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Diabetes Mellitus

Medical Author: Ruchi Mathur, MD

Medical Editor: William C. Shiel, Jr., MD, FACP, FACR

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What is diabetes?

Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar (glucose) levels, that result from defects in insulin secretion, or action, or both. Diabetes mellitus, commonly referred to as diabetes (as it will be in this article) was first identified as a disease associated with "sweet urine," and excessive muscle loss in the ancient world. Elevated levels of blood glucose (hyperglycemia) lead to spillage of glucose into the urine, hence the term sweet urine.

Normally, blood glucose levels are tightly controlled by insulin, a hormone produced by the pancreas. Insulin lowers the blood glucose level. When the blood glucose elevates (for example, after eating food), insulin is released from the pancreas to normalize the glucose level. In patients with diabetes, the absence or insufficient production of insulin causes hyperglycemia. Diabetes is a chronic medical condition, meaning that although it can be controlled, it lasts a lifetime.

What is the impact of diabetes?

Over time, diabetes can lead to blindness, kidney failure, and nerve damage. These types of damage are the result of damage to small vessels, referred to as microvascular disease. Diabetes is also an important factor in accelerating the hardening and narrowing of the arteries (atherosclerosis), leading to strokes, coronary heart disease, and other large blood vessel diseases. This is referred to as macrovascular disease. Diabetes affects approximately 17 million people (about 8% of the population) in the United States. In addition, an estimated additional 12 million people in the United States have diabetes and don't even know it.

From an economic perspective, the total annual cost of diabetes in 1997 was estimated to be 98 billion dollars in the United States. The per capita cost resulting from diabetes in 1997 amounted to \$10,071.00; while healthcare costs for people without diabetes incurred a per capita cost of \$2,699.00. During this same year, 13.9 million days of hospital stay were attributed to diabetes, while 30.3 million physician office visits were diabetes related. Remember, these numbers reflect only the population in the United States. Globally, the statistics are staggering.

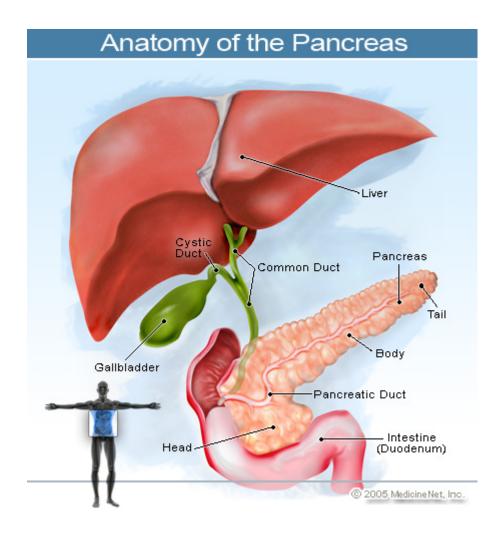
Diabetes is the third leading cause of death in the United States after heart disease and cancer.

What causes diabetes?

Insufficient production of insulin (either absolutely or relative to the body's needs), production of defective insulin (which is uncommon), or the inability of cells to use insulin properly and efficiently leads to hyperglycemia and diabetes. This latter condition affects mostly the cells of muscle and fat tissues, and results in a condition known as "insulin resistance." This is the primary problem in type 2 diabetes. The absolute lack of insulin, usually secondary to a destructive process affecting the insulin producing beta cells in the pancreas, is the main disorder in type 1 diabetes. In type 2 diabetes, there also is a steady decline of beta cells that adds to the process of elevated blood sugars. Essentially, if someone is resistant to insulin, the body can, to some degree, increase production of insulin and overcome the level of resistance. After time, if production decreases and insulin cannot be released as vigorously, hyperglycemia develops.

