Diabetes - Type 1

Highlights

Type 1 Diabetes

In type 1 diabetes, the pancreas does not produce insulin. Insulin is a hormone that is involved in regulating how the body converts sugar (glucose) into energy. People with type 1 diabetes need to take daily insulin shots and carefully monitor their blood glucose levels.

Type 1 diabetes is less common that type 2 diabetes. This type of diabetes can occur at any age, but usually first develops in childhood or adolescence. Type 1 diabetes accounts for 5 - 10% of all diabetes cases.

Symptoms of Diabetes

Symptoms of both type 1 and type 2 diabetes include:

- Frequent urination
- Excessive thirst
- Extreme hunger
- Sudden weight loss
- Extreme fatigue
- Irritability
- Blurred vision

Warning Signs of Hypoglycemia

Hypoglycemia (low blood sugar) occurs when blood sugar (glucose) levels fall below normal. Patients with type 1 diabetes should be aware of these symptoms of hypoglycemia:

- Sweating
- Trembling
- Hunger
- Rapid heartbeat
- Confusion

It is important to quickly treat hypoglycemia and raise blood sugar levels by eating sugar, sucking on hard candy, or drinking fruit juice. Patients who are at risk for hypoglycemia should carry some sugar product with them in case an attack occurs. In rare and worst cases, hypoglycemia can lead to coma and death. Regular blood sugar monitoring throughout the day can help you avoid hypoglycemia. Patients are also encouraged to wear a medical alert ID bracelet or necklace that states they have diabetes and that they take insulin.

Introduction

The two major forms of diabetes are type 1, previously called insulin-dependent diabetes mellitus (IDDM) or juvenile-onset diabetes, and type 2, previously called non-insulin-dependent diabetes mellitus (NIDDM) or maturity-onset diabetes.

Insulin

Both type 1 and type 2 diabetes share one central feature: elevated blood sugar (*glucose*) levels due to absolute or relative insufficiencies of *insulin*, a hormone produced by the pancreas. Insulin is a key regulator of the body's metabolism. It works in the following way:

- During and immediately after a meal, digestion breaks carbohydrates down into sugar molecules (of which *glucose* is one) and proteins into *amino acids.*
- Right after the meal, glucose and amino acids are absorbed directly into the bloodstream, and blood glucose levels rise sharply. (Glucose levels after a meal are called *postprandial* levels.)
- The rise in blood glucose levels signals important cells in the pancreas, called *beta cells*, to secrete insulin, which pours into the bloodstream. Within 20 minutes after a meal insulin rises to its peak level.
- Insulin enables glucose to enter cells in the body, particularly muscle and liver cells. Here, insulin and other hormones direct whether glucose will be burned for energy or stored for future use.
- When insulin levels are high, the liver stops producing glucose and stores it in other forms until the body needs it again.
- As blood glucose levels reach their peak, the pancreas reduces the production of insulin.
- About 2 - 4 hours after a meal both blood glucose and insulin are at low levels, with insulin being slightly higher. The blood glucose levels are then referred to as *fasting blood glucose concentrations*.

The pancreas is located behind the liver and stomach. In addition to secreting digestive enzymes, the pancreas secretes the hormones insulin and glucagon into the bloodstream. The release of insulin into the blood lowers the level of blood glucose (simple sugars from food) by enhancing glucose to enter the body cells, where it is metabolized. If blood glucose levels get too low, the pancreas secretes glucagon to stimulate the release of glucose from the liver.

Type 1 Diabetes

In type 1 diabetes, the body does not produce insulin. Onset is usually in childhood or adolescence. Type 1 diabetes is considered an autoimmune disorder that involves:

- Beta cells in the pancreas that produce insulin are gradually destroyed. Eventually insulin deficiency is absolute.
- Without insulin to move glucose into cells, blood glucose levels become excessively high, a condition known as hyperglycemia.
- Because the body cannot utilize the sugar, it spills over into the urine and is lost.

- Weakness, weight loss, frequent urination, and excessive hunger and thirst are among the initial symptoms.
- Patients with type 1 diabetes need to take daily insulin for survival.

Type 2 Diabetes

Type 2 diabetes is the most common form of diabetes, accounting for 90 - 95% of cases. In type 2 diabetes, the body does not respond properly to insulin, a condition known as insulin resistance.

Gestational Diabetes

About 5% of pregnant women develop a form of type 2 diabetes, usually temporary, in their third trimester called gestational diabetes.

Gestational diabetes is diabetes that first appears during pregnancy. It usually develops during the third trimester of pregnancy. After delivery, blood sugar (glucose) levels generally return to normal, although 25% of these women develop type 2 diabetes within 15 years.

Gestational diabetes is not the same as the situation for women who have type 1 or type 2 diabetes before their pregnancy.

Causes

Autoimmune Response

Type 1 diabetes is usually a progressive *autoimmune* disease, in which the beta cells that produce insulin are slowly destroyed by the body's own immune system. It is unknown what first starts this cascade of immune events, but evidence suggests that both a genetic predisposition and environmental factors, such as a viral infection, are involved.

Islets of Langerhans contain beta cells and are located within the pancreas. Beta cells produce insulin which is needed to metabolize glucose within the body.

Genetic Factors

Researchers have found at least 18 genetic locations, labeled IDDM1 - IDDM18, that are related to type 1 diabetes. The IDDM1 region contains the HLA genes that encode proteins called major histocompatibility complex. The genes in this region affect the immune response. New advances in genetic research are identifying other genetic components of type 1 diabetes. Other chromosomes and genes continue to be identified.

Most people who develop type 1 diabetes, however, do not have a family history of the disease. The odds of inheriting the disease are only 10% if a first-degree relative has diabetes, and even in identical twins, one twin has only a 33% chance of having type 1 diabetes if the other has it.

Children are more likely to inherit the disease from a father with type 1 diabetes than from a mother with the disorder.

Genetic factors cannot fully explain the development of diabetes. Over the past 40 years, a major increase in the incidence of type 1 diabetes has been reported in certain European countries, and the incidence has tripled in the U.S.

Viruses

Some research suggests that viral infections may trigger the disease in genetically susceptible individuals.

Among the viruses under scrutiny are *enteric* viruses, which attack the intestinal tract. Coxsackieviruses are a family of enteric viruses of particular interest. Epidemics of Coxsackie virus, as well as mumps and congenital rubella, have been associated with incidence of type 1 diabetes.

Diabetes Secondary to Other Conditions

Conditions that damage or destroy the pancreas, such as pancreatitis, pancreatic surgery, or certain industrial chemicals can cause diabetes. Certain drugs can also cause temporary diabetes, including corticosteroids, beta blockers, and phenytoin. Rare genetic disorders (Klinefelter syndrome, Huntington's chorea, Wolfram syndrome, leprechaunism, Rabson-Mendenhall syndrome, lipoatrophic diabetes, and others) and hormonal disorders (acromegaly, Cushing syndrome, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma) also increase the risk for diabetes.

Risk Factors

Type 1 diabetes is much less common than type 2 diabetes consisting of only 5 - 10% of all cases of diabetes. Nevertheless, like type 2 diabetes, the incidence of type 1 diabetes among children and adolescents has been rising over the past few decades. While type 2 diabetes has been increasing among African-American and Hispanic adolescents, the highest rates of type 1 diabetes are found among Caucasian youth.

