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COVER

Why So Many Of Us Are Getting Diabetes

Never have doctors known so much about how to prevent or control this disease, yet the epidemic keeps on raging. How you can protect yourself

By [CHRISTINE GORMAN](#)



STEVE LISS FOR TIME

DAILY TESTS: Hillary Carroll, who has adult onset diabetes, tests her blood sugar level

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December 162

ADVERT

Sunday, Nov. 30, 2003

Hillary Carroll knew something was amiss. she had spent Memorial Day happily frolicking in her grandmother's swimming pool, but by that evening she was doubling over in pain every time she went to the bathroom. Her

mother figured it was probably an infection and the next day took Hillary, then 10, to the pediatrician. Instead of getting a prescription for an antibiotic, however, the 220-lb. youngster was immediately admitted to the hospital. Lab tests showed that she had something far more serious—Type 2 diabetes.

Hillary is not the first overweight child to learn she has this form of diabetes, a chronic metabolic disorder that used to be called adult onset but was renamed in part because so many kids Hillary's age were getting it. As doctors have repeatedly warned, the U.S. is experiencing a diabetes epidemic. Some 18 million Americans suffer from one form or another, with 1.3 million new cases diagnosed last year—up from 878,000 in 1997. And although Type 2 diabetes still tends to strike people in their fifth or sixth decade, more children are getting it, a fact of grave concern to health officials. Not only are these kids likely to face a lifetime of problems—including higher risks of blindness, heart disease and

stroke—they are also a warning sign that something in our way of life has gone terribly wrong.

And yet scientists in just the past decade have learned that the most devastating complications of diabetes—and in some cases the disease itself—are almost entirely preventable. There are better techniques for monitoring diabetes and more effective drugs for treating it, and a major study published last year shows that by making only modest changes in diet and exercise, people at high risk of Type 2 diabetes can stave off the disease for at least three years and perhaps a lot longer (more on Type 1 in just a bit).

It's a puzzle. Never have physicians known so much about Type 2 diabetes and how to control it, yet the number of cases is expected to rise at an alarming rate. Epidemiologists predict that by 2025 the incidence in the U.S. will double. Annual treatment costs are projected to rise, from \$132 billion to \$192 billion in 2020—not counting inflation. Hardest hit will be certain ethnic groups—including African Americans and Native Americans, Hispanics and Asians—that for complicated reasons are more prone to the disorder.

To the dismay of health experts, diabetes is becoming a global problem. In the next couple of decades, the prevalence of diabetes is expected to triple in Africa, the eastern Mediterranean, the Middle East and Southeast Asia, to double in the western Pacific and to nearly double in Europe. With an estimated 33 million cases, India has the most people with diabetes; China has 23 million.

Lots of doctors will tell you that the reason for the explosion is obvious: Americans are eating too much and exercising too little, and much of the world is following our bad example. There is no question that excessive weight increases your risk of becoming diabetic. But that explains only part of the problem. Diabetes has a strong genetic component, and scientists are beginning to suspect that certain evolutionary factors, as well as your mother's metabolic or nutritional status during pregnancy, may predispose you to develop diabetes. That may explain why Indians from the subcontinent often become diabetic after gaining just a few pounds and why the consequences of obesity seem far more devastating for Americans of African, as opposed to European, descent.

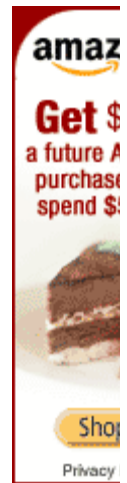
A complex picture is emerging that is changing the way we think about what was already a complex disease. It turns out that patients are not as helpless against its ravages as was once thought, especially if they are warned at the disease's very earliest stages. Changes in lifestyle and diet can, in the vast majority of cases, make a big difference. The future for anyone with diabetes has never been brighter, provided he or she has access to the right treatments. But the consequences of inaction have never been more broadly devastating. This year more than 200,000 Americans with diabetes will die from its complications.

What Is Diabetes?



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To understand the latest insights into the disease, it helps to know a little more about two key molecules—glucose and insulin—and the roles they play in the conditions doctors call Type 1 and Type 2 diabetes. We'll start with glucose, the sugar molecule that is a major source of fuel for the body. You can get your glucose levels tested at a doctor's office or at home with a device called a glucometer. What you're looking for is a reading measured in milligrams of glucose per deciliter of blood (or, on some glucometers, in millimoles per liter). Anyone whose glucose level before breakfast—the fasting level—is 126 mg/dL (7 mmol/L) or higher is considered diabetic. A normal fasting level runs anywhere from 65 mg/dL to just under 100 mg/dL (3.6 mmol/L to 5.6 mmol/L). Insulin is a hormone made by specialized cells in the pancreas, whose job is to push glucose out of the blood into various cells in the body.