Glucose is a simple sugar found in food. Glucose is an essential nutrient that provides energy for the proper functioning of the body cells. Carbohydrates are broken down in the small intestine and the glucose in digested food is then absorbed by the intestinal cells into the bloodstream, and is carried by the bloodstream to all the cells in the body where it is utilized. However, glucose cannot enter the cells alone and needs insulin to aid in its transport into the cells. Without insulin, the cells become starved of glucose energy despite the presence of abundant glucose in the bloodstream. In certain types of diabetes, the cells' inability to utilize glucose gives rise to the ironic situation of "starvation in the midst of plenty". The abundant, unutilized glucose is wastefully excreted in the urine.

Insulin is a hormone that is produced by specialized cells (beta cells) of the pancreas. (The pancreas is a deep-seated organ in the abdomen located behind the stomach.) In addition to helping glucose enter the cells, insulin is also important in tightly regulating the level of glucose in the blood. After a meal, the blood glucose level rises. In response to the increased glucose level, the pancreas normally releases more insulin into the bloodstream to help glucose enter the cells and lower blood glucose levels after a meal. When the blood glucose levels are lowered, the insulin release from the pancreas is turned down. It is important to note that even in the fasting state there is a low steady release of insulin than fluctuates a bit and helps to maintain a steady blood sugar level during fasting. In normal individuals, such a regulatory system helps to keep blood glucose levels in a tightly controlled range. As outlined above, in patients with diabetes, the insulin is either absent, relatively insufficient for the body's needs, or not used properly by the body. All of these factors cause elevated levels of blood glucose (hyperglycemia).



What are the different types of diabetes?

There are two major types of diabetes, called type 1 and type 2. Type 1 diabetes was also called insulin dependent diabetes mellitus (IDDM), or juvenile onset diabetes mellitus. In type 1 diabetes, the pancreas undergoes an autoimmune attack by the body itself, and is rendered incapable of making insulin. Abnormal antibodies have been found in the majority of patients with type 1 diabetes. Antibodies are proteins in the blood that are part of the body's immune system. The patient with type 1 diabetes must rely on insulin medication for survival.

In autoimmune diseases, such as type 1 diabetes, the immune system mistakenly manufactures antibodies and inflammatory cells that are directed against and cause damage to patients' own body tissues. In persons with type 1 diabetes, the beta cells of the pancreas, which are responsible for insulin production, are attacked by the misdirected immune system. It is believed that the tendency to develop abnormal antibodies in type 1 diabetes is, in part, genetically inherited, though the details are not fully understood.

Exposure to certain viral infections (mumps and Coxsackie viruses) or other environmental toxins may serve to trigger abnormal antibody responses that cause damage to the pancreas cells where insulin is made. Some of the antibodies seen in type 1 diabetes include anti-islet cell antibodies, anti-insulin antibodies and anti-glutamic decarboxylase antibodies. These antibodies can be measured in the majority of patients, and may help determine which individuals are at risk for developing type 1 diabetes.

At present, the American Diabetes Association does not recommend general screening of the population for type 1 diabetes, though screening of high risk individuals, such as those with a first degree relative (sibling or parent) with type 1 diabetes should be encouraged. Type 1 diabetes tends to occur in young, lean individuals, usually before 30 years of age, however, older patients do present with this form of diabetes on occasion. This subgroup is referred to as latent autoimmune diabetes in adults (LADA). LADA is a slow, progressive form of type 1 diabetes. Of all the patients with diabetes, only approximately 10% of the patients have type 1 diabetes and the remaining 90% have type 2 diabetes.

Type 2 diabetes was also referred to as non-insulin dependent diabetes mellitus (NIDDM), or adult onset diabetes mellitus (AODM). In type 2 diabetes, patients can still produce insulin, but do so relatively inadequately for their body's needs, particularly in the face of insulin resistance as discussed above. In many cases this actually means the pancreas produces larger than normal quantities of insulin. A major feature of type 2 diabetes is a lack of sensitivity to insulin by the cells of the body (particularly fat and muscle cells).