Type 1 diabetes can occur at any age but usually appears between infancy and the late 30s, most typically in childhood or adolescence. Males and females are equally at risk. Studies report the following may be risk factors for developing type 1 diabetes:

- Being ill in early infancy
- Having a parent with type 1 diabetes (the risk is greater if a father has the condition)
- Having an older mother
- Having a mother who had preeclampsia during pregnancy
- Having other autoimmune disorders such as Grave's disease, Hashimoto's thyroiditis (a form of hypothyroidism), Addison's disease, multiple sclerosis (MS), or pernicious anemia

Symptoms

The process that destroys the insulin-producing beta cells can be long and insidious. At the point when insulin production bottoms out, however, type 1 diabetes usually appears suddenly and progresses quickly. Warning signs of type 1 diabetes include:

- Frequent urination (in children, a recurrence of bed-wetting after toilet training has been completed)
- Unusual thirst, especially for sweet, cold drinks
- Extreme hunger
- Sudden, sometimes dramatic, weight loss
- Weakness
- Extreme fatigue
- Blurred vision or other changes in eyesight
- Irritability
- Nausea and vomiting (acute symptoms)

Children with type 1 diabetes may also be restless, apathetic, and have trouble functioning at school. In severe cases, diabetic coma may be the first sign of type 1 diabetes.

Complications

Type 1 diabetes reduces the normal lifespan by about 5 - 8 years. However, survival rates are improving in all ethnic groups and both genders. Longer survival rates are probably due to improvements in monitoring and tighter control of blood glucose. There are two important approaches to preventing complications from type 1 diabetes:

- Intensive control of blood glucose and keeping glycosylated hemoglobin (HbA1c) levels below 7%. This approach can help prevent complications due to vascular (blood vessel) abnormalities and nerve damage (neuropathy) that can cause major damage to organs, including the eyes, kidneys, and heart.
- Managing risk factors for heart disease. Blood glucose control helps the heart, but it is also very important that people with diabetes control blood pressure, cholesterol levels, and other factors associated with heart disease.

Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is a life-threatening complication caused by insulin deficiency. For some, it may be the first sign that someone has diabetes. It may also occur in a person with type 1 diabetes who is not consistent with insulin therapy, or who has an acute illness or infection that makes their diabetes difficult to control. Other contributing factors are lack of health insurance and intentionally reducing insulin doses in order to lose weight, which occurs with adolescent girls in an effort to keep weight down.

Diabetic ketoacidosis often develops as follows:

- The process is usually triggered in insulin-deficient patients by a stressful event, most often pneumonia or urinary tract infections. Other triggers include alcohol abuse, physical injury, pulmonary embolism, heart attacks, or other illnesses.
- Severely low insulin levels cause excessive amounts of glucose in the bloodstream (hyperglycemia).
- Fat breakdown then accelerates and increases the production of fatty acids.
- These fatty acids are converted into chemicals called ketone bodies, which are toxic at high levels.

Symptoms and complications include:

- Nausea and vomiting
- Deep and rapid breathing may occur with frequent sighing
- Rapid heartbeat
- Severe dehydration
- Cerebral edema, or brain swelling, is a rare but very dangerous complication that occurs in 1% of ketoacidosis cases and results in coma, brain damage, or death in many cases.
- Other serious complications from DKA include aspiration pneumonia and adult respiratory distress syndrome.
- If the condition persists, coma and eventually death may occur, although over the past 20 years, death from DKA has decreased to about 2% of all cases.

Life-saving treatment uses rapid replacement of fluids with a salt (saline) solution followed by low-dose insulin and potassium replacement.

Ketoacidosis is a serious condition of glucose build-up in the blood and urine. A simple urine test can determine if high ketone levels are present.

Hypoglycemia

Tight blood sugar (glucose) control increases the risk of low blood sugar (hypoglycemia). Hypoglycemia occurs if blood glucose levels fall below normal. It is generally defined as a blood sugar below 70 mg/dL, although this level may not necessarily cause symptoms in all patients. Insufficient intake of food and excess exercise or alcohol intake may cause hypoglycemia. Usually the condition is manageable, but, occasionally, it can be severe or even life threatening, particularly if the patient fails to recognize the symptoms, especially while continuing to take insulin or other hypoglycemic drugs.

Risk Factors for Severe Hypoglycemia. Among young patients, the youngest children and boys of any age are at higher risk for hypoglycemia. Specific risk factors for severe hypoglycemia include:

- Patients attempting tight control of blood glucose and HbA1c levels
- Long-term diabetes

- Patients who do not comply with treatment
- Infections such as gastroenteritis or respiratory illnesses

Hypoglycemia unawareness. Hypoglycemia unawareness is a condition in which people become accustomed to hypoglycemic symptoms. They may no longer notice the signs of hypoglycemia until they become more severe. It affects about 25% of patients who use insulin, nearly always people with type 1 diabetes. In such cases, hypoglycemia appears suddenly, without warning, and can escalate to a severe level. Even a single recent episode of hypoglycemia may make it more difficult to detect the next episode. With vigilant monitoring and by rigorously avoiding low blood glucose levels, patients can often regain the ability to sense the symptoms. However, even very careful testing may fail to detect a problem, particularly one that occurs during sleep.

Symptoms. Mild symptoms usually occur at moderately low and easily correctable levels of blood glucose. They include:

- Sweating
- Trembling
- Hunger
- Rapid heartbeat

Severely low blood glucose levels can cause neurologic symptoms, such as:

- Confusion
- Weakness
- Disorientation
- Combativeness
- In rare and worst cases, coma, seizure, and death

Heart Disease and Stroke

Patients with type 1 diabetes are 10 times more at risk for heart disease than healthy patients. Heart attacks account for 60% of deaths in patients with diabetes, while strokes account for 25% of such deaths. Diabetes affects the heart in many ways:

- Both type 1 and 2 diabetes accelerate the progression of atherosclerosis (hardening of the arteries). Diabetes is often associated with low HDL ("good" cholesterol) and high triglycerides. This can lead to coronary artery disease, heart attack, or stroke.
- In type 1 diabetes, high blood pressure (hypertension) usually develops if the kidneys become damaged. High blood pressure is another major cause of heart attack, stroke, and heart failure. Children with diabetes are also at risk for hypertension.
- Impaired nerve function (neuropathy) associated with diabetes also causes heart abnormalities.

Atherosclerosis is a disease of the arteries in which fatty material is deposited in the vessel wall, resulting in narrowing and eventual impairment of blood flow. Severely restricted blood flow in

the arteries to the heart muscle leads to symptoms such as chest pain. Atherosclerosis shows no symptoms until a complication occurs.

Kidney Damage (Nephropathy)

Kidney disease (nephropathy) is a very serious complication of diabetes. With this condition, the tiny filters in the kidney (called glomeruli) become damaged and leak protein into the urine. Over time this can lead to kidney failure. Urine tests showing microalbuminuria (small amounts of protein in the urine) are important markers for kidney damage.

Diabetic nephropathy, the leading cause of end-stage renal disease (ESRD), occurs in about 20 - 40% of patients with diabetes. Patients with ESRD have 13 times the risk of death compared to other patients with type 1 diabetes. If the kidneys fail, dialysis is required. Symptoms of kidney failure may include swelling in the feet and ankles, itching, fatigue, and pale skin color. The outlook of end-stage renal disease has greatly improved during the last four decades for patients with type 1 diabetes, and fewer people with type 1 diabetes are developing ESRD.

