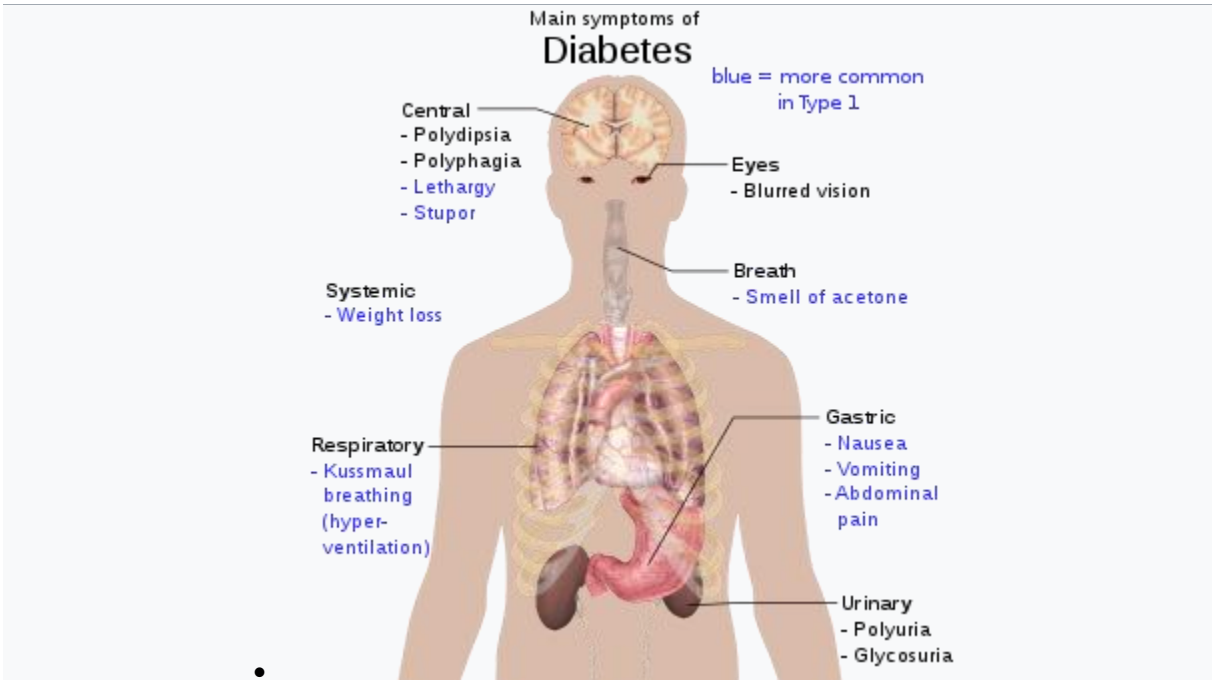
Diabetes Mellitus

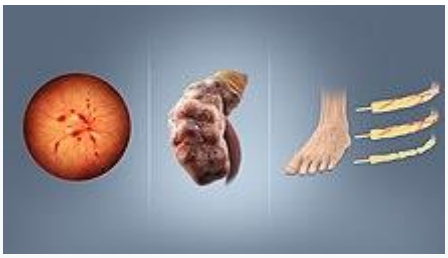
Diabetes, also known as **diabetes mellitus**, is a group of metabolic disorders characterized by a high blood sugar level (hyperglycemia) over a prolonged period of time. Symptoms often include frequent urination, increased thirst and increased appetite.

- Type 1 diabetes results from failure of the pancreas to produce enough insulin due to loss of beta cells. This form was previously referred to as "insulin-dependent diabetes mellitus" or "juvenile diabetes".
- Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" or "adult-onset diabetes".
- Gestational diabetes is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels. In women with gestational diabetes, blood sugar usually returns to normal soon after delivery. However, women who had gestational diabetes during pregnancy have a higher risk of developing type 2 diabetes later in life

- **Signs and symptoms**

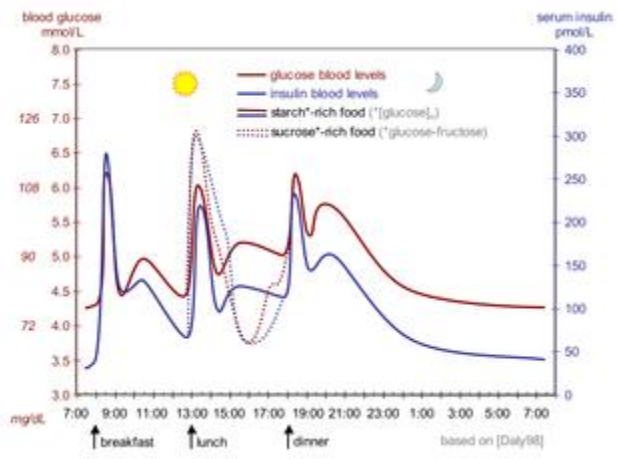


Complications[edit]

