BIOTECH Basics
Diabetes

What you need to know:

- There are several types of diabetes, each with different causes, treatments and outcomes, but all characterized by high blood sugar.
- Type 1 diabetes is an auto-immune disease with no cure.
- 285 million people worldwide live with diabetes, with 349 million expected by 2030.
- About 90-95 percent of people living with diabetes have type 2 and 5-10 percent have type 1.
- Diabetes is the fifth leading cause of death in the world. More than $174 billion is spent in direct and indirect costs associated with diabetes.

Introduction to diabetes

Diabetes is a disorder of metabolism, affecting the way the body uses food for energy. There are several types of diabetes with different causes, treatments and outcomes, but each type of diabetes is characterized by high blood glucose, or high blood sugar. These include type 1, type 2, type 1.5 or latent autoimmune diabetes of adults, gestational diabetes and MODY (maturity-onset diabetes of the young). There is no cure for diabetes, though some forms can be managed through diet and exercise, oral medication or insulin injections.

It's estimated that more than 285 million people worldwide live with diabetes and that number is predicted to reach 349 million by 2030. Diabetes is the fifth leading cause of death in the world, and it's estimated that $174 billion is spent in direct and indirect costs associated with diabetes. In America, 25 million people live with a form of diabetes – roughly 1 in 4 adults. About 90-95 percent of diabetics live with type 2 diabetes while 5-10 percent live with type 1 diabetes.

Understanding glucose metabolism

The body's glucose levels, or blood sugar levels, rise naturally from eating and the body's beta cells in the pancreas release insulin which stabilizes those blood sugar levels. Insulin "opens" the receptor molecules on cells so glucose enters and is converted into energy. In the liver, glucose units are assembled into glycogen. A variety of things cause a person's glucose levels to drop including exercise or minor illnesses. When glucose concentrations fall below a specific level, another type of pancreatic cells release the hormone glucagon. Glucagon causes liver cells to break up glycogen which produces multiple glucose units that enter the bloodstream and are passed to other body cells for energy.

Types

Type 1 diabetes, also known as juvenile diabetes, is an auto-immune disease. The body attacks and kills the insulin-producing beta cells so no insulin is produced. The immune system is constantly balancing between attacking what it perceives to be foreign invaders and suppressing those attacks. Too much suppression risks allowing infectious agents unrestricted access to the body or allowing cancer cells to escape detection. In contrast, constant attacking can destroy the body's own cells, as occurs in an auto-immune disease like type 1 diabetes. The immune system has several players in the defense process, many being designed to recognize a different foreign invader. This provides immunity to a broad spectrum of potential pathogens. Some components of the immune system go through a "training process" in the thymus to select against those defenders that recognize and improperly attack "self" proteins. In autoimmune disorders like type 1 diabetes, this selection process is incomplete or weakened – the immune system misrecognizes self proteins as foreign and mounts an attack, over time destroying that part of the body.

In the past, type 1 diabetes was more commonly diagnosed in children, but it can be diagnosed at any age. This form of diabetes is not something a person can outgrow, and it cannot be managed with diet alone. A person with type 1 diabetes will always be required to take a synthetic form of the insulin. More than 85 percent of all people living with type 1 diabetes are adults and about 10 percent of all diabetes cases are type 1.

Type 2 diabetes, or adult onset diabetes, is the most common form of diabetes. When a person develops type 2 diabetes, cells become resistant to the effect of insulin. The pancreas produces more insulin to compensate and ultimately, the pancreas stops making insulin altogether, causing blood glucose levels to rise and complications to appear. Sometimes, improvements in diet and exercise can achieve good results in the first few years after a type 2 diabetes diagnosis. In some cases, weight loss and exercise reduce insulin resistance. Diet plus exercise can often reduce the progression from prediabetes to diabetes. A prescription drug is often required to help stabilize blood sugar levels. There is no cure for type 2 diabetes, but in cases where weight management and dietary modifications stabilize a person's blood sugar levels, the symptoms of type 2 diabetes will return if a person regains lost weight or reverts back to unhealthy eating habits. Like type 1 diabetes, the disease requires constant attention and management.

Type 1.5 diabetes or LADA is a relatively new term but reflects the slow onset of type 1 diabetes in adults. Often, adults are misdiagnosed with type 2 diabetes when in fact, they have type 1.5. This form of diabetes is also an auto-immune disease. The person's body still makes insulin, but at some point, it will stop. Not all people diagnosed with type 1.5 diabetes will immediately require insulin, but as beta cells are destroyed slowly, the person will eventually become insulin-dependent.