Neuropathy

Diabetes reduces or distorts nerve function, causing a condition called neuropathy. Neuropathy refers to a group of disorders that affect nerves. The two main types of neuropathy are:

- *Peripheral* (affects nerves in the toes, feet, legs, hand, and arms)
- *Autonomic* (affects nerves that help regulate digestive, bowel, bladder, heart, and sexual function)

Peripheral neuropathy particularly affects sensation. It is a common complication that affects nearly half of people with type 1 or type 2 diabetes after 25 years. The most serious consequences of neuropathy occur in the legs and feet and pose a risk for ulcers and, in unusually severe cases, amputation. Peripheral neuropathy usually starts in the fingers and toes and moves up to the arms and legs (called a stocking-glove distribution). Symptoms include:

- Tingling
- Weakness
- Burning sensations
- Loss of the sense of warm or cold
- Numbness (if the nerves are severely damaged, the patient may be unaware that a blister or minor wound has become infected)
- Deep pain

Autonomic neuropathy can cause:

- Digestive problems (constipation, diarrhea, nausea, vomiting)
- Bladder infections and incontinence
- Erectile dysfunction

- Heart problems. Neuropathy may mask angina, the warning chest pain for heart disease and heart attack. Patients with diabetes should be aware of other warning signs of a heart attack, including sudden fatigue, sweating, shortness of breath, nausea, and vomiting.
- Rapid heart rates
- Lightheadedness when standing up (orthostatic hypotension)

Blood sugar control is an essential component in the treatment for neuropathy. Studies show that tight control of blood glucose levels delays the onset and slows progression of neuropathy. Heart disease risk factors may increase the likelihood of developing neuropathy. Lowering triglycerides, losing weight, reducing blood pressure, and quitting smoking may help prevent the onset of neuropathy.

Foot Ulcers and Amputations

About 15% of patients with diabetes experience serious foot problems. They are the leading cause of hospitalizations for these patients. The consequences of both poor circulation and peripheral neuropathy make this a common and serious problem for all patients with diabetes.

Diabetes is responsible for more than half of all lower limb amputations performed in the U.S. Each year there are about 88,000 non-injury amputations, 50 - 75% of them due to diabetes. About 85% of amputations start with foot ulcers, which develop in about 12% of people with diabetes.

People with diabetes who are overweight, smokers, and have a long history of diabetes tend to be at most risk. People who have the disease for more than 20 years and are insulin-dependent are at the highest risk. Related conditions that put people at risk include peripheral neuropathy, peripheral artery disease, foot deformities, and a history of ulcers. [For more information, see *In-Depth Report* #102: Peripheral artery disease and intermittent claudication.]

In general, foot ulcers develop from infections, such as those resulting from blood vessel injury. Numbness from nerve damage, which is common in diabetes, compounds the danger since the patient may not be aware of injuries. About one-third of foot ulcers occur on the big toe.

Charcot Foot. Charcot foot or Charcot joint (medically referred to as neuropathic arthropathy) occurs in up to 2.5% of people with diabetes. Early changes appear similar to an infection, with the foot becoming swollen, red, and warm. Gradually, the affected foot can become deformed. The bones may crack, splinter, and erode, and the joints may shift, change shape, and become unstable. It typically develops in people who have neuropathy to the extent that they cannot feel sensation in the foot and are not aware of an existing injury. Instead of resting an injured foot or seeking medical help, the patient often continues normal activity, causing further damage.

Charcot foot is initially treated with strict immobilization of the foot and ankle; some centers use a cast that allows the patient to move and still protects the foot. When the acute phase has passed, patients usually need lifelong protection of the foot using a brace initially and custom footwear.

Retinopathy and Eye Complications

Diabetes accounts for thousands of new cases of blindness annually and is the leading cause of new cases of blindness in adults ages 20 - 74. The most common eye disorder in diabetes is retinopathy. People with diabetes are also at higher risk for developing cataracts and certain types of glaucoma. [For more information, see *In-Depth Report* #26: Cataracts and *In-Depth Report* #25: Glaucoma.]

Retinopathy. Retinopathy is a condition in which the retina becomes damaged. The two primary abnormalities that occur are a weakening of the blood vessels in the retina and the obstruction in the capillaries -- probably from very tiny blood clots. Retinopathy generally occurs in one or two phases:

- The early and more common type of this disorder is called *nonproliferative or background retinopathy*. The blood vessels in the retina are abnormally weakened. They rupture and leak, and waxy areas may form. If these processes affect the central portion of the retina, swelling may occur, causing reduced or blurred vision.
- If the capillaries become blocked and blood flow is cut off, soft, "woolly" areas may develop in the retina's nerve layer. These woolly areas may signal the development of *proliferative retinopathy*. Often there are no symptoms of progressing retinopathy. In this more severe condition, new abnormal blood vessels form and grow on the surface of the retina. They may spread into the cavity of the eye or bleed into the back of the eye. Major hemorrhage or retinal detachment can result, causing severe visual loss or blindness. The sensation of seeing flashing lights may indicate retinal detachment.

All patients with diabetes should begin having a professional eye exam according to the following schedule:

- Children older than 10 years and with diabetes for at least 3 - 5 years
- Adolescents and adults with type 1 diabetes, within 5 years of diagnosis
- Adults with type 2 diabetes soon after diagnosis is made

After the first exam, most patients should have a yearly eye examination. Patients with no signs of retinal damage or low risk factors for retinopathy may only require screening every 2 - 3 years. Patients beginning a new or vigorous exercise program should have their eyes examined, as well as all patients planning pregnancy.

Infections

Respiratory Infections. People with diabetes face a higher risk for influenza and its complications, including pneumonia, possibly because the disorder neutralizes the effects of protective proteins on the surface of the lungs. Everyone with diabetes should have annual influenza vaccinations and a vaccination against pneumococcal pneumonia.

Urinary Tract Infections. Women with diabetes face a significantly higher risk for urinary tract infections, which are likely to be more complicated and difficult to treat than in the general population.

Depression

Diabetes doubles the risk for depression. Depression, in turn, may increase the risk for hyperglycemia and complications of diabetes.

Osteoporosis

Type 1 diabetes is associated with a slightly reduced bone density, putting patients at risk for osteoporosis and possibly fractures.

Other Complications

Diabetes increases the risk for other conditions, including:

- Hearing loss
- Periodontal disease
- Carpal tunnel syndrome and other nerve entrapment syndromes
- Nonalcoholic fatty liver disease, also called nonalcoholic steatohepatitis (NASH); a particular danger for people who are obese
- Colorectal cancer
- Uterine cancer

Specific Complications in Women

Diabetes can cause specific complications in women. Women with diabetes have an increased risk of recurrent yeast infections. In terms of sexual health, diabetes may cause decreased vaginal lubrication, which can lead to pain or discomfort during intercourse.

Women with diabetes should also be aware that certain types of medication can affect their blood glucose levels. For example, birth control pills can raise blood glucose levels. Long-term use (more than 2 years) of birth control pills may increase the risk of health complications.

Diabetes and Pregnancy. Pregnancy in a patient with existing diabetes can increase the risk for birth defects. Studies indicate that high blood sugar levels (hyperglycemia) can affect the developing fetus during the critical first 6 weeks of organ development. Therefore, it is important that women with pre-existing diabetes (both type 1 and type 2) who are planning on becoming pregnant strive to maintain good glucose control for 3 - 6 months before pregnancy.

It is also important for women to closely monitor their blood sugar levels during pregnancy. For women with type 1 diabetes, pregnancy can affect their insulin dosing needs. Insulin dosing may also need to be adjusted during and following delivery. [For more information, see “Treatment of Diabetes During Pregnancy” in *Treatment of Complications* section of this report.]

Diabetes and Menopause. The changes in estrogen and other hormonal levels that occur during perimenopause can cause major fluctuations in blood glucose levels. Women with diabetes also face an increased risk of premature menopause, which can lead to higher risk of heart disease.

Specific Problems for Adolescents with Type 1 Diabetes

Lack of Blood Glucose Control. Control of blood glucose levels is generally very poor in adolescents and young adults. Adolescents with diabetes are at higher risk than adults for ketoacidosis resulting from noncompliance. Young people who do not control glucose are also at high risk for permanent damage in small vessels, such as those in the eyes.

Eating Disorders. Up to a third of young women with type 1 diabetes have eating disorders and under-use insulin to lose weight. Anorexia and bulimia pose significant health risks in any young person, but they can be especially dangerous for people with diabetes.

Diagnosis

Testing for Glucose Abnormalities

Fasting Plasma Glucose. The fasting plasma glucose (FPG) test is the standard test for diagnosing diabetes. It is a simple blood test taken after 8 hours of fasting.