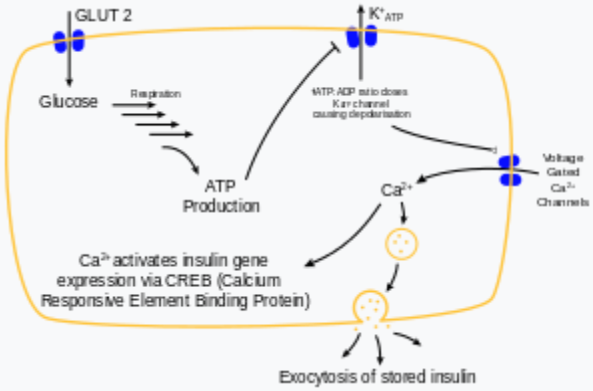


Retinopathy, nephropathy, and neuropathy are potential complications of diabetes

Pathophysiology[edit]



The fluctuation of blood sugar (red) and the sugar-lowering hormone insulin (blue) in humans during the course of a day with three meals. One of the effects of a sugar-rich vs a starch-rich meal is highlighted.



Mechanism of insulin release in normal pancreatic beta cells. Insulin production is more or less constant within the beta cells. Its release is triggered by food, chiefly food containing absorbable glucose.

Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle, except smooth muscle, in which insulin acts via the IGF-1.[*citation needed*] Therefore, deficiency of insulin or the insensitivity of its receptors play a central role in all forms of diabetes mellitus.

The body obtains glucose from three main sources: the intestinal absorption of food; the breakdown of glycogen (glycogenolysis), the storage form of glucose found in the liver; and gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body. insulin plays a critical role in regulating glucose levels in the body. Insulin can inhibit the breakdown of glycogen or the process of gluconeogenesis, it can stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen.

Insulin is released into the blood by beta cells (β-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. This process is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin.[87]

If the amount of insulin available is insufficient, or if cells respond poorly to the effects of insulin (insulin resistance), or if the insulin itself is defective, then glucose is not absorbed properly by the body cells that require it, and is not stored appropriately in the liver and muscles. The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as metabolic acidosis in cases of complete insulin deficiency.

When glucose concentration in the blood remains high over time, the kidneys reach a threshold of reabsorption, and the body excretes glucose in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume is replaced osmotically from water in body cells and other body compartments, causing dehydration and increased thirst (polydipsia). In addition, intracellular glucose deficiency stimulates appetite leading to excessive food intake (polyphagia).

Diagnosis

- Fasting plasma glucose level ≥ 7.0 mmol/L (126 mg/dL).
- Plasma glucose ≥ 11.1 mmol/L (200 mg/dL) two hours after a 75 gram oral glucose load as in a glucose tolerance test (OGTT)
- Glycated hemoglobin (HbA_{1C}) ≥ 48 mmol/mol (≥ 6.5 DCCT %)

Medication

Insulin

Insulin is the most common type of medication used in type 1 diabetes treatment.

Insulin is also used in type 2 diabetes treatment. It's given by injection and comes in different types. The type of insulin you need depends on how severe your insulin depletion is.

Options include:

Short-acting insulin

- regular insulin (Humulin and Novolin)

Rapid-acting insulins

- insulin aspart (NovoLog, FlexPen, Fiasp)
- insulin glulisine (Apidra)
- insulin lispro (Humalog)

Intermediate-acting insulin

- insulin isophane (Humulin N, Novolin N)

Long-acting insulins

- insulin degludec (Tresiba)
- insulin detemir (Levemir)
- insulin glargine (Lantus)
- insulin glargine (Toujeo)

Combination insulins

- NovoLog Mix 70/30 (insulin aspart protamine-insulin aspart)
- Humalog Mix 75/25 (insulin lispro protamine-insulin lispro)

- Humalog Mix 50/50 (insulin lispro protamine-insulin lispro)
- Humulin 70/30 (human insulin NPH-human insulin regular)
- Novolin 70/30 (human insulin NPH-human insulin regular)
- Ryzodeg (insulin degludec-insulin aspart)

Amylinomimetic drug

Pramlintide (SymlinPen 120, SymlinPen 60) is an amylinomimetic drug. It's an injectable drug used before meals.

