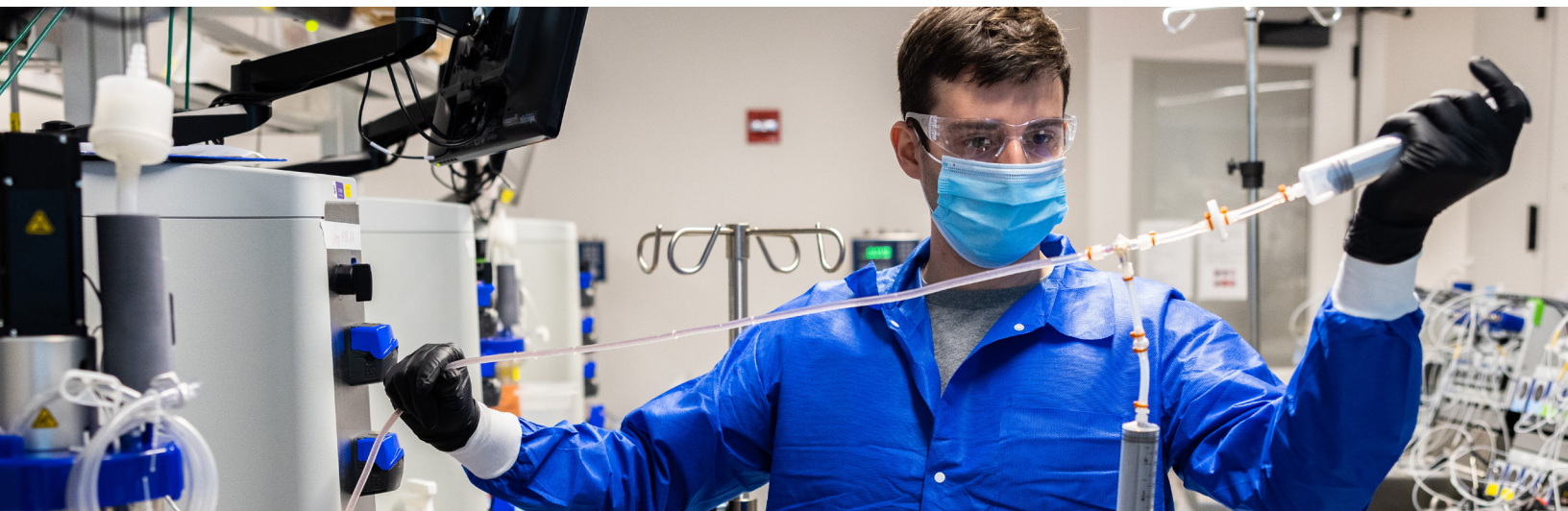




## Disease Education: Type 1 Diabetes

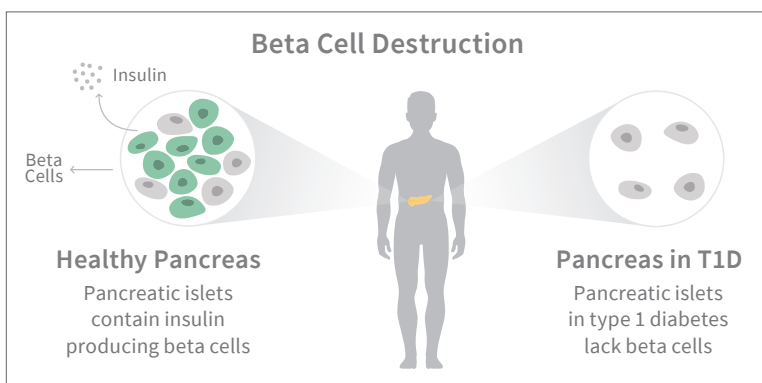




## What is type 1 diabetes (T1D)?

T1D is a lifelong disease caused by the autoimmune destruction of insulin-producing islet cells (beta cells) in the pancreas. This leads to a loss of insulin production and abnormal glucose (blood sugar) regulation. Genetic and environmental factors are thought to play a role in development of T1D, but the exact triggers for autoimmune cell destruction are not known and factors may vary between individuals.

When beta cells function normally, they produce insulin to respond to increases in blood sugar (e.g., after eating) as well as to maintain normal blood sugar (e.g. during sleep and between meals). The absence of beta cells results in insufficient insulin, which leads to abnormalities in how the body processes nutrients and can lead to acute symptoms from the accumulation of sugar in the blood.



*For illustrative purposes*

Treatment of T1D relies upon exogenous insulin administered through regular injections or device-based approaches such as insulin pumps. Despite being a life-saving drug, insulin has a narrow therapeutic window and hence requires careful monitoring of blood sugar levels throughout the day and night to avoid the consequences of both high and low blood sugar levels. This challenge imposes a significant burden for people living with T1D, as well as their caregivers.

## What is insulin?

Insulin is a hormone produced in the beta cells located in the islets of Langerhans in the pancreas, that plays a crucial role in the body, enabling transport of glucose and other nutrients into cells. Insulin was discovered as a life-saving therapy for type 1 diabetes over a century ago, in 1921, and administered for the first time in 1922.

Insulin was originally derived from the pancreases of cows and pigs. Today, insulin is made synthetically in both bacteria and yeast. Innovations over the last century have focused on improving the production and delivery of insulin, but patients continue to face relentless daily management of the disease.

## Insulin basics



Insulin is made in a lab, harvested and purified from different source materials.



Insulin is integral to managing type 1 diabetes today.