FPG levels indicate:

- Normal. U100 mg/dL (or 5.5 mmol/L) or below.
- Pre-Diabetes. (a risk factor for type 2 diabetes): Between 100 - 125 mg/dL (5.5 - 7.0 mmol/L).
- Diabetes.126 mg/dL (7.0 mmol/L) or higher

The FPG test is not always reliable, so a repeat test is recommended if the initial test suggests the presence of diabetes, or if the tests are normal in people who have symptoms or risk factors for diabetes. Widespread screening of patients to identify those at higher risk for diabetes type 1 is not recommended.

Glucose Tolerance Test. The oral glucose tolerance test (OGTT) is more complex than the FPG and may overdiagnose diabetes in people who do not have it. Some doctors recommend it as a follow-up after FPG, if the latter test results are normal but the patient has symptoms or risk factors of diabetes. The test uses the following procedures:

- It first uses an FPG test.
- A blood test is then taken 2 hours later after drinking a special glucose solution.

OGTT levels indicate:

- Normal. 140 mg/dL or below.
- Pre-Diabetes. Between 140 - 199 mg/dL

- Diabetes. 200 mg/dL or higher.

Patients who have the FPG and OGTT tests must not eat for at least 8 hours prior to the test.

The oral glucose tolerance test is used to diagnose diabetes. The first portion of the test involves drinking a special glucose solution. Blood is then taken several hours later to test for the level of glucose in the blood. Patients with diabetes will have higher than normal levels of glucose in their blood.

Test for Glycosylated Hemoglobin (Hemoglobin A1c). This test examines blood levels of glycosylated hemoglobin, also known as hemoglobin A1c (HbA1c). The test is not affected by recent food intake so it can be taken at any time.

- The results of a blood glucose test tell the patient and doctor how well the diabetes is controlled for only the day of the test.
- Once a blood sugar molecule sticks to a hemoglobin molecule, which are found in every red blood cell, it never lets go (a process called glycation). If a patient with diabetes has elevated blood glucose on many days, more blood glucose molecules will stick to the hemoglobin molecule. If that happens, the hemoglobin A1c level will be higher.
- Therefore, an elevated hemoglobin A1c level tells the doctor and the patient how well controlled the patients diabetes has been over the last 3 months or so.
- Measuring glycosylated hemoglobin is not generally used for making an initial diagnosis of diabetes, since a normal level does not rule out diabetes. In people without diabetes, a normal HbA1c range is between 4 - 6%.

Elevated levels of glycosylated hemoglobin are strongly associated with most if not all of the complications of diabetes.

In general, most adults with diabetes should aim for HbA1c levels below 7%. Higher levels indicate poor blood glucose control.

Goal HbA1c levels for children are:

- Between 7.5 - 8.5% for children under age 6 years
- Less than 8% for children age 6 - 12 years
- Less than 7.5% for children age 13 - 19 years

Schedule for HbA1c Monitoring:

- Every 6 months if diabetes is well controlled
- Every 3 months if not well controlled

Autoantibody Tests

Type 1 diabetes is characterized by the presence of a variety of antibodies that attack the islet cells. These antibodies are referred to as autoantibodies because they attack the body's own cells

-- not a foreign invader. Blood tests for these autoantibodies can help differentiate between type 1 and type 2 diabetes.

Screening Tests for Complications

Screening Tests for Heart Disease. All patients with diabetes should be tested for:

- Blood pressure. Your doctor should check your blood pressure at every visit. Blood pressure goals should be 130/80 mm Hg or lower.
- Lipid levels, including cholesterol. People with diabetes should aim for LDL levels below 100 mg/dL, HDL levels over 40 mg/dL, and triglyceride levels below 150 mg/dL. Testing should be performed yearly and perhaps every other year for patients with good lipid control and no evidence of heart disease.
- Cardiac exercise testing should be considered for adult patients with any symptoms or electrocardiogram findings, or before starting an exercise program.

Screening Tests for Kidney Damage. The earliest manifestation of kidney disease is microalbuminuria, in which tiny amounts (30 - 300 mg per day) of protein called albumin are found in the urine. Microalbuminuria is also a marker for other complications involving blood vessel abnormalities, including heart attack and stroke.

People with diabetes should have an annual microalbuminuria urine test. Patients should also have their blood creatinine tested at least once a year. Creatinine is a waste product that is removed from the blood by the kidneys. High levels of creatinine may indicate kidney damage. A doctor uses the results from a creatinine blood test to calculate the glomerular filtration rate (GFR). The GFR is an indicator of kidney function; it estimates how well the kidneys are cleaning the blood.

Screening for Retinopathy. The American Diabetes Association recommends that patients with type 1 diabetes have an annual comprehensive eye exam, with dilation, to check for signs of retina disease (retinopathy). Patients at low risk may need exams only every 2 - 3 years.

Screening for Neuropathy. All patients should be screened for nerve damage (neuropathy), including a comprehensive foot exam. Patients who lose sensation in their feet should have a foot exam every 3 - 6 months to check for ulcers or infections.

Screening for Thyroid Abnormalities. Thyroid function tests should be performed.

Lifestyle Changes

The treatment goals for a diabetes diet are:

- Achieve near-normal blood glucose levels. People with type 1 diabetes must coordinate calorie intake with medication or insulin administration, exercise, and other variables to control blood glucose levels. New forms of insulin now allow more flexibility in timing meals.

- Protect the heart and aim for healthy lipid (cholesterol and triglyceride) levels and control of blood pressure.
- Achieve healthy weight. (A reasonable weight is usually defined as a weight that is achievable and sustainable, rather than one that is culturally defined as desirable or ideal.) Children, pregnant women, and people recovering from illness should maintain adequate calories for health.
- Manage or prevent complications of diabetes. People with diabetes, whether type 1 or 2, are at risk for a number of medical complications, including heart and kidney disease. Dietary requirements for diabetes must take these disorders into consideration.
- Promote overall health.

Overall Guidelines. There is no single diabetes diet. Patients should meet with a professional dietitian to plan an individualized diet within the general guidelines that takes into consideration their own health needs.

Healthy eating habits, along with good control of blood glucose, are the basic goals, and several good dietary methods are available to meet them. General dietary guidelines for diabetes recommend:

- Carbohydrates should provide 45 - 65% of total daily calories. The type and amount of carbohydrate are both important. Best choices are vegetables, fruits, beans, and whole grains. These foods are also high in fiber. Patients with diabetes should monitor their carbohydrate intake either through carbohydrate counting or meal planning exchange lists.
- Fats should provide 25 - 35% of daily calories. Monounsaturated (olive, peanut, and canola oils; avocados; and nuts) and omega-3 polyunsaturated (fish, flaxseed oil, and walnuts) fats are the best types. Limit saturated fat (red meat, butter) to less than 7% of daily calories. Choose nonfat or low-fat dairy instead of whole milk products. Limit trans-fats (hydrogenated fat found in snack foods, fried foods, and commercially baked goods) to less than 1% of total calories.
- Protein should provide 12 - 20% of daily calories, although this may vary depending on a patient's individual health requirements. Patients with kidney disease should limit protein intake to less than 10% of calories. Fish, soy, and poultry are better protein choices than red meat

[For more information, see *In-Depth Report* #42: Diabetes diet.]

Healthy Weight Control

Weight gain is a potential side effect of intense diabetic control with insulin. Being overweight can increase the risk for health problems. On the other hand, studies suggest that more than one-third of women with diabetes omit or underuse insulin in order to lose weight. Eating disorders have become a serious problem within the general population and are especially dangerous in patients with diabetes. Some evidence suggests that they contribute to about 20% of cases of recurrent ketoacidosis in young women. Ketoacidosis is a significant complication of insulin depletion and can be life threatening.

