

Diabetes Mellitus

What is diabetes?

*Note: This article addresses diabetes mellitus, not **diabetes insipidus**. Although the two share the same reference term "diabetes" (which means increased urine production), diabetes insipidus is much rarer and has a different underlying cause.*

Diabetes is a group of conditions linked by an inability to produce sufficient insulin and/or to respond to insulin. This causes high **blood glucose levels (hyperglycemia)** and can lead to a number of **acute** and **chronic** health problems, some of them life-threatening.

Glucose is the body's primary energy source. After a meal, carbohydrates usually are broken down into glucose and other simple sugars. This causes blood glucose levels to rise and stimulates the pancreas to release insulin into the bloodstream. Insulin is a **hormone** produced by the **beta cells** in the pancreas. It regulates the transport of glucose into most of the body's cells and works with glucagon, another pancreatic hormone, to maintain blood glucose levels within a narrow range. If someone is unable to produce enough insulin, or if the body's cells are resistant to its effects (**insulin resistance**), then less glucose is transported from the blood into cells. Blood glucose levels remain high and the body's cells "starve." This can cause both acute and chronic problems depending on the severity of the insulin deficiency.

Acute hyperglycemia can be a medical emergency. The body tries to rid the blood of excess glucose by flushing it out of the system with increased urination. This process can cause **dehydration** and upset the body's electrolyte balance as sodium and potassium are lost in the urine. With severe insulin deficiency, glucose is not available to the cells and the body may attempt to provide an alternate energy source by metabolizing fatty acids. This less efficient process leads to a buildup of **ketones** and upsets the body's **acid-base balance**, producing a state known as **ketoacidosis**. Left unchecked, acute hyperglycemia can lead to severe dehydration, loss of consciousness, and even death.

Glucose levels that rise over time and become chronically elevated may not be initially noticed. The body tries to control the amount of glucose in the blood by increasing insulin production and by eliminating glucose in the urine. Symptoms usually begin to arise when the body is no longer able to compensate for the higher levels of blood glucose. Chronic hyperglycemia can cause long-term damage to blood vessels, nerves, and organs throughout the body and can lead to other conditions such as kidney failure, loss of vision, **strokes, cardiovascular disease** and circulatory problems in the legs. Damage from hyperglycemia is cumulative and may begin before a person is aware that he or she has diabetes. The sooner that the condition is detected and treated, the better the chances of minimizing complications.

According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK, 2010 data), about 26 million people in the United States have diabetes, but as many as 7 million of them are not yet aware that diabetes is affecting their health.

Types of Diabetes

There are three main types of diabetes: type 1, type 2, and gestational diabetes. **Pancreatic disease** and/or damage can also cause diabetes if the insulin-producing **beta cells** are destroyed.

Type 1 diabetes, which used to be called insulin dependent or juvenile diabetes, makes up about 10% of the diabetes cases in the United States. Most cases of type 1 diabetes are diagnosed in those under the age of 30. Symptoms often develop abruptly and the diagnosis is often made in an emergency room setting. The affected person may be seriously ill, even comatose, with very high **glucose levels** and high **levels of ketones (ketoacidosis)**. Type 1 diabetics make very little or no insulin. Any insulin-producing beta cells they do have at the time of diagnosis are usually completely destroyed within 5 to 10 years, leaving them entirely reliant on insulin injections to live.

The exact cause of type 1 diabetes is unknown, but a family history of diabetes, **viruses** that injure the pancreas, and autoimmune processes, in which the body's own **immune system** destroys the beta cells, are all thought to play a role. Type 1 diabetics may have more severe medical complications sooner than other diabetics. About 40% of those with type 1 diabetes will develop serious kidney problems leading to kidney failure by the age of 50.

Type 2 diabetes used to be known as non-insulin dependent diabetes or adult onset diabetes. Those affected do make their own insulin, but it is either not in a sufficient amount to meet their needs or their body has become resistant to its effects. At the time of diagnosis, people with type 2 diabetes will frequently have both high glucose levels and high **insulin levels**, but they may not have any symptoms. About 90% of diabetes cases in the United States are type 2. It generally occurs later in life, in those who are obese, sedentary, and over 45 years of age.

