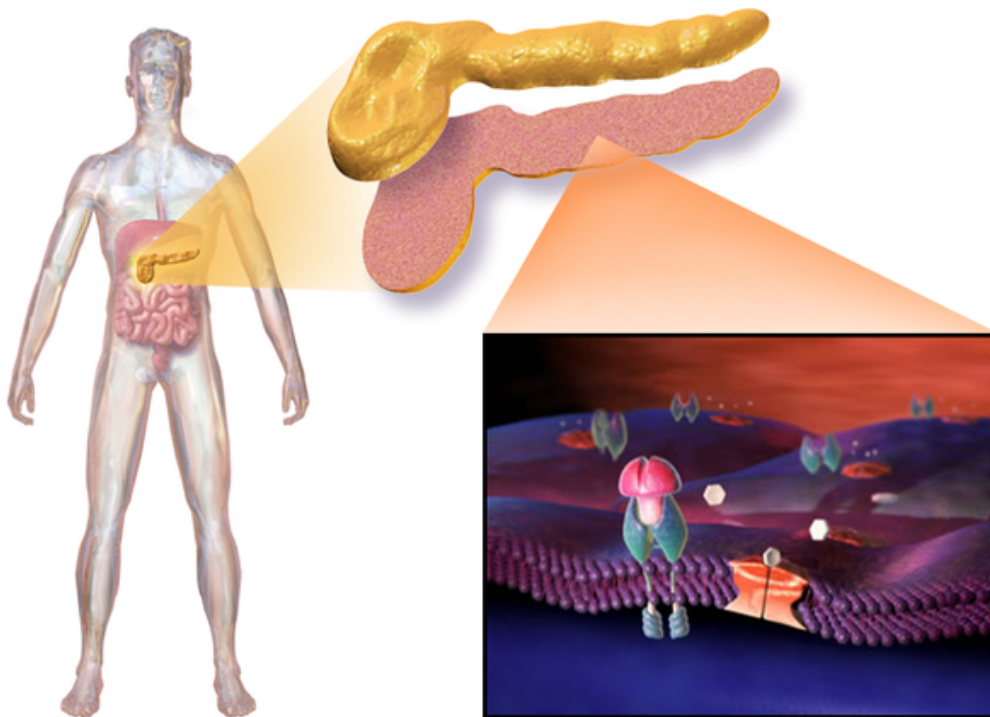


Types of Diabetes: Types 1, 2, and Gestational Diabetes

[See online here](#)

Early diagnosis is important to slow disease progression, even in diabetes mellitus. Especially with type 2 diabetes, timely detection of symptoms may limit the severity of damage and lead to asymptomatic life. Therefore, patients with obesity, weight loss, polydipsia, and polyuria should be evaluated and managed promptly.



Diabetes Mellitus

Diabetes mellitus (DM) is a chronic systemic disease associated with abnormal carbohydrate, fat, and protein metabolism. It results from insulin deficiency or peripheral tissue resistance to insulin.

Diabetes Subtypes

Type	Pathogenesis	Acute complications	Chronic complications
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<p>1 (IDDM)</p>	<ul style="list-style-type: none"> • B-cell destruction <ul style="list-style-type: none"> • Immune-mediated or idiopathic • Affects non-obese younger patients (< 30 years old) • Genetic basis (20-50% twin concordance) with HLA link 	<ul style="list-style-type: none"> • Diabetic ketoacidosis (DKA) • Hypoglycemia 	<p>Microvascular</p> <ul style="list-style-type: none"> • Retinopathy • Nephropathy • Neuropathy <p>Macrovascular</p> <ul style="list-style-type: none"> • Atherosclerosis
<p>2 (NIDDM)</p>	<ul style="list-style-type: none"> • Insulin resistance with relative insulin deficiency initially, progressing to type I diabetes-like pathology • Genetic component (60-90% twin concordance) <ul style="list-style-type: none"> • Correlation with obesity 	<ul style="list-style-type: none"> • DKA precipitated with stress <ul style="list-style-type: none"> • Nonketotic hyperosmolar coma 	<p>Microvascular</p> <ul style="list-style-type: none"> • Retinopathy • Nephropathy • Neuropathy <p>Macrovascular</p> <ul style="list-style-type: none"> • Atherosclerosis