Exercise

Aerobic exercise has significant and particular benefits for people with type 1 diabetes. It increases sensitivity to insulin, lowers blood pressure, improves cholesterol levels, and decreases body fat. Because glucose levels swing dramatically during workouts, people with type 1 diabetes need to take certain precautions:

- Monitor glucose levels carefully before, during, and after workouts.
- Avoid exercise if glucose levels are above 300 mg/dL or under 100 mg/dL.
- To avoid hypoglycemia, patients should inject insulin in sites away from the muscles they use the most during exercise.
- Before exercising, avoid alcohol and if possible certain drugs, including beta blockers, which make it difficult to recognize symptoms of hypoglycemia.
- Insulin-dependent athletes may need to decrease insulin doses or take in more carbohydrates, especially in the form of pre-exercise snacks. Skim milk is particularly helpful. They should also drink plenty of fluids.
- Good, protective footwear is essential to help avoid injuries and wounds to the feet.

Avoid resistance or high impact exercises. They can strain weakened blood vessels in the eyes of patients with retinopathy. High-impact exercise may also injure blood vessels in the feet. Because patients with diabetes may have silent heart disease, they should always check with their doctors before undertaking vigorous exercise.

Warning on Dietary Supplements

Various fraudulent products are often sold on the Internet as “cures” or treatments for diabetes. These dietary supplements have not been studied or approved. The US Food and Drug Administration (FDA) and Federal Trade Commission (FTC) warn patients with diabetes not to be duped by bogus and unproven remedies.

Treatment

Insulin is essential for strict control of blood glucose levels in type 1 diabetes. Tight blood glucose control is the best way to prevent major complications in type 1 diabetes, including those that affect the kidneys, eyes, nerve pathways, and blood vessels. Intensive insulin treatment in early diabetes may even help preserve any residual insulin secretion for at least 2 years.

There are, however, some significant problems with intensive insulin therapy:

- There is a greater risk for low blood sugar (hypoglycemia).
- Many patients experience significant weight gain from insulin administration, which may have adverse effects on blood pressure and cholesterol levels. It is important to manage heart disease risk factors that might develop as a result of insulin treatment.

A diet plan that compensates for insulin administration and supplies healthy foods is extremely important. [For more information, see *In-Depth Report* #42: Diabetes diet.] Pancreas

transplantation may eventually be recommended for patients who cannot control glucose levels without frequent episodes of severe hypoglycemia.

Regimens for Intensive Insulin Treatment

The goal of intensive insulin therapy is to keep blood glucose levels as close to normal as possible.

Glucose Goals for Patients with Diabetes		
	Normal	**Goal**
Blood glucose levels before meals	Less than 110 mg/dL	90 - 130 mg/dL for adults 100 - 180 mg/dL for children under age 6 90 - 180 mg/dL for children 6 - 12 years old 90 - 130 mg/dL for children 13 - 19 years old
Bedtime blood glucose levels	Less than 120 mg/dL	110 - 150 mg/dL for adults 110 - 200 mg/dL for children under age 6 100 - 186 mg/dL for children 6 - 12 years old 90 - 150 mg/dL for children 13 - 19 years old
Glycosylated hemoglobin (HbA1c) levels	4 - 6%	Less than 7%
Source: *Standards of Medical Care In Diabetes -- 2008*, American Diabetes Association.		

Standard insulin therapy usually consists of one or two daily insulin injections, one daily blood sugar test, and visits to the health care team every 3 months. For strictly controlling blood glucose, however, intensive management is required. The regimen is complicated although newer insulin forms may make it easier.

There are two components to flexible insulin administration and a number of variations of insulin delivery for accomplishing them:

- Basal insulin administration. The *basal* component of the treatment attempts to provide a steady amount of background insulin throughout the day. Basal insulin levels maintain

regular blood glucose needs. Insulin glargine now offers the most consistent insulin activity level, but other intermediate and long-acting forms may be beneficial when administered twice a day. Short-acting insulin delivered continuously using a pump is proving to a very good way to provide basal rates of insulin.
- Mealtime insulin administration. Meals require a boost (a bolus) of insulin to regulate the sudden rise in glucose levels after a meal.

In achieving insulin control the patient must also take other steps:

- The patient should perform four or more blood glucose tests during the day.
- Patients should coordinate insulin administration with calorie intake. In general, they should eat three meals each day at regular intervals. Snacks are often necessary.
- Insulin requirements vary depending on many non-nutritional situations during the day, including exercise and sleep. People are at enhanced risk for low blood sugar during exercise. Some patients experience a sudden rise in blood glucose levels in the morning -- the so-called "dawn phenomenon."
- The patient must also maintain a good diet plan and should visit the health care team of doctors, nurses, and dietitians once a month.

Because of the higher risk for hypoglycemia in children, doctors recommend that intensive treatment be used very cautiously in children under 13 and not at all in very young children.

Types of Insulin

Insulin cannot be taken orally because the body's digestive juices destroy it. Injections of insulin under the skin ensure that it is absorbed slowly by the body for a long-lasting effect. The timing and frequency of insulin injections depend upon a number of factors:

- The duration of insulin action. Insulin is available in several forms, including: standard, intermediate, long-acting, and rapid-acting.
- Amount and type of food eaten. Ingestion of food makes the blood glucose level rise. Alcohol lowers levels.
- The person's level of physical activity. Exercise lowers glucose levels.

Fast-Acting Insulin. Insulin lispro (Humalog) and insulin aspart (Novo Rapid, Novolog) lower blood sugar very quickly, usually within 5 minutes after injection. Insulin peaks in about 4 hours and continues to work for about 4 more hours. This rapid action reduces the risk for hypoglycemic events after eating (postprandial hypoglycemia). Optimal timing for administering this insulin is about 15 minutes before a meal, but it can also be taken immediately after a meal (but within 30 minutes). Fast-acting insulins may be especially useful for meals with high carbohydrates.

Regular Insulin. Regular insulin begins to act 30 minutes after injection, reaches its peak at 2 - 4 hours, and lasts about 6 hours. Regular insulin may be administered before a meal and may be better for high-fat meals.

Intermediate Insulin. NPH (neutral protamine Hagedorn) insulin has been the standard intermediate form. It works within 2 - 4 hours, peaks 4 - 12 hours later, and lasts up to 18 hours. Lente (insulin zinc) is another intermediate insulin that peaks 4 - 12 hours and lasts up to 18 hours.

Long-Acting (Ultralente) Insulin. Long-acting insulins, such as insulin glargine (Lantus), are released slowly. Insulin glargine matches parts of natural insulin and maintains stable activity for more than 24 hours. Studies suggest that it poses less of a risk for hypoglycemia and weight gain than NPH. It has a higher incidence of pain at the injection site than NPH. Ultralente insulin peaks at 10 hours and lasts up to 20 hours but varies greatly in activity from day to day.

Combinations. Regimens generally include combinations of short and longer-acting insulins to help match the natural cycle. For example, one approach in patients who are intensively controlling their glucose levels uses 3 injections of insulin, which includes a mixture of regular insulin and NPH at dinner. Another approach uses 4 injections, including a separate short-acting form at dinner and NPH at bedtime, which may pose a lower risk for nighttime hypoglycemia than the 3-injection regimen.

Insulin Pens. Insulin pens, which contain cartridges of insulin, have been available for some time. Until recently, they were fairly complicated and difficult to use. Newer, prefilled pens (Humulin Pen, Humalog) are disposable and allow the patient to dial in the correct amount.

Insulin Pumps

Insulin Pumps. An insulin pump can improve blood glucose control and quality of life with fewer hypoglycemic episodes than multiple injections. The pumps correct for the “dawn phenomenon” (sudden rise of blood glucose in the morning) and allow quick reductions for specific situations, such as exercise. Many different brands are available.