Factors associated with diabetes include:

- Obesity
- Lack of exercise
- Family history of diabetes
- Pre-diabetes
- Ethnicity: African-American, Hispanic-American, Native American, Asian-American, Pacific Islander
- Gestational diabetes during **pregnancy** or baby weighing more than 9 pounds
- **High blood pressure**
- High **triglycerides**, high **cholesterol**, low **HDL**

Since Americans are becoming more obese and not getting enough regular exercise, the number of those diagnosed with type 2 diabetes is continuing to rise and it is developing at younger ages.

Gestational diabetes is a form of **hyperglycemia** seen in some pregnant women, usually late in their pregnancy. The cause is unknown, but it is thought that some **hormones** from the placenta increase **insulin resistance** in the mother, causing elevated blood glucose levels. Most women are **screened** for gestational diabetes between their 24th and 28th week of pregnancy. If gestational diabetes is found and not addressed, the baby is likely to be larger than normal, be born with low glucose levels, and be born prematurely. The hyperglycemia associated with gestational diabetes usually goes away after the baby's birth, but both the women diagnosed with gestational diabetes and their babies are at an increased risk of eventually developing type 2 diabetes. A woman who has gestational diabetes with one pregnancy will frequently experience it with subsequent pregnancies.

Pre-Diabetes is a term for impaired fasting glucose or impaired glucose tolerance. It is characterized by glucose levels that are higher than normal, but not high enough to be diagnostic of diabetes. Recent data suggest that at least 79 million adults in the U.S. had pre-diabetes in 2010. Usually those who have pre-diabetes do not have any symptoms but, if nothing is done to lower their glucose levels, they are at an increased risk of developing diabetes within about 10 years. Experts are recommending that everyone who has any of the risk factors for type 2 diabetes be tested for pre-diabetes.

Signs and Symptoms

The **signs** and **symptoms** of diabetes are related to high **glucose levels (hyperglycemia)**, low glucose levels (**hypoglycemia**), and complications associated with diabetes. The complications can be related to lipid production, damage to blood vessels (vascular and microvascular), organ damage - for example, kidney (diabetic nephropathy), nerve (**diabetic neuropathy**), and eye (diabetic retinopathy) damage - and/or to the slower healing associated with diabetes. Type 1 diabetics are often diagnosed with **acute** severe symptoms that require hospitalization. With pre-diabetes, early type 2 diabetes, and gestational diabetes, there usually are no symptoms.

Symptoms of type 1 and type 2 diabetes with hyperglycemia:

- Increased thirst
- Increased urination
- Increased appetite (with type 1, weight loss is also seen)
- Fatigue
- Nausea, vomiting, abdominal pain (especially in children)
- Blurred vision
- Slow-healing infections
- Numbness, tingling, and pain in the feet
- **Erectile dysfunction** in men

- Absence of menstruation in women
- Rapid breathing (acute)
- Decreased consciousness, coma (acute)

Symptoms of impending hypoglycemia:

Temporary hypoglycemia in the diabetic may be caused by the accidental injection of too much insulin, not eating enough or waiting too long to eat, exercising strenuously, or by the swings in glucose levels seen with "brittle" diabetes. Hypoglycemia needs to be addressed as soon as it is noticed as it can rapidly progress to unconsciousness. Symptoms include:

- Sudden severe hunger
- Headache
- Anxiety, confusion
- Sweating
- Trembling, weakness
- Double vision
- Convulsions
- Coma

Tests

The goals with testing are to screen for high **blood glucose levels (hyperglycemia)**, to detect and diagnose diabetes and pre-diabetes, to monitor and control glucose levels over time, and to detect and monitor complications.

Tests for screening

There are a few tests that may be used to screen for and/or diagnose diabetes and pre-diabetes. They may be used:

- As part of a regular physical
- When someone has symptoms suggesting diabetes
- When a person has a condition that is associated with diabetes
- When a person presents to the emergency room with an **acute** condition
- For pregnant women as a screen for gestational diabetes

Screening tests include:

- **Fasting glucose** (fasting blood glucose, FBG) – this test measures the level of glucose in the blood after an 8-12 hour fast.
- **A1c** (also called hemoglobin A1c or glycohemoglobin) – this test evaluates the average amount of glucose in the blood over the last 2 to 3 months and has been recommended more recently as another test to screen for diabetes. (For more on this test, see below.)
- For pregnant women, some professional organizations recommend a glucose challenge test (GCT) to screen for gestational diabetes at 24-28 weeks of **pregnancy**. This involves a fasting blood glucose followed by the woman drinking a standard glucose solution and another glucose test one hour after consuming the glucose. If results are abnormal, then a 3-hour oral glucose tolerance test (OGTT, GTT) is performed to help establish a diagnosis. However, the American Diabetes Association in 2011 adopted new guidelines that recommend the use of a 2-hour glucose tolerance test for screening and diagnosing gestational diabetes. See "Tests for diagnosis" below.
- Sometimes a random blood glucose level is used for screening when a fasting test is not possible, such as when a person is seriously ill.
- Sometimes random urine samples are tested for glucose, protein, and ketones during a physical. If glucose and/or protein or **ketones** are present on the indicator strip dipped in the urine sample, the person has a problem that needs to be addressed. This is a screening tool, but it is not **sensitive** enough for diagnosis or monitoring.

Tests for diagnosis

According to the American Diabetes Association (ADA), a fasting blood glucose, an oral glucose tolerance test, or an A1c test may be used to diagnose diabetes and pre-diabetes. Each test has advantages, disadvantages, and limitations.

- The FBG requires an 8-hour fast.
- The OGTT requires that the person have a fasting glucose test, followed by the person drinking a standard amount of glucose solution to "challenge" their system, followed by another glucose test 2 hours later.
- With the A1c, people don't have to fast for 8 hours or endure multiple blood samples being taken over several hours, but the test is not recommended for everyone. It should not be used for diabetes diagnosis in pregnant women, people who have had recent severe bleeding or blood transfusions, those with **chronic kidney** or **liver disease**, and people with blood disorders such as **iron-deficiency anemia**, **vitamin B12 anemia**, and **hemoglobin variants**. Also, only A1c tests that have been referenced to an accepted

laboratory method (standardized) should be used for diagnostic or screening purposes. Currently, point-of-care tests, such as those that may be used at a doctor's office or a patient's bedside, are too variable for use in diagnosis but can be used to monitor treatment (lifestyle and drug therapies).

If the initial result from one of the above tests is abnormal, the test should be repeated on another day to confirm a diagnosis of diabetes.

- Gestational diabetes may be diagnosed using a glucose challenge test as a screen, followed by a 3-hour OGTT using a 100-gram glucose drink if the screen is abnormal, per recommendations of the U.S. Preventive Services Task Force and the American Congress of Obstetricians and Gynecologists (ACOG). If at least two of the glucose levels at fasting, 1 hour, 2 hour, or 3 hour are above a certain level, then a diagnosis of gestational diabetes is made. The ADA, however, recommends that a 2-hour glucose tolerance test using a 75-gram glucose drink be used to screen for and diagnose gestational diabetes. Only one of the values needs to be above a cutpoint for diagnosis.
- **Diabetes autoantibodies** – this test may help distinguish between type 1 and type 2 diabetes if the diagnosis is unclear. The presence of one or more of these antibodies indicates type 1 diabetes.

Tests for monitoring

- Glucose – diabetics must monitor their own blood glucose levels, often several times a day, to determine how far above or below normal their glucose is and, based on their doctor's instructions, what modifications they should make to their medications. This is usually done by placing a drop of blood (obtained by pricking your skin with a small lancet device), onto a glucose strip and then inserting the strip into a glucose meter, a small machine that provides a digital readout of the blood glucose level.
- A1c and estimated average glucose (eAG) – this is a test and a calculation that are ordered several times a year to monitor people with type 1 or type 2 diabetes. A1c is a measure of the average amount of glucose present in the blood over the last 2 to 3 months and helps the doctor to determine how well a treatment plan is working to control the person's blood glucose levels over time.

Several other laboratory tests may be used to monitor diabetes, evaluate organ function, and detect emerging complications. These include:

- To monitor kidney function: **Microalbumin** (increased urinary albumin), **Creatinine Clearance**, **eGFR**, **CMP**, **BUN**, **Creatinine**, **Cystatin C**
- To monitor cholesterol and other lipids: **Cholesterol**, **HDL cholesterol**, **LDL cholesterol**, **Triglycerides**, **Lipid profile**
- To monitor insulin production: **Insulin**, **C-Peptide**

- Urine and/or **blood ketone** tests may be ordered to monitor people who present at the emergency room with symptoms suggesting acute hyperglycemia and to monitor those who are being treated for **ketoacidosis**. A build-up of ketones can occur whenever there is a decrease in the amount or effectiveness of insulin in the body

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