In addition to the problems with an increase in insulin resistance, the release of insulin by the pancreas may also be defective and suboptimal. In fact, there is a known steady decline in beta cell production of insulin in type 2 diabetes that contributes to worsening glucose control. (This is a major factor for many patients with type 2 diabetes who ultimately require insulin therapy.) Finally, the liver in these patients continues to produce glucose through a process called gluconeogenesis despite elevated glucose levels. The control of gluconeogenesis becomes compromised.

While it is said that type 2 diabetes occurs mostly in individuals over 30 years old and the incidence increases with age, we are seeing an alarming number patients with type 2 diabetes who are barely in their teen years. In fact, for the first time in the history of humans, type 2 diabetes is now more common than type 1 diabetes in childhood. Most of these cases are a direct result of poor eating habits, higher body weight, and lack of exercise.

While there is a strong genetic component to developing this form of diabetes, there are other risk factors - the most significant of which is obesity. There is a direct relationship between the degree of obesity and the risk of developing type 2 diabetes, and this holds true in children as well as adults. It is estimated that the chance to develop diabetes doubles for every 20% increase over desirable body weight.

Regarding age, data shows that for each decade after 40 years of age regardless of weight there is an increase in incidence of diabetes. The prevalence of diabetes in persons 65 to 74 years of age is nearly 20%. Type 2 diabetes is also more common in certain ethnic groups. Compared with a 6% prevalence in Caucasians, the prevalence in African Americans and Asian Americans is estimated to be 10%, in Hispanics 15%, and in certain Native American communities 20% to 50%. Finally, diabetes occurs much more frequently in women with a prior history of diabetes that develops during pregnancy (gestational diabetes - see below).

Diabetes can occur temporarily during pregnancy. Significant hormonal changes during pregnancy can lead to blood sugar elevation in genetically predisposed individuals. Blood sugar elevation during pregnancy is called gestational diabetes. Gestational diabetes usually resolves once the baby is born. However, 25%-50% of women with gestational diabetes will eventually develop type 2 diabetes later in life, especially in those who require insulin during pregnancy and those who remain overweight after their delivery. Patients with gestational diabetes are usually asked to undergo an oral glucose tolerance test about six weeks after giving birth to determine if their diabetes has persisted beyond the pregnancy, or if any evidence (such as impaired glucose tolerance) is present that may be a clue to the patient's future risk for developing diabetes.

"Secondary" diabetes refers to elevated blood sugar levels from another medical condition. Secondary diabetes may develop when the pancreatic tissue responsible for the production of insulin is destroyed by

disease, such as chronic pancreatitis (inflammation of the pancreas by toxins like excessive alcohol), trauma, or surgical removal of the pancreas.

Diabetes can also result from other hormonal disturbances, such as excessive growth hormone production (acromegaly) and Cushing's syndrome. In acromegaly, a pituitary gland tumor at the base of the brain causes excessive production of growth hormone, leading to hyperglycemia. In Cushing's syndrome, the adrenal glands produce an excess of cortisol, which promotes blood sugar elevation.

In addition, certain medications may worsen diabetes control, or "unmask" latent diabetes. This is seen most commonly when steroid medications (such as prednisone) are taken and also with medications used in the treatment of HIV infection (AIDS).

What are diabetes symptoms?

- The early symptoms of untreated diabetes are related to elevated blood sugar levels, and loss of glucose in the urine. High amounts of glucose in the urine can cause increased urine output and lead to dehydration. Dehydration causes increased thirst and water consumption.
- The inability of insulin to perform normally has effects on protein, fat and carbohydrate metabolism. Insulin is an anabolic hormone, that is, one that encourages storage of fat and protein.
- A relative or absolute insulin deficiency eventually leads to weight loss despite an increase in appetite.
- Some untreated diabetes patients also complain of fatigue, nausea and vomiting.
- Patients with diabetes are prone to developing infections of the bladder, skin, and vaginal areas.
- Fluctuations in blood glucose levels can lead to blurred vision. Extremely elevated glucose levels can lead to lethargy and coma.

How is diabetes diagnosed?