The typical pump is about the size of a beeper and has a digital display. Some are worn externally and are programmed to deliver insulin through a catheter in the skin or the abdomen. They generally use rapid-acting insulin, the most predictable type. They work by administering a small amount of insulin continuously (the basal rate) and a higher dose (a bolus dose) when food is eaten.

Many adults, adolescents, and school children use insulin pumps. Studies indicate that even very young children (ages 2 - 7 years) can successfully use insulin pumps and that the pumps may help improve blood sugar control.

The catheter at the end of the insulin pump is inserted through a needle into the abdominal fat of a person with diabetes. Dosage instructions are entered into the pump's small computer, and the appropriate amount of insulin is then injected into the body in a calculated, controlled manner.

Learning to use the pump can be complicated, although over time most patients find the devices are fairly easy to use. To achieve good control, patients and parents of children must undergo some training. The patient and doctor must determine the amount of insulin used -- it is not

automatically calculated. This requires an initial learning period, including understanding insulin needs over the course of the day and in different situations and knowledge of carbohydrate counting. Frequent blood testing is very important, particularly during the training period.

Insulin pumps are more expensive than insulin shots and occasionally have some complications, such as blockage in the device or skin irritation at the infusion site. In spite of early reports of a higher risk for ketoacidosis with pumps, more recent studies have found no higher risk.

Supplementary Drugs for Hyperglycemia

Pramlintide (Symlin) is a new type of injectable drug that can help control postprandial hyperglycemia, the sudden increase in blood sugar after a meal. Pramlintide is injected before meals and can help lower blood sugar levels in the 3 hours after meals. Pramlintide is used in addition to insulin for patients who take insulin regularly but still need better blood sugar control. The FDA approved this drug in 2005 for adults with type 1 and type 2 diabetes. Pramlintide and insulin are the only two drugs approved for treatment of type 1 diabetes.

Pramlintide is a synthetic form of amylin, a hormone that is related to insulin. Side effects may include nausea, vomiting, abdominal pain, headache, fatigue, and dizziness. Patients with type 1 diabetes have an increased risk of severe low blood sugar (hypoglycemia) that may occur within 3 hours following a pramlintide injection. This drug should not be used if patients have trouble knowing when their blood sugar is low or have slow stomach emptying (gastroparesis).

Treatment of Complications

Treatment of Complications

High Blood Pressure and Heart Disease

All patients with diabetes and high blood pressure should adopt lifestyle changes. These include weight reduction (when needed), following the Dietary Approaches to Stop Hypertension (DASH) diet, smoking cessation, limiting alcohol intake, and limiting salt intake to no more than 1,500 mg of sodium per day.

High Blood Pressure Control. Strict control of blood pressure is critical for preventing complications of diabetes and has proven to improve survival rates. Patients should strive for blood pressure levels of less than 130/80 mm Hg (systolic/diastolic).

Patients with diabetes and high blood pressure need an individualized approach to drug treatment, based on their particular health profile. Dozens of anti-hypertensive drugs are available. The most beneficial fall into the following categories

- Diuretics rid the body of extra sodium (salt) and water. There are three main types of diuretics: Potassium-sparing, thiazide, and loop.
- Angiotensin-converting enzyme (ACE) inhibitors reduce the production of angiotensin, a chemical that causes arteries to narrow.

- Angiotensin-receptor blockers (ARBs) block angiotensin.
- Beta blockers block the effects of adrenaline and ease the heart's pumping action.
- Calcium-channel blockers (CCBs) decrease the contractions of the heart and widen blood vessels.

Nearly all patients who have diabetes and high blood pressure should take an ACE inhibitor (or ARB) as part of their regimen for treating their hypertension. These drugs help prevent kidney damage.[For more information, see *In-Depth Report* #14: High blood pressure.]

Improving Cholesterol and Lipid Levels. Abnormal cholesterol and lipid levels are common in diabetes. High LDL ("bad") cholesterol should always be lowered, but people with diabetes also often have additional harmful imbalances, including low HDL ("good") cholesterol and high triglycerides.

Adult patients should aim for LDL levels below 100 mg/dL, HDL levels over 50 mg/dL, and triglyceride levels below 150 mg/dL. Patients with diabetes and existing heart disease should strive for even lower LDL levels; the American Diabetes Association recommends LDL levels below 70 mg/dL for these patients.

Children should be treated for LDL cholesterol above 160 mg/dL, or above 130 mg/dL if they have other cardiovascular risk factors.

For medications, statins are the best cholesterol-lowering drugs. They include atorvastatin (Lipitor), lovastatin (Mevacor and generics), pravastatin (Pravachol), simvastatin (Zocor and generics), fluvastatin (Lescol), and rosuvastatin (Crestor). These drugs are very effective for lowering LDL cholesterol levels.

The primary safety concern with statins has involved myopathy, an uncommon condition that can cause muscle damage and, in some cases, muscle and joint pain. A specific myopathy called rhabdomyolysis can lead to kidney failure. People with diabetes and risk factors for myopathy should be monitored for muscle symptoms.

Although lowering LDL cholesterol is beneficial, statins are not as effective as other medications -- such as niacin and fibrates -- in addressing HDL and triglyceride imbalances. This is a common problem in type 2 diabetes. Combining a statin with one of these drugs may be helpful for people with diabetes who have heart disease, low HDL, and near-normal LDL levels. Although combinations of statins and fibrates or niacin increase the risk of myopathy, both combinations are considered safe if used with extra care.

Fibrates, such as gemfibrozil (Lopid) and fenofibrate (Tricor), are usually the second choice after statins. Niacin has the most favorable effect on raising HDL and lowering triglycerides of all the cholesterol drugs. However, some patients who take high-dose niacin can experience increased blood glucose levels. Moderate doses of niacin can control lipids without causing serious blood glucose problems. [For more information, see *In-Depth Report* #23: Cholesterol.]

Aspirin for Reducing the Risk for Blood Clots. Taking a daily aspirin reduces the risk for blood clotting and may help protect against heart attacks. The recommended dose is 75 - 162 mg/day. Patients with diabetes for whom aspirin is recommended include those who have:

- Age over 40 years old
- History of heart problems
- Family history of heart disease
- High blood pressure or elevated cholesterol and
- Smokers

Prevention and Treatment of Retinopathy

Prevention of Retinopathy. Fortunately, severe and even moderate vision loss is largely preventable with tight control of blood glucose levels. (Intense glucose control can cause early worsening of retinopathy, although this is nearly always counterbalanced by long-term benefits.) Tight control of blood pressure can also help protect against retinopathy. Aspirin therapy does not help prevent retinopathy.

Treatment of Retinopathy. Patients with severe diabetic retinopathy or macular edema (swelling of the retina) should see an eye specialist who is experienced in the management and treatment of diabetic retinopathy. Once damage to the eye develops, laser or photocoagulation eye surgery may be needed. Laser surgery can help reduce vision loss in high-risk patients.

Treatment of Foot Ulcers

About a third of foot ulcers will heal within 20 weeks with good wound care treatments. Some treatments are as follows:

- Antibiotics are generally given. In some cases, hospitalization and intravenous antibiotics for up to 28 days may be needed for severe foot ulcers.
- In virtually all cases, wound care requires debridement, which is the removal of injured tissue until only healthy tissue remains. Debridement may be accomplished using chemical (enzymes), surgical, or mechanical (irrigation) means.
- Hydrogels (such as Nu-Gel) may help soothe and heal ulcers.
- Felted foam may be helpful in healing ulcers on the sole of the foot. Felted foam uses a multi-layered foam pad over the bottom of the foot with an opening over the ulcer.