Symptoms of Diabetes Mellitus Type 1

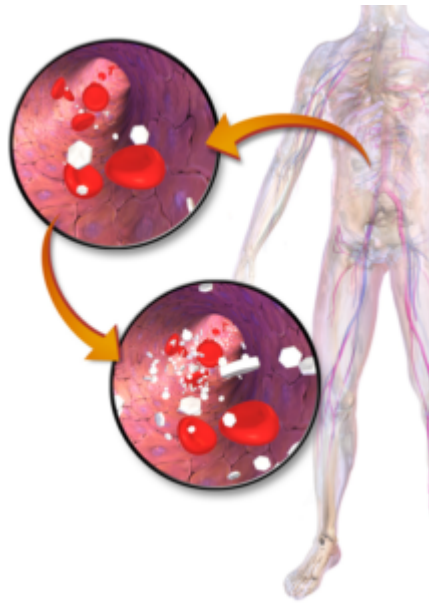


Image: 'Diabetes and High Blood Sugar' by Bruce Blaus. License: [CC BY 3.0](#)

Type-1 diabetes, formerly known as **juvenile diabetes**, is common in children and young adults. In rare cases, **type-1 diabetes occurs in adulthood**, which is then known as **LADA** (latent autoimmune diabetes in the adult).

The pathophysiology of type 1 DM involves autoimmune reaction leading to the destruction of insulin-producing beta cells in the islets of Langerhans of the [pancreas](#). The first symptoms of type 1 diabetes appear only after the destruction of 80-90% of the beta cells. Stressful situations can accelerate the disease onset, leading to an acute condition.

As diabetes is only symptomatic when 80-90% of beta cells are destroyed, the **onset** of the disease is **often sudden** and dramatic. Noticeable symptoms include **weight loss, polydipsia, and polyuria**. Due to the absence of insulin hormone, the serum glucose level is greatly elevated as glucose needs insulin to enter the cells. Normally, the kidneys completely reabsorb the filtered glucose, and it is not excreted in the urine. **However, as**

serum glucose concentration rises over 180 mg/dL (10 mmol/L), the renal threshold is exceeded, and glucose is released into the urine via the [kidney](#).

Glucose, being a solvent, when excreted by the kidneys, carries free water with itself. Therefore, these patients suffer from **frequent urination** (polyuria) and **excessive thirst**. In young children, this process may lead to **enuresis**, which is a warning sign of diabetes. Since glucose cannot enter the cells and is processed as an energy source, the body relies on the energy reserves in the fatty tissues, which leads to significant weight loss.

In addition, **non-specific symptoms of the disease**, such as malaise, **fatigue**, [anorexia](#), [amenorrhoea](#), impotence, and **dehydration (exsiccosis) may appear**. The consequential harm caused by diabetes is apparent during the subsequent course of the disease. **Dry skin, pruritus, muscle cramps**, delayed wound healing, and visual disturbances are the first indications of progressive diabetes.

In **emergency cases**, type 1 diabetes may present with life-threatening metabolic acidosis, known as **diabetic ketoacidosis**. Due to insulin deficiency, serum glucose cannot be utilized. The fatty acids are then transformed into **ketone bodies**, which enter the cells **independently** of insulin and are utilized for energy purposes. However, [ketone bodies](#) are acidic in nature, and their excessive accumulation decreases the blood pH, leading to metabolic acidosis.