The fasting blood glucose (sugar) test is the preferred way to diagnose diabetes. It is easy to perform and convenient. After the person has fasted overnight (at least 8 hours), a single sample of blood is drawn and sent to the laboratory for analysis. This can also be done accurately in a doctor's office using a glucose meter.

- Normal fasting plasma glucose levels are less than 100 milligrams per deciliter (mg/dl).
- Fasting plasma glucose levels of more than 126 mg/dl on two or more tests on different days indicate diabetes.
- A random blood glucose test can also be used to diagnose diabetes. A blood glucose level of 200 mg/dl or higher indicates diabetes.

When fasting blood glucose stays above 100mg/dl, but in the range of 100-126mg/dl, this is known as impaired fasting glucose (IFG). While patients with IFG do not have the diagnosis of diabetes, this condition carries with it its own risks and concerns, and is addressed elsewhere.

The oral glucose tolerance test

Though not routinely used anymore, the oral glucose tolerance test (OGTT) is a gold standard for making the diagnosis of type 2 diabetes. It is still commonly used for diagnosing gestational diabetes and in conditions of pre-diabetes, such as polycystic ovary syndrome. With an oral glucose tolerance test, the person fasts overnight (at least eight but not more than 16 hours). Then first, the fasting plasma glucose is tested. After this test, the person receives 75 grams of glucose (100 grams for pregnant women). There are several methods employed by obstetricians to do this test, but the one described here is standard. Usually, the glucose is in a sweet-tasting liquid that the person drinks. Blood samples are taken at specific intervals to measure the blood glucose.

For the test to give reliable results:

- the person must be in good health (not have any other illnesses, not even a cold).
- the person should be normally active (not lying down, for example, as an inpatient in a hospital),
 and
- the person should not be taking medicines that could affect the blood glucose.
- For three days before the test, the person should have eaten a diet high in carbohydrates (200-300 grams per day).
- The morning of the test, the person should not smoke or drink coffee.

The classic oral glucose tolerance test measures blood glucose levels five times over a period of three hours. Some physicians simply get a baseline blood sample followed by a sample two hours after drinking the glucose solution. In a person without diabetes, the glucose levels rise and then fall quickly. In someone with diabetes, glucose levels rise higher than normal and fail to come back down as fast.

People with glucose levels between normal and diabetic have impaired glucose tolerance (IGT). People with impaired glucose tolerance do not have diabetes, but are at high risk for progressing to diabetes. Each year, 1%-5% of people whose test results show impaired glucose tolerance actually eventually develop diabetes. Weight loss and exercise may help people with impaired glucose tolerance return their glucose levels to normal. In addition, some physicians advocate the use of medications, such as metformin (Glucophage), to help prevent/delay the onset of overt diabetes.

Recent studies have shown that impaired glucose tolerance itself may be a risk factor for the development of heart disease. In the medical community, most physicians are now understanding that impaired glucose tolerance is nor simply a precursor of diabetes, but is its own clinical disease entity that requires treatment and monitoring.

Evaluating the results of the oral glucose tolerance test

Glucose tolerance tests may lead to one of the following diagnoses:

- **Normal response:** A person is said to have a normal response when the 2-hour glucose level is less than 140 mg/dl, and all values between 0 and 2 hours are less than 200 mg/dl.
- **Impaired glucose tolerance**: A person is said to have impaired glucose tolerance when the fasting plasma glucose is less than 126 mg/dl and the 2-hour glucose level is between 140 and 199 mg/dl.
- **Diabetes:** A person has diabetes when two diagnostic tests done on different days show that the blood glucose level is high.

• **Gestational diabetes:** A woman has gestational diabetes when she has any two of the following: a 100g OGTT, a fasting plasma glucose of more than 95 mg/dl, a 1-hour glucose level of more than 180 mg/dl, a 2-hour glucose level of more than 155 mg/dl, or a 3-hour glucose level of more than 140 mg/dl.

Why is blood sugar checked at home?