Whenever the amount of glucose in the blood starts to rise, which happens just about whenever you eat, the pancreas pumps out more insulin to keep sugar levels stable.

Here's where the difference between Type 1 and Type 2 is clearest. Type 1 diabetics have high glucose levels because their pancreas can no longer make insulin. By definition, Type 1 diabetics must eventually take insulin shots to get their diabetes under control. Type 2 diabetics can still make their own insulin, but their bodies don't respond as well to it—a situation called insulin resistance.

Any scientist who can figure out why Type 2 diabetics are insulin resistant will probably be a candidate for a Nobel Prize. It's not a simple consequence of being overweight. Many obese people are not insulin resistant, and not everyone who is insulin resistant is overweight. Researchers at the Salk Institute in La Jolla, Calif., believe that at least part of the answer lies not in the pancreas but in the liver. In a study of mice published in the Nov. 13 issue of *Nature*, scientists identified a protein that tells the liver to favor the metabolism of fat over that of glucose. The result is a buildup of glucose levels in the blood, a hallmark of insulin resistance.

Evolutionary biologists suspect that a predisposition toward diabetes developed among certain ethnic groups—such as Pima Indians or Americans of African descent—as a result of repeated, perhaps even recent, bouts of starvation. Those individuals who were better able to decrease energy expenditures during a famine survived and passed on the trait to their offspring. Unfortunately, that ability seems to cause insulin resistance when food is plentiful. In other words, says Dr. Peter Nathanielsz, director of the Center for Women's Health Research at New York University, "you come out into the world—at least the developed world—and there is no shortage of cheap, fast food. Your thrifty metabolism has prepared you for the wrong future."

The Sugar Blues

What's so bad about being insulin resistant and having too much glucose in your blood? For reasons that researchers are still trying to figure out,

having diabetes greatly increases your risk of suffering a heart attack or a stroke. A man with diabetes appears to have the same risk of cardiovascular problems as a nondiabetic who has had a heart attack. A woman who develops diabetes loses the cardioprotective benefits of being female. And kids with Type 2 diabetes are more likely to develop heart disease in their 20s and 30s.

The condition also damages small blood vessels throughout the body—particularly those in the eyes and kidneys. As many as 24,000 diabetics in the U.S. become blind each year, more than 100,000 require dialysis or kidney transplantation, and 82,000 need to have a toe, foot or leg amputated. Diabetics are twice as likely as nondiabetics to suffer from depression.

It doesn't have to be this way. Back in 1993 doctors proved that Type 1 diabetics could greatly reduce their risk of complications by intensively managing their glucose levels to keep them as close to normal as possible (using a glucometer to measure the level of sugar in a pinprick of blood and an insulin shot when necessary to bring the level down). Similar results have since been seen with Type 2 diabetics.

But most Type 2 diabetics don't have to resort to insulin shots to manage their condition. Because the fundamental problem in Type 2 diabetes is insulin resistance—not the inability to produce insulin as in Type 1—other options are available. Your physician may first give you pills that can either sensitize your body to insulin's effects or help your body produce more of the hormone. But some of your best allies in this struggle are your muscles.

Building them up and using them regularly in such pursuits as walking or dancing draw more glucose out of the bloodstream and increase insulin's efficiency. It also pays to avoid easily digested foods—like chips, nondiet soda and other junk food—which require large amounts of insulin to metabolize. Finally, losing a little weight usually makes insulin's job a lot easier.

Donna Black Bradley, 52, of Los Angeles is living proof. Bradley was driving home from work one evening when she suddenly was unable to read the freeway signs. When her doctor diagnosed diabetes, she felt paralyzed. "Then I said O.K., I got something I got to do here," Bradley says. "I got to change." And change she did. The 5-ft. 7-in. mother and grandmother started eating better and working out on a treadmill several times a week. Her weight dropped from 272 lbs. to 210 lbs., and her fasting glucose fell from 300 mg/dL to 103 mg/dL. "It's amazing how your cravings diminish when you're eating the right food groups," Bradley says. Her vision problems have disappeared, and her doctor believes she will no longer need to take insulin-sensitizing drugs if she can get her weight under 200 lbs.—something she's determined to do, both for herself and for her grandson Isaiah. Says she: "I want to be around for that 2-year old."