Patients with [diabetic ketoacidosis](#) initially present with **nausea, vomiting, dehydration, and abdominal pain**. Metabolic acidosis may lead to disturbed breathing pattern (**Kussmaul breathing**), where the patient takes rapid, shallow breaths in order to hyperventilate, which leads to decreased carbon dioxide levels as a compensatory mechanism. Further, the ketone bodies are composed of acetoacetate, β -hydroxybutyrate, and their spontaneous breakdown product, acetone. Therefore, patients presenting with diabetic ketoacidosis may have an **acetone-like** smell in their breath and urine.

Symptoms of Diabetes Mellitus Type 2

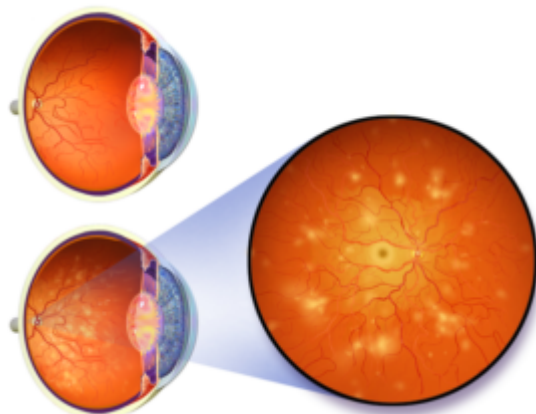
Type 2 DM is most common in adults **aged above 40 years**. However, due to the increased prevalence of obesity in children and adolescents, the younger population is also increasingly diagnosed with type 2 diabetes mellitus. The etiology of type 2 diabetes is multifactorial, with a strong hereditary component. These patients often exhibit **metabolic syndrome** characterized by central obesity, elevated triglycerides, insulin resistance, and [hypertension](#).

The pathophysiology of [type 2 DM](#) involves a combination of peripheral insulin resistance and inadequate insulin secretion by beta cells of the pancreas.

While the onset of **type 1 DM is sudden**, the progression of **type 2 DM is insidious** and is often discovered incidentally during other investigations. Therefore, these patients carry undetected type 2 DM for years and may have developed various microvascular and macrovascular complications, such as visual disturbances, [polyneuropathy](#), chronic renal disease, and impaired wound healing. For this reason, sometimes patients are first diagnosed with type 2 diabetes when they present with these late complications.

Symptoms are **nonspecific**, similar to those of type 1 diabetes. They include **polyuria, polydipsia, and polyphagia**. **Glucosuria** may occur when the renal threshold is

exceeded due to high serum glucose levels. However, these symptoms are more frequent in type 1 diabetes. Other nonspecific symptoms include:



[Image](#): "Diabetic retinopathy.", by Bruce Blaus. License: [CC BY 3.0](#)

- Fatigue, exhaustion

- Concentration problems
- [Headache](#), dizziness
- Increased susceptibility to infection (cold, flu)
- Impaired wound healing
- Blurred vision
- Muscle cramps
- Pruritus
- [Amenorrhea](#), impotence
- Frequent infections due to increased sugar content, in particular, in urine (fungi, cystitis, etc.)
- Acanthosis nigricans



[Image](#): "Acanthosis nigricans," by Madhero88. License: [CC BY-SA 3.0](#)

In **emergency**, patients with type 2 DM may develop **hyperosmolar hyperglycemic state (HHS)**, which is different from diabetic ketoacidosis. In the case of HHS, the serum glucose is **markedly elevated**, often more than **500 mg/dL**, increasing serum osmolarity. These patients often manifest a concomitant illness that leads to reduced fluid intake exacerbating the serum hyperosmolarity. These patients present with features of dehydration, altered sensorium, one or more neurological focal deficits, or even coma. Diabetic ketoacidosis is less common in type 2 diabetes than in type 1 diabetes.

Note: Acanthosis nigricans of the inguinal and axillary region is typically seen in young patients with insulin resistance.