Home blood sugar (glucose) testing is an important part of controlling blood sugar. One important goal of diabetes treatment is to keep the blood glucose levels near the normal range of 70 to 120 mg/dl before meals and under 140 mg/dl at two hours after eating. Blood glucose levels are usually tested before and after meals, and at bedtime. The blood sugar level is typically determined by pricking a fingertip with a lancing device and applying the blood to a glucose meter, which reads the value. There are many meters on the market, for example, Accu-Check Advantage, One Touch Ultra, Sure Step and Freestyle. Each meter has its own advantages and disadvantages (some use less blood, some have a larger digital readout, some take a shorter time to give you results, etc). The test results are then used to help patients make adjustments in medications, diets, and physical activities.

There are some interesting developments in blood glucose monitoring. Currently, at least three continuous glucose sensors are approved in the United States (Dexcom, Medtronic and Navigator). The new continuous glucose sensor systems involve an implantable cannula placed just under the skin in the abdomen or in the arm. This cannula allows for frequent sampling of blood glucose levels. Attached to this is a transmitter that sends the data to a pager-like device. This device has a visual screen that allows the wearer to see, not only the current glucose reading, but also the graphic trends. In some devices, the rate of change of blood sugar is also shown. There are alarms for low and high sugar levels. Certain models will alarm if the rate of change indicates the wearer is at risk for dropping or rising blood glucose too rapidly. The Medtronic version is specifically designed to interface with their insulin pumps. However, at this time the patient still must manually approve any insulin dose (the pump cannot blindly respond to the glucose information it receives, it can only give a calculated suggestion as to whether the wearer should give insulin, and if so, how much). All of these devices need to be correlated to fingersticks for a few hours before they can function independently. The devices can then provide readings for 3-5 days.

Diabetes experts feel that these blood glucose monitoring devices give patients a significant amount of independence to manage their disease process; and they are a great tool for education as well. It is also important to remember that these devices can be used intermittently with fingersticks. For example, a well-controlled patient with diabetes can rely on fingerstick glucose checks a few times a day and do well. If they become ill, if they decide to embark on a new exercise regimen, if they change their diet and so on, they can use the sensor to supplement their fingerstick regimen, providing more information on how they are responding to new lifestyle changes or stressors. This kind of system takes us one step closer to closing the loop, and to the development of an artifical pancreas that senses insulin requirements based on glucose levels and the body's needs and releases insulin accordingly - the ultimate goal.

Hemoglobin A1c (A1c)

To explain what an hemoglobin A1c is, think in simple terms. Sugar sticks, and when it's around for a long time, it's harder to get it off. In the body, sugar sticks too, particularly to proteins. The red blood cells that circulate in the body live for about three months before they die off. When sugar sticks to these cells, it gives us an idea of how much sugar is around for the preceding three months. In most labs, the normal range is 4%-5.9 %. In poorly controlled diabetes, its 8.0% or above, and in well controlled patients it's less than 7.0% (optimal is <6.5%). The benefits of measuring A1c is that is gives a more reasonable and stable view of what's happening over the course of time (three months), and the value does not bounce as much as finger stick blood sugar measurements. There is a direct correlation between A1c levels and average blood sugar levels as follows.

While there are no guidelines to use A1c as a screening tool, it gives a physician a good idea that someone is diabetic if the value is elevated. Right now, it is used as a standard tool to determine blood sugar control in patients known to have diabetes.

A1c(%)	Mean blood sugar (mg/dl)
6	135
7	170
8	205
9	240
10	275
11	310
12	345

The American Diabetes Association currently recommends an A1c goal of less than 7.0%. Other Groups such as the American Association of Clinical Endocrinologists feel that an A1c of <6.5% should be the goal.

Of interest, studies have shown that there is about a 10% decrease in relative risk for microvascular disease for every 1% reduction in A1c. So, if a patient starts off with an A1c of 10.7 and drops to 8.2, though there are not yet at goal, they have managed to decrease their risk of microvascular complications by about 20%. The closer to normal the A1c, the lower the absolute risk for microvascular complications. Data also suggests that the risk of macrovascular disease decreases by about 24% for every 1% reduction in A1c values.