It works by delaying the time your stomach takes to empty itself. It reduces glucagon secretion after meals. This lowers your blood sugar.

It also reduces appetite through a central mechanism.

Biguanides

Biguanides decrease how much sugar your liver makes. They decrease how much sugar your intestines absorb, make your body more sensitive to insulin, and help your muscles absorb glucose.

The most common biguanide is metformin (Glucophage, Metformin Hydrochloride ER, Glumetza, Riomet, Fortamet).

Metformin can also be combined with other drugs for type 2 diabetes. It's an ingredient in the following medications:

Dopamine agonist

Bromocriptine (Cycloset) is a dopamine agonist.

Dipeptidyl peptidase-4 (DPP-4) inhibitors

DPP-4 inhibitors help the body continue to make insulin. They work by reducing blood sugar without causing hypoglycemia (low blood sugar).

These drugs can also help the pancreas make more insulin. These drugs include:

- alogliptin (Nesina)
- alogliptin-metformin (Kazano)
- alogliptin-pioglitazone (Oseni)
- linagliptin (Tradjenta)
- linagliptin-empagliflozin (Glyxambi)
- linagliptin-metformin (Jentadueto)
- saxagliptin (Onglyza)
- saxagliptin-metformin (Kombiglyze XR)
- sitagliptin (Januvia)
- sitagliptin-metformin (Janumet and Janumet XR)
- sitagliptin and simvastatin (Juvisync)

Glucagon-like peptide-1 receptor agonists (GLP-1 receptor agonists)

These drugs are similar to the natural hormone called incretin.

They increase B-cell growth and how much insulin your body uses. They decrease your appetite and how much glucagon your body uses. They also slow stomach emptying.

These are all important actions for people with diabetes.

For some people, atherosclerotic cardiovascular disease, heart failure, or chronic kidney disease may predominate over their diabetes. In these cases, the American Diabetes Association (ADA) recommends certain GLP-1 receptor agonists as part of an antihyperglycemic treatment regimen.

These drugs include:

- albiglutide (Tanzeum)
- dulaglutide (Trulicity)
- exenatide (Byetta)
- exenatide extended-release (Bydureon)
- liraglutide (Victoza)
- semaglutide (Ozempic)

Meglitinides

These medications help your body release insulin. However, in some cases, they may lower your blood sugar too much.

These drugs aren't for everyone. They include:

- nateglinide (Starlix)
- repaglinide (Prandin)
- repaglinide-metformin (Prandimet)

Sodium-glucose transporter (SGLT) 2 inhibitors

Sodium-glucose transporter (SGLT) 2 inhibitors work by preventing the kidneys from holding on to glucose. Instead, your body gets rid of the glucose through your urine.

In cases where atherosclerotic cardiovascular disease, heart failure, or chronic kidney disease predominate, the ADA recommends SGLT2 inhibitors as a possible treatment option.

- dapagliflozin (Farxiga)
- dapagliflozin-metformin (Xigduo XR)
- canagliflozin (Invokana)
- canagliflozin-metformin (Invokamet)
- empagliflozin (Jardiance)
- empagliflozin-linagliptin (Glyxambi)
- empagliflozin-metformin (Synjardy)
- ertugliflozin (Steglatro)

Sulfonylureas

These are among the oldest diabetes drugs still used today. They work by stimulating the pancreas with the help of beta cells. This causes your body to make more insulin.

These drugs include:

- glimepiride (Amaryl)

- glimepiride-pioglitazone (Duetact)
- glimepiride-rosiglitazone (Avandaryl)
- gliclazide
- glipizide (Glucotrol)
- glipizide-metformin (Metaglip)
- glyburide (DiaBeta, Glynase, Micronase)
- glyburide-metformin (Glucovance)
- chlorpropamide (Diabinese)
- tolazamide (Tolinase)
- tolbutamide (Orinase, Tol-Tab)

Thiazolidinediones

- rosiglitazone (Avandia)
- rosiglitazone-glimepiride (Avandaryl)
- rosiglitazone-metformin (Amaryl M)
- pioglitazone (Actos)
- pioglitazone-alogliptin (Oseni)
- pioglitazone-glimepiride (Duetact)
- pioglitazone-metformin (Actoplus Met, Actoplus Met XR)

.