Metabolic Syndrome

Elevated waist circumference	Men: \geq 40 inches (102 cm)
	Women: \geq 35 inches (88 cm)
Elevated triglycerides	\geq 150 mg/dL
Reduced HDL (“good”) cholesterol	Men: $<$ 40 mg/dL
	Women: $<$ 50 mg/dL
Elevated blood pressure	\geq 130/85 mm Hg or use of medication for hypertension
Elevated fasting glucose	\geq 100 mg/dL or use of medication for hyperglycemia

Note: Patients with these findings are generally considered ‘high-risk’ for adverse cardiac events.

Type 1 Versus Type 2 Diabetes

	Type 1	Type 2
Weight	Normal or thin. Often lose weight prior to diagnosis	Overweight or obese
Age	Typically first-second decade of life but often occurs at any age as LADA	Typically $>$ age 40 years, but can present much earlier
Glycemic patterns	Highly variable	Less variable
Insulin sensitivity	Normal	Reduced
Response to oral agents	Not responsive	Responsive
Antibody status	Usually positive	Negative
C-peptide level	Low or undetectable	Detectable or high
Family history	First-degree relatives uncommonly affected	Strong family history of 1 st -degree relatives
Other autoimmune disorders	Autoimmune thyroid disease, adrenal insufficiency, vitiligo, and pernicious anemia	Absent

Symptoms of Gestational Diabetes

Gestational diabetes is often **asymptomatic**. Therefore, an oral glucose tolerance test (OGTT) is recommended during the 24th to 28th week of pregnancy. Untreated gestational diabetes can lead to **developmental problems** in the fetus, which results in

increased birth weight (greater than 4 kg requiring a [cesarean section](#)), [respiratory distress syndrome](#), [hypoglycemia](#), and [hyperbilirubinemia](#). In emergency cases, the fetus may suffer from **diabetic embryopathy**.

During pregnancy, due to hydramnios, in which the fetus is larger than average, urinary tract infections and preeclampsia can be noticed. Usually, in gestational diabetes, **type 2 DM occurs** as the hormonal changes lead to insulin resistance in 3–5% of females. In rare cases, pregnancy may trigger type 1 DM.

Diabetes due to genetic defects in beta cells of the islets of Langerhans

Maturity onset diabetes of the young (MODY) is caused by genetic defects in glucose metabolism and occurs mainly in adolescence. MODY is attributed to specific gene defects leading to **monogenic autosomal dominant** disorders. Eleven different forms of MODY have been recognized so far:

- **MODY 1:** mutation in chromosome 20, resulting in defective hepatic transcription factor HNF4A
- **MODY 2:** mutation in chromosome 7, resulting in defective enzyme glucokinase
- **MODY 3:** mutation in chromosome 12, resulting in defective hepatic transcription factor HNF1A
- **MODY 4:** mutation in chromosome 13, resulting in defective PDX1
- **MODY 5:** mutation in chromosome 17, resulting in defective hepatic transcription factor TCF2
- **MODY 6:** mutation in chromosome 2, resulting in defective NEUROD1
- **MODY 7:** mutation in chromosome 2, resulting in defective KLF11
- **MODY 8:** mutation in chromosome 9, resulting in defective CEL
- **MODY 9:** mutation in chromosome 7, resulting in defective PAX4
- **MODY 10:** mutation in chromosome 11, resulting in defective INS
- **MODY 11:** mutation in chromosome 8, resulting in defective BLK

If MODY is detected early, initial treatment with oral hypoglycemic agents such as **sulfonylureas** is sufficient. However, it is quite probable that insulin therapy might be necessary.

Diabetes due to genetic defects in insulin action

Two types of diabetes are distinguished based on **insulin resistance due to genetic defects**. **Type A insulin resistance syndrome** is characterized by hyperinsulinemia, skin disorders such as acanthosis nigricans (hyperpigmentation and hyperkeratosis (cornification) mostly involving the groin and armpits) and hyperandrogenism in women. **Lawrence syndrome or Lipodystrophy** is characterized by a massive reduction in subcutaneous fat, which is accompanied by insulin resistance due to previously unknown reasons.

