insulin production declines. The ADA and EASD suggest keeping your eye on the A1C bull's-eye of 7 percent or less. Work with your provider to increase or add medicines as quickly as possible to hit your goal. For example, the process of starting metformin to reaching the maximum dose should occur within two months.

"Way too often people and their providers wait too long to start, increase, or add medicines to the mix," Valentine says. Contact your provider to get the necessary changes made between office visits, if necessary.

Beginning insulin

Many people who have had type 2 diabetes for 10 years or longer do not make enough of their own insulin to satisfy the body's needs. Insulin is the oldest and most widely used blood glucose-lowering medicine. It's very effective, and there's no maximum dose. June Johnson, BS, PharmD, BC-ADM, associate professor of pharmacy practice at Drake University and a researcher, tells her patients: "If you live long enough with type 2, you will likely need to take insulin, because your beta cells simply poop out over time." The infrequently used c-peptide test can reveal how much beta cell function remains. "If it's time for you to start taking insulin, don't delay," Valentine says. "Your beta cells have failed. You haven't."

Unfortunately, insulin has been mistakenly used as the last-resort treatment. That's in part because it must be injected, it can cause hypoglycemia, and it may cause weight gain. "Insulin carries an

outdated stigma that you must have a 'bad case' of diabetes if you need it," says Richard Ruth, PWD type 2, a psychologist in Arlington, Virginia. Richard, 58, began taking insulin three years ago. He started with long-acting insulin before bed, and after several months he and his provider decided to add rapid-acting insulin before each meal.

Other helpful medications

Insulin is not the only blood glucose-lowering medication. "The ADA and EASD guidelines focus too much on the dwindling supply of

insulin and insulin resistance and not enough on another hormone in diminishing supply: incretin," says Davida Kruger, M.S.N., APN-BC, BC-ADM, a nurse practitioner at Henry Ford Health System in Detroit. Incretins enhance the release of insulin after eating, slowing stomach-emptying and balancing postmeal blood glucose peaks.



Hormones and blood glucose

Several hormones affect blood glucose levels:

- ◆ **Insulin:** The beta cells in the pancreas make and release this hormone. Insulin helps the body use the glucose derived from food by allowing the glucose to move into the body's cells. **Medications:** Long-acting background (basal) and rapid-acting mealtime (bolus) insulins.
- ◆ **Glucagon:** The alpha cells in the pancreas make and release this hormone. It breaks down glucose stored in the liver and muscle and releases it to power the body. **Medication:** Glucagon is injected to treat severe hypoglycemia.
- ◆ **Amylin:** This hormone is secreted from the beta cells. It regulates the release of glucose into the bloodstream after food intake by slowing stomach-emptying and increasing the feeling of fullness. People with diabetes are amylin-deficient as well as insulin-deficient. **Medication:** Injectable pramlintide (Symlin). This drug is approved for people who take mealtime insulin.
- ◆ **Incretins:** Incretins are secreted mainly from the small intestine and enhance the release of insulin after eating. This slows stomach-emptying and delays the release of glucose into the bloodstream. Incretins also promote a feeling of fullness and prevent the release of glucagon from the pancreas, putting less glucose into circulation from the liver. **Medications:** Injectable incretin mimetics, such as the GLP-1 agonist exenatide (Byetta), and oral dipeptidyl peptidase-4 (DPP-4) inhibitors, such as sitagliptin (Januvia) and newly approved saxagliptin (Onglyza).

Less than 10 percent of adults with diabetes meet the goals for three important health markers: blood glucose, blood pressure, and blood lipids.

—*Current Diabetes Reviews*, 2007

Two classes of blood glucose-lowering medications—the oral dipeptidyl peptidase-4 (DPP-4) inhibitors, such as sitagliptin (Januvia), and the injectable incretin mimetics, such as the GLP-1 agonist exenatide (Byetta)—help control blood glucose by maximizing the dwindling supply of incretin. These drugs temper the rise of blood glucose after eating by slowing stomach-emptying and decreasing hunger between meals. The incretin mimetics can promote weight loss and may replenish some beta cells.

Balancing your approach

Once you start on blood glucose-lowering medicine, your food and activity choices are still important. “Eating healthy and being physically active always help make the job of

getting and keeping your ABCs in control easier,” Shwive-Slavin says—“perhaps with fewer pills to pop.”

Valentine reminds herself of the benefits of being aggressive with medications and lifestyle changes by keeping before-and-after pictures on her desk. She lost 100 pounds over six years and hits her ABC targets (see “Goals for Control: ABCs,” page 53) with the help of portion control, workouts, and twice-daily Byetta injections. Valentine says she’s “on a 29-year, one-rat study, and so far the rat is living well with no complications.”



Hope Warshaw, a registered dietitian and certified diabetes educator, coauthored *Real-Life Guide to Diabetes* (American Diabetes Association, 2009).

How low to go?

Last year, results from three studies looked at intensive glucose control (A1C of 6–7 percent) in certain diabetes populations and raised cautions about heart attacks and strokes. The National Institutes of Health’s ACCORD trial, the ADVANCE Trial, and the Veterans Affairs Diabetes Trial investigated tight blood glucose control in people with long-time type 2 diabetes already at high risk for heart attack and stroke.

“The results of these studies have caused me to less aggressively manage people with many years of type 2 diabetes,” says one of the principal ACCORD investigators, Faramarz Ismail-Beigi, M.D., Ph.D., professor of medicine at Case Medical Center in Cleveland. “I may strive for an A1C of 7.5 percent in these people, whereas in people with recently recognized type 2 diabetes without heart and blood vessel disease, I’ll shoot for an A1C of 6.5 percent (or lower), if it can be done safely.”

The 2009 American Diabetes Association Standards of Medical Care continues to promote the A1C goal of 7 percent or less for most people. Check with your provider for your personal target. 📌

Typical treatment route

Finding the right mix of blood glucose-lowering medications is an individual journey for each person with diabetes and his or her health care provider. Here’s a basic road map:

STEP 1

At diagnosis: Healthful eating + physical activity + metformin

STEP 2

If A1C climbs above target: Healthful eating + physical activity + metformin + long-acting (inject once or twice daily) insulin or Healthful eating + physical activity + metformin + sulfonylurea or pioglitazone (Actos) or GLP-1 agonist (Byetta, inject twice daily)

STEP 3

If A1C climbs above target: Healthful eating + physical activity + metformin + long-acting insulin (inject once or twice daily) and rapid-acting insulin (inject at meals)