It should be mentioned here that there are a number of conditions in which an A1c value may not be accurate. For example, with significant anemia, the red blood cell count is low, and thus the A1c is altered. This may also be the case in sickle cell disease and other hemoglobinopathies.

What are the acute complications of diabetes?

- 1. Severely elevated blood sugar levels due to an actual lack of insulin or a relative deficiency of insulin.
- 2. Abnormally low blood sugar levels due to too much insulin or other glucose-lowering medications.

Insulin is vital to patients with type 1 diabetes - they cannot live with out a source of exogenous insulin. Without insulin, patients with type 1 diabetes develop severely elevated blood sugar levels. This leads to increased urine glucose, which in turn leads to excessive loss of fluid and electrolytes in the urine. Lack of insulin also causes the inability to store fat and protein along with breakdown of existing fat and protein stores. This dysregulation, results in the process of ketosis and the release of ketones into the blood. Ketones turn the blood acidic, a condition called diabetic ketoacidosis (DKA). Symptoms of diabetic ketoacidosis include nausea, vomiting, and abdominal pain. Without prompt medical treatment, patients with diabetic ketoacidosis can rapidly go into shock, coma, and even death.

Diabetic ketoacidosis can be caused by infections, stress, or trauma all which may increase insulin requirements. In addition, missing doses of insulin is also an obvious risk factor for developing diabetic ketoacidosis. Urgent treatment of diabetic ketoacidosis involves the intravenous administration of fluid, electrolytes, and insulin, usually in a hospital intensive care unit. Dehydration can be very severe, and it is not unusual to need to replace 6-7 liters of fluid when a person presents in diabetic ketoacidosis. Antibiotics are given for infections. With treatment, abnormal blood sugar levels, ketone production, acidosis, and dehydration can be reversed rapidly, and patients can recover remarkably well.

In patients with type 2 diabetes, stress, infection, and medications (such as corticosteroids) can also lead to severely elevated blood sugar levels. Accompanied by dehydration, severe blood sugar elevation in patients with type 2 diabetes can lead to an increase in blood osmolality (hyperosmolar state). This condition can lead to coma (hyperosmolar coma). A hyperosmolar coma usually occurs in elderly patients with type 2 diabetes. Like diabetic ketoacidosis, a hyperosmolar coma is a medical emergency. Immediate treatment with intravenous fluid and insulin is important in reversing the hyperosmolar state. Unlike patients with type 1 diabetes, patients with type 2 diabetes do not generally develop ketoacidosis solely on the basis of their diabetes. Since in general, type 2 diabetes occurs in an older population, concomitant medical conditions are more likely to exist, and these patients may actually be sicker overall. The complication and death rates from hyperosmolar coma is thus higher than in DKA.

Hypoglycemia means abnormally low blood sugar (glucose). In patients with diabetes, the most common cause of low blood sugar is excessive use of insulin or other glucose-lowering medications, to lower the blood sugar level in diabetic patients in the presence of a delayed or absent meal. When low blood sugar levels occur because of too much insulin, it is called an insulin reaction. Sometimes, low blood sugar can be the result of an insufficient caloric intake or sudden excessive physical exertion.

Blood glucose is essential for the proper functioning of brain cells. Therefore, low blood sugar can lead to central nervous system symptoms such as:

- · dizziness.
- · confusion,
- · weakness, and
- tremors.

The actual level of blood sugar at which these symptoms occur varies with each person, but usually it occurs when blood sugars are less than 65 mg/dl. Untreated, severely low blood sugar levels can lead to coma, seizures, and, in the worse case scenario, irreversible brain death. At this point, the brain is suffering from a lack of sugar, and this usually occurs somewhere around levels of <40 mg/dl.

The treatment of low blood sugar consists of administering a quickly absorbed glucose source. These include glucose containing drinks, such as orange juice, soft drinks (not sugar-free), or glucose tablets in doses of 15-20 grams at a time (for example, the equivalent of half a glass of juice). Even cake frosting applied inside the cheeks can work in a pinch if patient cooperation is difficult. If the individual becomes unconscious, glucagon can be given by intramuscular injection.