Small Steps, Big Rewards

The more scientists learn about diabetes and the complications it causes, the more they find themselves looking at the conditions that precede it. "The big question now is, When does the diabetes clock start ticking?" says Dr. Frank Vinicor, director of the diabetes program at the Centers for Disease Control. "For eye or small-vessel disease, we think the clock starts ticking when blood sugar starts to go up. But for heart disease, we think the clock may start ticking much, much earlier, even before the first sign of blood sugar going up."

That's why researchers are focusing on a precursor condition called prediabetes, in which glucose levels are only slightly elevated but which may put at risk an additional 20 million Americans. In 2002 researchers published the results of the Diabetes Prevention Program (D.P.P.), one of the largest, most rigorous clinical trials ever conducted on the subject. More than 3,000 people from all over the U.S. participated. All were overweight, and blood tests indicated that their bodies were having trouble handling glucose, though none had yet developed diabetes. Half were from ethnic communities that are at higher risk. Participants in the D.P.P. were divided into three groups. One was given the diabetes drug metformin, one was given a dummy pill, and one was enrolled in a nutrition and exercise program with the goal for participants to lose 7% of their initial weight and to exercise 30 minutes a day, five times a week.

The D.P.P. trial was halted a full year early "because the results were just so remarkable," says Dr. David Nathan, director of the Diabetes Center at Massachusetts General Hospital in Boston, who chaired the study. During the three years of the study, nearly 30% of the placebo group developed diabetes. For the metformin group the figure was 22%. The subjects who exercised moderately and lost weight had the lowest incidence of all—just 14%. (The first two groups were given diet and exercise information but did not lose as much weight as the last group.) The study is continuing to see if lifestyle changes can prevent diabetes for life or merely delay its occurrence. At the very least, the trial proves that the point of no return is not as early or as fixed as was once feared.

Diabetes researchers have been so impressed by the D.P.P. results that many would like to lower the thresholds that determine who is prediabetic. In January the American Diabetes Association plans to officially recommend that physicians consider treating anyone with a fasting glucose of 100 mg/dL or higher, down from 110 mg/dL or higher in the previous guidelines. "If your fasting blood sugar is below 100, your chances of getting diabetes are quite low," says Dr. Robert Rizza, an endocrinologist at the Mayo Clinic in Rochester, Minn., and a vice president of the American Diabetes Association. "But if your fasting glucose is over 100, you have a 10% to 15% chance of getting diabetes in the next seven years."

You don't have to convince Tom Marinello, 51, of Carson, Calif., that prediabetes should be taken seriously. After his father-in-law died of

complications from diabetes, Marinello, unaware that he was at risk, enrolled in the Diabetes Prevention Program at the University of California, Los Angeles, hoping to help others with the disease. He was surprised to learn that he was prediabetic. By paying closer attention to what he eats and by making sure to walk nearly every day, Marinello dropped 28 lbs. from his 260-lb., 6-ft. 1-in. frame, and his fasting-glucose level is down to 110 mg/dL. "I may still be at risk, but I'm not diabetic," Marinello says. "I'm kind of proud of that."

Beyond Apples and Pears

Is it possible to turn the clock back even further to find who is at greatest risk of developing prediabetes and lower their risk of future health problems?

That turns out to be much more complicated.

Cardiologists have long known that if you carry extra weight around your waist, which they liken to being shaped like an apple, you are at greater risk of heart disease. The other configuration, being shaped like a pear, with excess weight around the hips, doesn't eliminate your risk but seems to lessen it. Over the years it has become clear that apple-shaped folks have a certain kind of metabolism: they are more likely to be resistant to insulin, have high amounts of triglycerides (one of the fatty molecules you don't want too much of in your blood) and have low levels of hdl (the "good" cholesterol). They also tend to have high blood pressure.

Coincidence? Probably not, which is why physicians have lumped all these symptoms together in one condition that they now call metabolic syndrome. They believe that anyone with metabolic syndrome is at much greater risk of developing not just heart disease but diabetes as well. They're not sure whether there is a primary trigger for metabolic syndrome—say, obesity or insulin resistance—or if several biological pathways are involved.

Whatever the case, says Dr. Scott Grundy, a leading expert on cholesterol who chaired the American Heart Association's first clinical conference on metabolic syndrome in September, "right now there's no single drug that can treat the whole metabolic syndrome." Individual symptoms like high blood pressure still have to be treated separately. But your best bet for an overall solution is to eat better, lose weight and get more exercise.

