

# Type 1 Diabetes Mellitus

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## Key Points

- Pathogenesis of diabetes mellitus
- Islet- targeting autoantibodies
- Symptoms of risk factors & treatment of diabetes mellitus

Type 1 diabetes mellitus (T1DM), also known as autoimmune diabetes, is a chronic disease in which pancreatic beta cells are lost which leads to insulin deficiency in the body and causes hyperglycemia. The symptoms start during childhood or adolescence, or sometimes it may develop later. But the pathogenesis of T1DM is not completely understood, the pathogenesis of the disease is thought to involve T cell-mediated destruction of  $\beta$ -cells. Islet-targeting autoantibodies that target insulin, 65 kDa glutamic acid decarboxylase, insulinoma-associated protein 2 and zinc transporter 8—all of these are proteins associated with secretory granules in  $\beta$ -cells—are biomarkers of T1DM-associated autoimmunity that are found months to years before symptom start, and can be used to identify and study individuals who are at risk of developing T1DM. The type of autoantibody that appears first depends on the environmental trigger and on genetic factors. The pathogenesis of T1DM can be divided into three stages depending on the absence or presence of hyperglycaemia and hyperglycaemia-associated symptoms (such as polyuria and thirst). A cure is not available, and patients depend on lifelong insulin injections; novel approaches to insulin treatment, such as insulin pumps, continuous glucose monitoring and hybrid closed-loop systems, are in development. But intensive glycaemic control has decreased the occurrence of microvascular and macrovascular complications, the majority of patients with T1DM are still developing these complications. Major research efforts are needed to achieve early diagnosis, prevent  $\beta$ -cell loss and develop better

treatment options to improve the quality of life and prognosis of those affected. <sup>1</sup>

Over the past decade, knowledge of the pathogenesis and natural history of type 1 diabetes has grown substantially, particularly with regard to disease prediction and heterogeneity, pancreatic pathology, and epidemiology. Technological improvements in insulin pumps and continuous glucose monitors help patients with type 1 diabetes manage the challenge of lifelong insulin administration. Agents that show promise for averting debilitating disease-associated complications have also been identified. However, despite broad organizational, intellectual, and fiscal investments, no means for preventing or curing type 1 diabetes exists, and, globally, the quality of diabetes management remains uneven. This forum discusses current progress in epidemiology, pathology, diagnosis, and treatment of type 1 diabetes, and prospects for an improved future for individuals with this disease.<sup>2</sup>

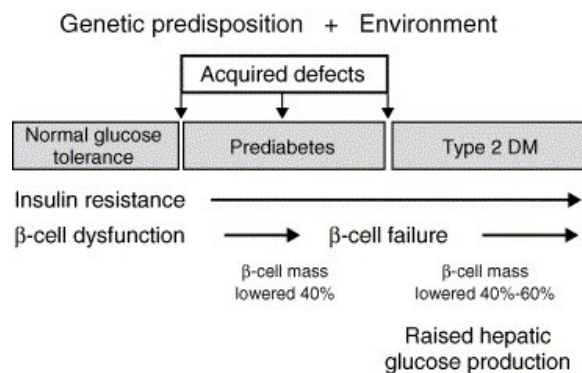
Type 1 diabetes mellitus (T1DM) results from the destruction of pancreatic  $\beta$ -cells that is mediated by the immune system. Genetic risk is defined by the presence of particular allele combinations, which in the major susceptibility locus (the HLA region) affect T cell recognition and tolerance to foreign and autologous molecules.

Multiple other loci also regulate and affect features of specific immune responses and modify the vulnerability of  $\beta$ -cells to inflammatory mediators. Compared with the genetic factors, environmental

factors that affect the development of T1DM are less well characterized but contact with particular microorganisms is emerging as an important factor.

Certain infections might affect immune regulation, and the role of commensal microorganisms, such as the gut microbiota, are important in the education of the developing immune system. Some evidence also suggests that nutritional factors are important. Multiple islet-specific autoantibodies are found in the circulation from a few weeks to up to 20 years before the onset of clinical disease and this prediabetic phase provides a potential opportunity to manipulate the islet-specific immune response to prevent or postpone  $\beta$ -cell loss.

The latest developments in understanding the heterogeneity of T1DM and characterization of major disease subtypes might help in the development of preventive treatments.<sup>3</sup>



**Figure 1:** Pathogenesis of Diabetes mellitus (*The lancet*)

## References:

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2. Atkinson MA, Eisenbarth GS, Michels AW. Type 1 diabetes. *The Lancet*. 2014 Jan 4;383(9911):69-82.
3. Ilonen J, Lempainen J, Veijola R. The heterogeneous pathogenesis of type 1 diabetes mellitus. *Nature Reviews Endocrinology*. 2019 Nov;15(11):635-50.