During pregnancy, some women develop a form of diabetes called gestational diabetes. In most cases, after the child is born, blood sugar levels return to normal. Having gestational diabetes does increase the mother's risk for developing type 1 or type 2 diabetes later in life.

For more information:

JDRF, formerly Juvenile Diabetes Research Foundation – information on type 1 diabetes research initiatives, treatment options, mentoring possibilities and local support groups
www.jdrf.org/index.cfm?page_id=101006

ADA, American Diabetes Association – information on type 1 and type 2 diabetes treatment, complications, health insurance options, discrimination and legal advice
www.diabetes.org/living-with-diabetes/treatment-and-care/?loc=DropDownLWD-treatment

National Diabetes Information Clearinghouse, organized by NIH – easy-to-read information focusing on new research and current findings related to awareness and preventions
http://diabetes.niddk.nih.gov/dm/pubs/overview/

Incidence of diabetes in the U.S.

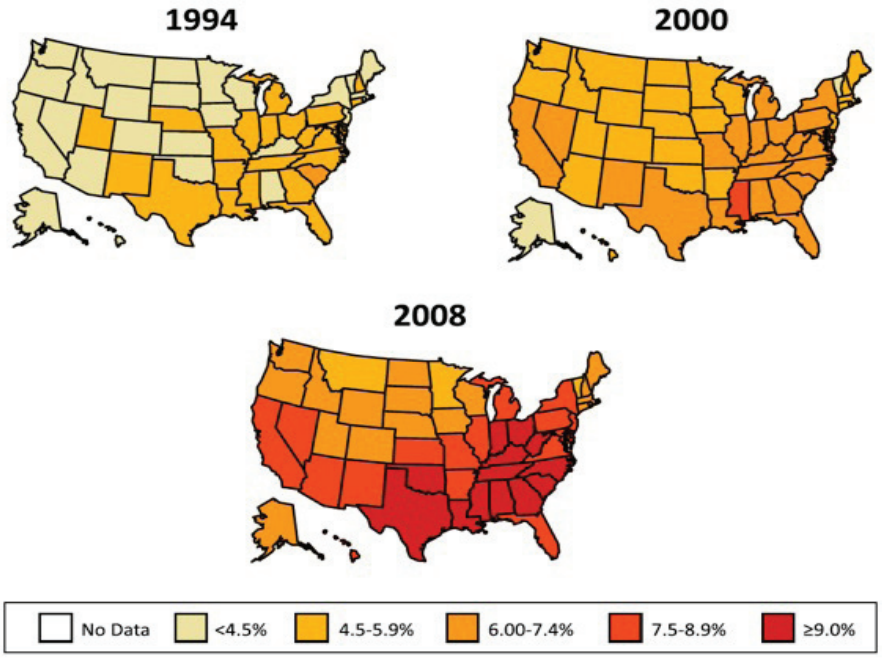


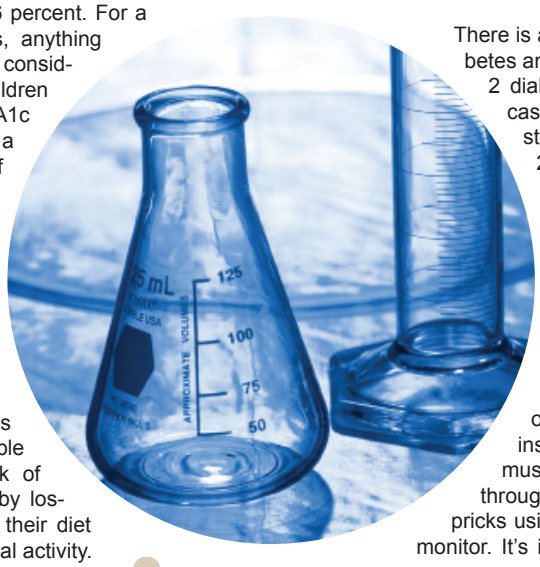
Figure 1: *source: cdc.gov/diabetes/statistics*

Diagnosis

To diagnose diabetes, doctors look for elevated plasma glucose levels. This can be measured in a number of ways. Doctors may check blood sugar levels in the morning hours after overnight fasting. Normal fasting blood sugar level is between 70-99 milligrams/deciliter. A fasting blood sugar level of 100-125 mg/dL is a sign of prediabetes (a transitional stage that precedes diabetes), and levels higher than 126 mg/dL are consistent with diabetes. Blood sugar levels may also be tested after eating - commonly referred to as an oral glucose tolerance test. With this approach, normal blood sugar ranges between 70-145 mg/dL. If higher than 200 mg/dL, diabetes is diagnosed.