## What is the patient experience?

People with T1D can be diagnosed in childhood or adulthood. Due to high blood sugar levels, people with T1D develop symptoms including increased thirst or hunger, frequent urination and weight loss. In the body's attempt to compensate for the inability to use blood glucose for energy, muscle and fat are broken down, leading to muscle wasting and buildup of toxic ketones in the blood. This can result in diabetic ketoacidosis, which can be life-threatening.



Increased Thirst/Hunger



Excessive Urination



Unexplained Weight Loss

If type 1 diabetes is suspected, blood tests are used to assess blood sugar (glucose) levels, auto-antibodies and/or C-peptide levels (a biomarker of insulin production) are checked to confirm the diagnosis.

There is currently no cure for type 1 diabetes, and living with diabetes requires lifelong treatment. People with type 1 diabetes need to give themselves multiple injections of insulin per day or wear an insulin pump at all times and check their blood sugar frequently.

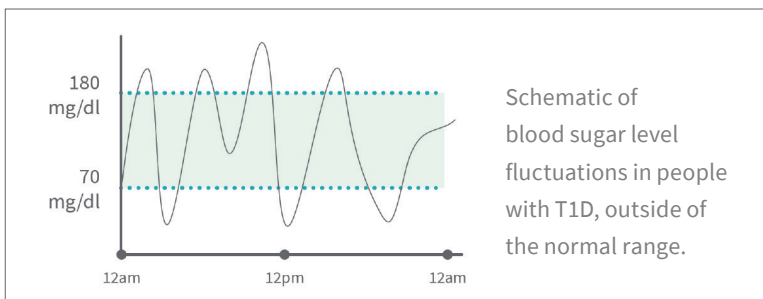


Monitoring Blood Sugar



Insulin Use

The goal of diabetes management is to maintain a healthy blood sugar range to avoid complications. Insulin administration aims to reduce chronic exposure to higher than normal levels of blood sugar, which are associated with the development of long-term multi-organ complications (see column at right). However, an excess of insulin can result in low blood sugar (hypoglycemia). Reduced glucose supply to the central nervous system can cause tremors, shaking, confusion and sweating. If untreated, blood glucose can fall to dangerously low levels resulting in coma, convulsions and even death. Therefore, living with T1D is a constant balancing act, imposing a lifelong emotional and physical burden on patients and their families.



People with type 1 diabetes are also at an increased risk for cardiovascular disease and have a reduced life expectancy. Uncontrolled high blood sugar levels can, over a lifetime, result in kidney failure leading to dialysis and kidney transplant, eye problems leading to blindness and nerve problems leading to potential complications that could result in lower limb amputations.



Kidney Disease



Eye Disease



Heart Disease



Nerve Problems



## FAQ

### What is type 1 diabetes?

T1D results from the autoimmune destruction of insulin-producing islet cells in the pancreas, leading to loss of insulin production and impairment of blood glucose control. The absence of insulin leads to abnormalities in how the body processes nutrients, leading to high blood glucose levels. If glucose levels are not appropriately managed, over time they can lead to complications such as kidney disease/failure, eye disease (including vision loss), heart disease, stroke, nerve damage and even death.

Due to the limitations and complexities of insulin delivery systems, it can be difficult for patients to achieve and maintain balance in glucose control with T1D. Hypoglycemia often results because of the difficulty in balancing the different factors that impact glucose levels, including insulin, diet and exercise. Hypoglycemia remains a critical limiting factor in glycemic management, and severe hypoglycemia can cause loss of consciousness, coma, seizures, injury and can be fatal. Over time, patients with T1D can develop impaired awareness of hypoglycemia, meaning they are no longer able to perceive the early signs of a hypoglycemic event, which can be dangerous and result in life-threatening events.

Current standards of care do not address the underlying cause of the disease, the destruction of the pancreatic islet cells, and there are limited treatment options beyond insulin for the management of T1D. There is currently no cure for type 1 diabetes.

### How is T1D diagnosed?

T1D may be diagnosed after an individual develops symptoms such as excessive hunger, increased thirst, increased urination, blurred vision, fatigue and weight loss. A person may develop ketoacidosis which can lead to coma. If type 1 diabetes is suspected, the diagnosis is often made by testing for glucose in the blood or urine. Islet autoantibody or C-peptide level tests can be performed in order to assist in the diagnosis of type 1 diabetes.

### What are islets?

Islets are the clusters of cells within the pancreas that produce hormones such as insulin made by beta cells and glucagon made by alpha cells – two essential hormones for the regulation of blood sugar levels.

### What is a c-peptide?

C-peptide (connecting peptide of the proinsulin molecule) is a polypeptide that is produced when insulin is made by the islet cells in equal proportion to insulin. C-peptide is not included in exogenous insulin that is injected, and therefore can be used to assess the amount of insulin production from the islets. As insulin is secreted in response to a meal, c-peptide can be used as a surrogate to evaluate stimulated insulin secretion during a controlled setting using a mixed meal tolerance test. A low level of C-peptide indicates that a low level of insulin is being made by cells in the body, which is what is observed chronically in people with T1D. A fasting value of <200 pmol/L is used as a threshold value in the diagnosis of T1D.

### What is the difference between type 1 and type 2 diabetes?

T1D is caused by the destruction of insulin-producing pancreatic islet cells leading to insulin deficiency and abnormal glucose regulation, and accounts for 5 to 10% of all diabetes. In contrast, type 2 diabetes is characterized by progressive islet cell dysfunction and loss of adequate insulin secretion, frequently on the background of insulin resistance.