Diabetes as a result of pancreatic disease

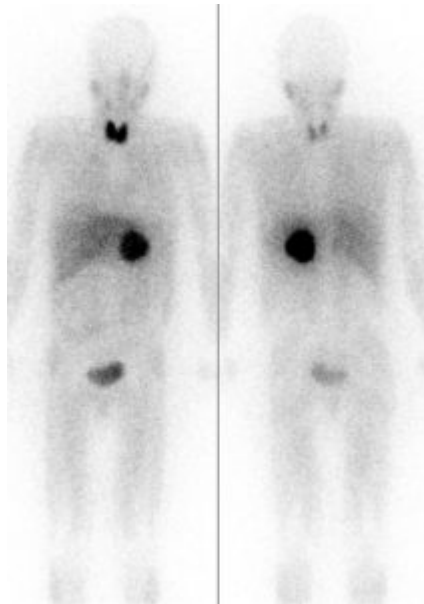
All the exocrine pancreatic disorders due to defective pancreas or as a consequence of another disease may lead to diabetes. **Such disorders include:**

- [Pancreatitis](#)

- Trauma or pancreatectomy
- [Pancreatic cancer](#)
- [Cystic fibrosis](#)
- [Hemochromatosis](#)

Diabetes due to abnormal hormone synthesis or regulation (endocrinopathy)

Diabetes can accompany the following disorders due to hormonal imbalances:



- **Image:** "Body scintigraphy 24 hours after intravenous administration of ¹²³Iod-MIBG. Physiological occupancy of the thyroid, liver and bladder. Pathological accumulation in a tumor of the left adrenal glands (pheochromocytoma). Left: from the front. Right: from behind," by Drahhreg01. License: [CC BY-SA 3.0](#)

[Acromegaly](#) (abnormal growth hormone somatotropin)

- Aldosteronoma (elevated aldosterone production)
- Glucagonoma (tumor related to A-cells of the islets of Langerhans)
- [Hyperthyroidism](#) (overactive thyroid)
- [Cushing's disease](#) (increased ACTH production)
- [Pheochromocytoma](#) (tumors of the adrenal medulla)
- Somatostatinoma (tumor of the pancreas or duodenum, with increased somatostatin production)

Diabetes due to drugs or chemicals

Diabetes may occur as an adverse effect of certain drugs and chemicals, including:

- Alpha interferon (antiviral)
- Beta-adrenergic agonists (for stimulation of beta receptors in the sympathetic nervous system)

- Diazoxide (hyperglycemia)
- Glucocorticoids (against inflammation, overactive immune system, inflammatory rheumatic diseases)
- Nicotinic acid (to decrease increased blood cholesterol)
- Pentamidine (antiprotozoal, commonly used in tropical medicine)
- Phenytoin (for epilepsy, cardiac arrhythmia)
- [Thyroid hormones](#)
- [Thiazide diuretics](#)
- Vacor (rat poison)

Diabetes due to viral infection

In **congenital rubella**, caused by the rubella virus, the islet cells of the pancreas may be destroyed resulting in the deficiency of insulin hormone leading to type 1 diabetes. Human **cytomegalovirus (CMV)** infection also leads to the development of diabetes, as pancreatitis may occur with disease progression.

Diabetes due to immunological defects

In certain autoimmune diseases, such as Stiff-person syndrome (SPS), the endocrine glands may be affected adversely with negative effects on the beta cells of the pancreas, resulting in type 1 diabetes. Other immunological defects that trigger type 1 diabetes include the presence of **anti-insulin receptor antibodies** that block the insulin receptors of the cells.

Diabetes due to genetic disorders

Previously, diabetes was detected as a side effect of numerous genetic syndromes:

- [Huntington's disease](#) (HD)
- [Down syndrome](#)
- Myotonic dystrophy
- Friedreich's ataxia
- Klinefelter's syndrome (KS)
- [Porphyria](#)
- [Prader-Willi-Labhart syndrome](#)
- [Turner syndrome](#)
- Wolfram syndrome

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