An Inflammatory Question

As central as insulin resistance has become to understanding Type 2 diabetes, scientists are starting to wonder whether another factor, the inflammatory response, may also play a key role. Inflammation is a complex biological process the immune system uses to limit the damage caused by various injuries. (Ever notice how a turned ankle swells or a sunburn feels warm to the touch? That's inflammation in action.) But when inflammation becomes chronic, it no longer limits damage. In fact, it starts to do harm to the body.

Over the past five years, researchers have shown that inflammation is at least as important as high cholesterol levels in causing heart disease. (High levels in the blood of certain molecules, such as C-reactive protein (CRP), indicate a runaway inflammatory process and are better predictors of heart attacks than cholesterol.) Could the same be true for diabetes? "In 2001, when we published our first paper on inflammation and diabetes, everybody thought we were just wrong," recalls Dr. Paul Ridker, a cardiologist at Brigham & Women's Hospital in Boston. "Now there are half a dozen studies confirming that if you measure markers of inflammation, and CRP in particular, you can do a good job of predicting who's going to get diabetes."

If these results are confirmed and inflammation turns out to be as important as insulin resistance in triggering diabetes, then it should become much easier to identify incipient problems in metabolism before they get out of control. Why? Because inflammation is much easier to measure than insulin resistance; all that is required is a single blood test. (Abnormal glucose levels only suggest the possibility of insulin resistance; they don't prove it. Insulin resistance is difficult to measure directly.) It might also mean that anti-inflammatory agents like aspirin may be particularly effective in diabetics.

An Ounce of Prevention

Advances in diabetes research over the past few years have been swift and wide ranging. Scientists are beginning to identify the genetic and environmental factors that predispose some people to insulin resistance and increase their risk of diabetes. They are looking beyond glucose levels to gauge patients' health and progress. They have identified other pathways that may play a role in triggering diabetes. Every new insight into Type 2 diabetes, from its biochemistry to its metabolic roots, makes clear that it can be avoided—and that the earlier you intervene the better.

The real question is whether we as a society are up to the challenge. "Our health-care system is currently set up to deliver care for acute disease," says Ann Albright, chief of the California Diabetes Prevention and Control Program. "It's get in, get your shot, and away you go." Diabetes, however, is a chronic disorder that demands constant attention. You have to change your eating habits and incorporate physical exercise into each day's activities. You need to monitor your glucose levels several times a day to see how well you're doing. These prevention measures pay off in the long run in fewer heart attacks, strokes, amputations and cases of blindness and kidney failure. But very few insurance programs focus on them—or pay for health professionals who can teach folks how best to incorporate them into their lives.

Comprehensive prevention programs aren't cheap, but the cost of doing nothing is far greater. "If we don't take care of this issue now, we will have huge numbers of Type 2 diabetics, and we will be paying for them with our tax dollars," says Dr. Phyllis Preciado, an internist who runs a diabetes clinic in California's farming-rich Central Valley. As the U.S. loses productive members of the work force, she notes, more people will

turn to public assistance for treatment. And the increased toll in human suffering will be staggering.

There are ways to keep costs down. It doesn't take a physician to teach a patient the principles of better nutrition or how to use a glucometer. Nurses, nutritionists, diabetes educators and other non-M.D.s can play a key role. Experts say it's important to reach the communities that are hardest hit by diabetes—American Indians, for example—all the while taking cultural differences into account. "You can't give everybody the same diet to solve the problem," says Albright, a registered dietitian. "People obviously eat the foods they've grown up with. So you have to try to help them get as much of those things that they like into their eating plan but also make the changes that will help lower the fat or moderate the carbohydrates."

Hillary Carroll and her family have taken those lessons to heart. While still in the hospital, Hillary went through a kind of diabetes boot camp in which she learned how to monitor her blood-sugar levels, change the way she eats and boost the amount of physical activity in her life. Her parents bought her a turquoise BMX bike, which she rides at least an hour every day. She has lost 24 lbs. so far, and her glucose levels have stabilized. "Before she was diagnosed, she was happy to sit here by herself, playing with her Barbies," says Tammy Carroll, Hillary's mother. "I thought she was so calm then, but now that we have her sugar under control, she's more active." Hillary, now 11, is taking charge of her life. To get control of the diabetes epidemic, the rest of us may have to do the same.

—*Reported by David Bjerklie and Alice Park/New York, Dan Cray/ Los Angeles and Laura Randall/ Cincinnati*

From the Dec. 08, 2003 issue of TIME magazine

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