Glucagon causes the release of glucose from the liver (for example, it promotes gluconeogenesis). Glucagon can be lifesaving and every patient with diabetes who has a history of hypoglycemia (particularly those on insulin) should have a glucagon kit. Families and friends of those with diabetes need to be taught how to administer glucagon, since obviously the patients will not be able to do it themselves in an emergency situation. Another lifesaving device that should be mentioned is very simple; a medic alert bracelet should be worn by all patients with diabetes.

What are the chronic complications of diabetes?

These diabetes complications are related to blood vessel diseases and are generally classified into small vessel disease, such as those involving the eyes, kidneys and nerves (microvascular disease), and large vessel disease involving the heart and blood vessels (macrovascular disease). Diabetes accelerates hardening of the arteries (atherosclerosis) of the larger blood vessels, leading to coronary heart disease

(angina or heart attack), strokes, and pain in the lower extremities because of lack of blood supply (claudication).

Eye Complications

The major eye complication of diabetes is called diabetic retinopathy. Diabetic retinopathy occurs in patients who have had diabetes for at least five years. Diseased small blood vessels in the back of the eye cause the leakage of protein and blood in the retina. Disease in these blood vessels also causes the formation of small aneurysms (microaneurysms), and new but brittle blood vessels (neovascularization). Spontaneous bleeding from the new and brittle blood vessels can lead to retinal scarring and retinal detachment, thus impairing vision.

To treat diabetic retinopathy a laser is used to destroy and prevent the recurrence of the development of these small aneurysms and brittle blood vessels. Approximately 50% of patients with diabetes will develop some degree of diabetic retinopathy after 10 years of diabetes, and 80% of diabetics have retinopathy after 15 years of the disease. Poor control of blood sugar and blood pressure further aggravates eye disease in diabetes.

Cataracts and glaucoma are also more common among diabetics. It is also important to note that since the lens of the eye lets water through, if blood sugar concentrations vary a lot, the lens of the eye will shrink and swell with fluid accordingly. As a result, blurry vision is very common in poorly controlled diabetes. Patients are usually discouraged from getting a new eyeglass prescription until their blood sugar is controlled. This allows for a more accurate assessment of what kind of glasses prescription is required.

Kidney damage

Kidney damage from diabetes is called diabetic nephropathy. The onset of kidney disease and its progression is extremely variable. Initially, diseased small blood vessels in the kidneys cause the leakage of protein in the urine. Later on, the kidneys lose their ability to cleanse and filter blood. The accumulation of toxic waste products in the blood leads to the need for dialysis. Dialysis involves using a machine that serves the function of the kidney by filtering and cleaning the blood. In patients who do not want to undergo chronic dialysis, kidney transplantation can be considered.

The progression of nephropathy in patients can be significantly slowed by controlling high blood pressure, and by aggressively treating high blood sugar levels. Angiotensin converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers (ARBs) used in treating high blood pressure may also benefit kidney disease in diabetic patients.

Nerve damage

Nerve damage from diabetes is called diabetic neuropathy and is also caused by disease of small blood vessels. In essence, the blood flow to the nerves is limited, leaving the nerves without blood flow, and they get damaged or die as a result (a term known as ischemia). Symptoms of diabetic nerve damage include numbness, burning, and aching of the feet and lower extremities. When the nerve disease causes a complete loss of sensation in the feet, patients may not be aware of injuries to the feet, and fail to properly protect them. Shoes or other protection should be worn as much as possible. Seemingly minor skin injuries should be attended to promptly to avoid serious infections. Because of poor blood circulation, diabetic foot injuries may not heal. Sometimes, minor foot injuries can lead to serious infection, ulcers, and even gangrene, necessitating surgical amputation of toes, feet, and other infected parts.

Diabetic nerve damage can affect the nerves that are important for penile erection, causing erectile dysfunction (ED, impotence). Erectile dysfunction can also be caused by poor blood flow to the penis from diabetic blood vessel disease.