Other Treatments for Foot Ulcers. Doctors are also using or investigating other treatments to heal ulcers. These include:

- Administering hyperbaric oxygen (oxygen given at high pressure) is showing promise in promoting healing. It is generally reserved for patients with severe, full thickness diabetic foot ulcers that have not responded to other treatments, particularly when gangrene or an abscess is present.
- Total-contact casting (TCC) uses a cast that is designed to match the exact contour of the foot and distribute weight along the entire length of the foot. It is usually changed

weekly. It may be helpful for ulcer healing and for Charcot foot. Although it is very effective in healing ulcers, recurrence is common.

Treatment of Neuropathy

A number of different drugs are used for peripheral neuropathy pain relief: They include:

- Nonprescription analgesics, such as aspirin, acetaminophen, and non-steroidal anti-inflammatory drugs (NSAIDs). (Patients with stomach or kidney problems should check with their doctors before using these drugs.)
- Prescription painkillers, such as tramadol (Ultram). Tramadol is a drug that is similar to opioids. It can help relieve pain but has significant side effects, including nausea, constipation, and headache.
- Topical medications, particularly capsaicin (the active ingredient in hot peppers), are applied to the skin to relieve minor local pain. A 5% lidocaine patch has also shown good results in clinical trials.
- Tricyclic antidepressants, such as amitriptyline (Elavil) or doxepin (Sinequan), are effective in reducing pain from neuropathy in many patients. A combination of doxepin and capsaicin (applied to the skin) may also be helpful. Unfortunately, tricyclics may cause heart rhythm problems, so patients at risk need to be monitored carefully.
- Duloxetine (Cymbalta), a serotonin and norepinephrine reuptake inhibitor, is approved for treatment of pain associated with diabetic peripheral neuropathy.
- Anti-seizure drugs used for peripheral neuropathy pain relief include gabapentin (Neurontin), pregabalin (Lyrica), carbamazepine (Tegretol), and valproate (Depakote).

Although not proven to be beneficial, patients may also try transcutaneous electrostimulation (TENS), a treatment that involves administering mild electrical pulses to painful areas. Alternative treatments -- such as hypnosis, biofeedback, relaxation techniques, and acupuncture -- have also been reported to help some patients manage pain. Doctors also recommend lifestyle measures, such as walking and wearing elastic stockings.

Treatments for Other Complications of Neuropathy. Neuropathy also impacts other functions, and treatments are needed to reduce their effects. If diabetes affects the nerves in the autonomic nervous system, then abnormalities of blood pressure control and bowel and bladder function may occur. Erythromycin, domperidone (Motilium), or metoclopramide (Reglan) may be used to relieve delayed stomach emptying caused by neuropathy. Patients need to watch their nutrition if the problem is severe.

Erectile dysfunction is also associated with neuropathy. Studies indicate that phosphodiesterase type 5 (PDE-5) drugs, such as sildenafil (Viagra), vardenafil (Levitra), and tadalafil (Cialis), are safe and effective, at least in the short term, for many patients with diabetes. Typical side effects are minimal but may include headache, flushing, and upper respiratory tract and flu-like symptoms. Patients who take nitrate medications for heart disease cannot use PDE-5 drugs.

Treatment of Kidney Problems

Tight control of blood sugar and blood pressure is essential for preventing the onset of kidney disease. Strict control of these two conditions produces a reduction in new cases of nephropathy and a delay in progression of the disease.

ACE inhibitors are the best class of blood pressure medications for delaying kidney disease and slowing disease progression in patients with type 1 diabetes. Angiotensin-receptor blockers (ARBs) are also very helpful.

- For patients with diabetes who have microalbuminuria, the American Diabetes Association strongly recommends ACE inhibitors or ARBs. Microalbuminuria is an accumulation of protein in the blood, which can signal the onset of kidney disease (nephropathy).
- Nearly all patients who have diabetes and high blood pressure should take an ACE inhibitor (or ARB) as part of their regimen for treating their hypertension

A doctor may recommend a low-protein diet for patients whose kidney disease is progressing despite tight blood sugar and blood pressure control. Protein-restricted diets can help slow disease progression and delay the onset of end-stage renal disease (kidney failure). However, patients with end-stage renal disease who are on dialysis generally need higher amounts of protein. [For more information, see *In-Depth Report* #42: Diabetes diet.]

Anemia. Anemia is a common complication of end-stage kidney disease. Patients on dialysis usually need injections of erythropoiesis-stimulating drugs to increase red blood cell counts and control anemia. However, these drugs -- darbepoetin alfa (Aranesp) and epoetin alfa (Epogen and Procrit) -- can increase the risk of blood clots, stroke, heart attack, and heart failure in patients with end-stage kidney disease when they are given at higher than recommended doses.

The FDA recommends that patients with end-stage kidney disease who receive erythropoiesis-stimulating drugs should:

- Maintain hemoglobin levels between 10 - 12 g/dL
- Receive frequent blood tests to monitor hemoglobin levels
- Contact their doctors if they experience such symptoms as shortness of breath, pain, swelling in the legs, or increases in blood pressure

[For more information, see *In-Depth Report* #57: Anemia.]

Treatment of Diabetes During Pregnancy

Some recommendations for preventing pregnancy complications include:

- Intensive blood sugar control during pregnancy can reduce the risk for health complications for both mothers and babies. Doctors recommend that pregnant women with pre-existing diabetes monitor their blood sugar levels up to 8 times daily. This

includes checking your blood glucose before each meal, 1 - 2 hours after a meal, at bedtime, and possibly during the night.
- Insulin needs increase during the pregnancy, especially during the last 3 months. Your doctor may recommend increasing your insulin dosage during this time.
- Consult a registered dietician to help adjust your food plan during pregnancy.
- Low-impact aerobic exercise during pregnancy can lower glucose levels. (All pregnant women, particularly those with diabetes, should check with their doctors before embarking on a rigorous exercise regimen. This is especially important for women with eye, kidney, or high blood pressure or other heart problems.)
- To prevent birth defects that affect the heart and nervous system, women with diabetes should take a higher dose of folic acid from the time of conception up to week 12 of pregnancy. They should also be checked for any heart problems.
- Women with diabetes should have an eye examination during pregnancy and up to a year afterward.

Home Management

Glucose (Blood Sugar) Levels

Both low blood sugar (hypoglycemia) and high blood sugar (hyperglycemia) are of concern for patients who take insulin. It is important, therefore, to carefully monitor blood glucose levels. In general, patients with type 1 diabetes need to take readings four or more times a day. Patients should aim for the following measurements:

- Pre-meal glucose levels of 90 - 130 mg/dL
- Bedtime levels of 110 - 150 mg/dL

Different goals may be required for specific individuals, including pregnant women, very old and very young people, and those with accompanying serious medical conditions.

Finger-Prick Test. A typical blood sugar test includes the following:

- A drop of blood is obtained by pricking the finger.
- The blood is then applied to a chemically treated strip.
- Monitors read and provide results.

Home monitors are about 10 - 15% less accurate than laboratory monitors, and many do not meet the standards of the American Diabetes Association. Most doctors believe, however, that they are accurate enough to indicate when blood sugar is too low.

To monitor the amount of glucose within the blood a person with diabetes should test their blood regularly. The procedure is quite simple and can often be done at home.

Some simple procedures may improve accuracy:

- Testing the meter once a month.
- Recalibrating it whenever a new packet of strips is used.
- Using fresh strips; outdated strips may not provide accurate results.
- Keeping the meter clean.
- Periodically comparing the meter results with the results from a laboratory.