A blood test called the glycosolated hemoglobin, also known as the HbA1c or A1c test, is another indicator of diabetes. The A1c test measures the percentage of hemoglobin that contains a bound glucose molecule in the blood. It reflects the average blood glucose concentration during the past 2-3 months. The normal A1c range for a non-diabetic is between 4-6 percent. For a person with diabetes, anything below 7 percent is considered normal. In children with type 1 diabetes, A1c readings can range a bit higher because of various outside factors.

Patients are often diagnosed with prediabetes when blood glucose levels or A1c levels are higher than normal, but not high enough to be diagnosed as diabetes. Many people can reduce their risk of developing diabetes by losing weight, changing their diet and increasing physical activity.



Complications

Short-term complications from diabetes include high blood sugar or hyperglycemia and low blood sugar or hypoglycemia. If a person's blood sugar remains high for an extended period of time, they can develop diabetic ketoacidosis, or DKA. Symptoms of DKA include deep, rapid breathing, dry skin and mouth, flushed face, fruity-smelling breath, nausea and vomiting, stomach pain or decreased consciousness.

Long term complications include cardiovascular disease, stroke, high blood pressure, kidney disease or nephropathy, blindness or diabetic retinopathy, nerve damage or neuropathy, ulcerations, amputation and pregnancy complications. Diabetics have a 2-4 times higher risk of heart disease and strokes. The complications of diabetes, if left untreated, can lower life expectancy by up to 15 years.

Treatments

There is a link between type 2 diabetes and obesity, but not all type 2 diabetics are overweight. In cases where a person's lifestyle contributes to type 2 diabetes, a change in activity and diet can help a person manage blood sugar levels. In other cases, a change in lifestyle as well as oral medication is required. For type 1 diabetics, insulin in required through multiple daily injections or through an external insulin pump. All diabetics must test blood sugar levels through multiple daily finger pricks using a small blood glucose monitor. It's important for diabetics to keep an eye on blood pressure and lipid levels as well as look for other signs of complications.

Genetics and Environmental Risks

Until recently, the genetic basis underlying most forms of diabetes was unknown. Mutations in a few genes had been identified in rare forms of diabetes, but the genetic contributions for types 1 and 2 remained a mystery. It is likely that both forms of diabetes are caused by a combination of multiple small genetic changes that lead to disease only in the presence of risk-increasing environments. Thanks to high-throughput approaches like genome-wide association studies, the genetic players are beginning to surface. More than 50 genes have been linked to type 1 diabetes. Not surprisingly, most are associated with the development and maintenance of the immune system. Clinicians are beginning to combine this genetic information with other risk factors, such as the presence of autoantibodies, to identify individuals who are at the greatest risk of developing type 1 diabetes. As prevention and treatment options continue to emerge, this class of individuals is the first group to target.

Several genetic risk factors have also been identified for type 2 diabetes. Early indications suggest that many of these are associated with the declining function of the beta cells in response to increased insulin sensitivity. The genes identified to date represent only a small percentage of the expected overall genetic contribution. This points to the presence of a number of yet-unidentified genes - each contributing only modestly to overall disease risk. The advent of whole genome and/or whole exome sequencing is expected to speed the discovery of this large group of risk factors.

Scientists are also researching environmental risks and what roles they play in developing diabetes. Preliminary evidence has highlighted viral infections, stress, exposure to pets and other allergens, and maternal weight gain around pregnancy for type 1 diabetes. Obesity and the presence of specific intestinal bacteria have been implicated in type 2 diabetes. These do not represent the full total of all risk factors and none of the risks is, by itself, sufficient to develop diabetes.

Diabetes requires continual monitoring, across multiple aspects of daily life. Affected individuals must read food labels and know what ingredients are in the foods they consume. They must track their activities and pay particular attention to the signals being sent by their bodies. Even so, with proper care and treatment, individuals impacted by diabetes live full and productive lives.

- Dr. Neil Lamb
director of educational outreach
HudsonAlpha Institute for Biotechnology

- Victoria Cumbow
communications specialist
HudsonAlpha Institute for Biotechnology
type 1 diabetic and patient blogger
at victoriacumbow.com