Diabetic neuropathy can also affect nerves to the stomach and intestines, causing nausea, weight loss, diarrhea, and other symptoms of gastroparesis (delayed emptying of food contents from the stomach into the intestines, due to ineffective contraction of the stomach muscles).

The pain of diabetic nerve damage may respond to traditional treatments with:

- gabapentin (Neurontin),
- phenytoin (Dilantin),
- · carbamazepine (Tegretol),
- desipramine (Norpraminine),
- amitriptyline (Elavil), or
- with topically-applied capsaicin (an extract of pepper).

Gabapentin (Neurontin), phenytoin (Dilantin), and carbamazepine (Tegretol) are medications that are traditionally used in the treatment of seizure disorders. Amitriptyline (Elavil) and desipramine (Norpraminine) are medications that are traditionally used for depression. While many of these medications are not FDA indicated specifically for the treatment of diabetes related nerve pain, they are used by physicians commonly.

The pain of diabetic nerve damage may also improve with better blood sugar control, though unfortunately blood glucose control and the course of neuropathy do not always go hand in hand. Newer medications for nerve pain have recently come to market in the US. Pregabalin (Lyrica) which has an indication for diabetic neuropathic pain and duloxetine (Cymbalta) are newer agents used in the treatment of diabetic neuropathy.

What can be done to slow diabetes complications?

Findings from the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) have clearly shown that aggressive and intensive control of elevated levels of blood sugar in patients with type 1 and type 2 diabetes decreases the complications of nephropathy, neuropathy, retinopathy, and may reduce the occurrence and severity of large blood vessel diseases. Aggressive control with intensive therapy means achieving fasting glucose levels between 70-120 mg/dl; glucose levels of less than 160 mg/dl after meals; and a near normal hemoglobin A1C levels (see below).

Studies in type 1 patients have shown that in intensively treated patients, diabetic eye disease decreased by 76%, kidney disease decreased by 54%, and nerve disease decreased by 60%. More recently the EDIC trial has shown that type 1 diabetes is also associated with increased heart disease, similar to type 2 diabetes. However, the price for aggressive blood sugar control is a two to three fold increase in the incidence of abnormally low blood sugar levels (caused by the diabetes medications). For this reason, tight control of diabetes to achieve glucose levels between 70-120 mg/dl is not recommended for children under 13 years of age, patients with severe recurrent hypoglycemia, patients unaware of their hypoglycemia, and patients with far advanced diabetes complications. To achieve optimal glucose control without an undue risk of abnormally lowering blood sugar levels, patients with type 1 diabetes must monitor their blood glucose at least four times a day and administer insulin at least three times per day. In patients with type 2 diabetes, aggressive blood sugar control has similar beneficial effects on the eyes, kidneys, nerves and blood vessels.

Diabetes At A Glance

- Diabetes is a chronic condition associated with abnormally high levels of sugar (glucose) in the blood.
- Insulin produced by the pancreas lowers blood glucose.
- Absence or insufficient production of insulin causes diabetes.
- The two types of diabetes are referred to as type 1 (insulin dependent) and type 2 (non-insulin dependent).
- · Symptoms of diabetes include increased urine output, thirst and hunger as well as fatigue.
- Diabetes is diagnosed by blood sugar (glucose) testing.
- The major complications of diabetes are both acute and chronic.
 - Acutely: dangerously elevated blood sugar, abnormally low blood sugar due to diabetes medications may occur.
 - o **Chronically:** disease of the blood vessels (both small and large) which can damage the eye, kidneys, nerves, and heart may occur
- Diabetes treatment depends on the type and severity of the diabetes. Type 1 diabetes is treated
 with insulin, exercise, and a diabetic diet. Type 2 diabetes is first treated with weight reduction,
 a diabetic diet, and exercise. When these measures fail to control the elevated blood sugars,
 oral medications are used. If oral medications are still insufficient, insulin medications are
 considered.

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