Supplementary Monitoring Devices. Other devices are available for monitoring blood glucose. These devices are used in addition to traditional fingerstick test kits, and glucose meters but do not replace them:

- Continuous glucose monitoring systems (CGMS) use a needle-like sensor inserted under the skin of the abdomen to monitor glucose levels every 5 minutes. In 2007, the STS-7 System was approved. Using a disposable sensor, the STS-7 measures glucose levels for up to a week. An alarm will sound if glucose levels are too high or low. The older Minimed system measures glucose over a 72-hour period and has wireless communication between the monitor and an insulin pump.
- GlucoWatch is a battery-powered wristwatch-like device that measures glucose by sending tiny electric currents through the skin, a technique called reverse iontophoresis. It is painless and has a warning device when detecting high glucose levels. It takes 2 hours to warm up, and the sensor pads need to be changed every day. Glucowatch measures glucose levels three times per hour for up to 12 hours. About a quarter of the time, the results differ significantly from actual fingerstick tests, however.

Glycosylated Hemoglobin

Hemoglobin A1c (also called HbA1c , HA1c, or A1C) is measured periodically every 2 - 3 months, or at least twice a year, to determine the average blood-sugar level over the lifespan of the red blood cell. While fingerprick self-testing provides information on blood glucose for that day, the HbA1c test shows how well blood sugar has been controlled over the period of several months. For most people with well-controlled diabetes, HbA1c levels should be below 7%. Home tests are available for measuring A1C but they tend not to be as accurate as the laboratory tests ordered by doctors.

Urine Tests

Urine tests are useful for detecting the presence of ketones. These tests should always be performed during illness or stressful situations, when diabetes is likely to go out of control. The patient should also undergo yearly urine tests for microalbuminuria (small amounts of protein in the urine), a risk factor for future kidney disease.

Preventing Hypoglycemia

The following tips may help avoid hypoglycemia or prepare for attacks.

- Bedtime snacks are advisable if blood glucose levels are below 180 mg/dL (10 mmol/L). Protein snacks may be best.
- Some research has suggested that children (particularly thin children) are at higher risk for hypoglycemia because the injection goes into muscle tissue. Pinching the skin so that only fat (and not muscle) tissue is gathered or using shorter needles may help.
- Various insulin regimens are available that can reduce the risk. For example, taking a fast-acting insulin (insulin lispro) before the evening meal may be particularly helpful in preventing hypoglycemia at bedtime or during the night.
- Patients who intensively control their blood sugar should monitor blood levels as often as possible, four times or more per day. This is particularly important for patients with hypoglycemia unawareness.
- In adults, it is particularly critical to monitor blood glucose levels before driving, when hypoglycemia can be very hazardous.
- Patients who are at risk for hypoglycemia should always carry hard candy, juice, sugar packets, or commercially available glucose substitutes.

Family and friends should be aware of the symptoms and be prepared:

- If the patient is helpless (but not unconscious), family or friends should administer three to five pieces of hard candy, two to three packets of sugar, half a cup (four ounces) of fruit juice, or a commercially available glucose solution.
- If there is inadequate response within 15 minutes, the patient should receive additional sugar by mouth and may need emergency medical treatment, possibly including an intravenous glucose solution.
- Family members and friends can learn to inject glucagon, a hormone, which, in contrast to insulin, raises blood glucose.

Patients with type 1 diabetes should always wear a medical alert ID bracelet or necklace that states that they have diabetes and take insulin.

Foot Care

Measures to Prevent Foot Ulcers. Preventive foot care can significantly reduce the risk of ulcers and amputation. Some tips for preventing problems include:

- Patients should inspect their feet daily and watch for changes in color or texture, odor, and firm or hardened areas, which may indicate infection and potential ulcers.
- When washing the feet, the water should be warm (not hot) and the feet and areas between the toes should be thoroughly dried afterward. Check water temperature with the hand or a thermometer before stepping in.
- Apply moisturizers, but NOT between the toes.

- Gently use pumice to remove corns and calluses (patients should not use medicated pads or try to shave the corns or calluses themselves).
- Trim toenails short and file the edges to avoid cutting adjacent toes.
- Well-fitting footwear is very important. People should be sure the shoe is wide enough. Patients should also avoid high heels, sandals, thongs, and going barefoot. Shoes with a rocker sole reduce pressure under the heel and front of the foot and may be particularly helpful. Custom-molded boots increase the surface area over which foot pressure is distributed. This reduces stress on the ulcers and allows them to heal.
- Change shoes often during the day.
- Wear socks, particularly with extra padding (which can be specially purchased).
- Patients should avoid tight stockings or any clothing that constricts the legs and feet.
- Consult a specialist in foot care for any problems.

Transplantation Procedures

Islet-Cell Transplantation

Major advances in islet-cell transplantation are allowing more patients to come off insulin or reduce their use of it.

Major clinical trials are now using an investigational specific islet-cell (also called beta-cell) transplantation procedure called the Edmonton protocol, which usually involves the following steps:

- As soon as there are sufficient numbers of islets available for transplantation, the patient is given intravenous antibiotics and oral vitamins E, B6, and A.
- A machine isolates islet cells taken from donor pancreases, generally from cadavers. Two or three organs are usually needed in order to supply enough islet cells to have any effect on insulin production. (This is a major limitation of the procedure.)
- Once the islets have been isolated, they are injected directly in a major vein in the patient's liver.
- The islets are carried to capillaries in the liver where they produce insulin.
- Specific drugs, such as tacrolimus, sirolimus, or rapamycin (Rapamume), are used to suppress the immune system. (Unlike immunosuppressant drugs used in other transplantation procedures, these drugs do not contain steroids, which destroy islet cells.) Immunosuppressants are needed for the rest of the patient's life so that the body does not reject these foreign islet cells.
- The procedure has to be performed two or more times over a period of 2 - 3 months. This generally requires multiple pancreas donors in order to achieve complete independence from insulin therapy. This is a major limitation to the procedure.

This procedure is still investigational but has helped some patients with severe type 1 diabetes to become free of insulin injections. However, many of these insulin-independent patients needed to resume insulin injections within 2 years. Researchers are continuing to work on refining the Edmonton protocol so that its benefits can be more sustainable and long lasting.

A major obstacle for the islet cell transplantation is the need for two or more donor pancreases to supply sufficient islet cells. Unfortunately, there are not enough pancreases available to make this procedure feasible for even 1% of patients. Researchers are looking for alternative approaches including the use of umbilical cord cells, embryonic or adult stem cells, bone marrow transplantation, and other types of cellular therapies. These studies are still in very early stages, but researchers predict that there will be major advances in these fields in the coming years.

Organ Transplantation

Whole pancreas transplants and double transplants of pancreases and kidneys are proving to have a good long-term success rate for some patients with type 1 diabetes. The operations help to prevent further kidney damage, and long-term studies indicate that they may even eventually reverse some existing damage. There is some evidence that heart disease and diabetic neuropathy improve after pancreas transplantation (although not retinopathy). However, this procedure has significant surgical and postsurgical complications in patients with diabetes. One 10-year study reported that survival rate at 10 years was 76%, and two-thirds of the patients had both pancreas and kidney function. Immunosuppressive drugs are needed lifelong with this procedure. Doctors generally recommend transplants in cases of end-stage kidney failure or when diabetes poses more of a threat to the patient's life than the transplant itself.

Uncontrolled diabetes causes damage to many tissues of the body, including the kidneys. Kidney damage caused by diabetes most often involves thickening and hardening of the internal kidney structures. Strict blood glucose control may delay the progression of kidney disease in type 1 and type 2 diabetics.

Resources

- www.diabetes.org -- American Diabetes Association
- www.niddk.nih.gov -- National Institute of Diabetes and Digestive and Kidney Diseases
- www.jdrf.org -- Juvenile Diabetes Research Foundation
- www.nei.nih.gov -- National Eye Institute
- www.eatright.org -- American Dietetic Association
- www.kidney.org -- National Kidney Foundation
- www.diabetestrialnet.org -- Type 1 Diabetes International Clinical Trial Net
- www.medicalert.org -- Bracelets or neck chain emblems with personal medical information
- www.childrenwithdiabetes.com -- Children with diabetes online community