

# Diagnosis and Treatment

## Learning Outcomes

- Describe the different disease stages of type 1 diabetes leading to clinical diagnosis
- Know the basic risk factors and biomarkers used for predicting risk and disease progression
- Explain basic principles for treatment and management of type 1 diabetes

### Type 1 Diabetes

Type 1 diabetes results from the immune system destroying beta cells, leading to an absolute deficiency of insulin. This destruction causes dysregulated blood glucose levels, requiring insulin injections from the onset of the disease. The immune-mediated destruction is irreversible, and no lifestyle changes can prevent this process. Despite the need for insulin therapy, maintaining a healthy diet and exercise regimen remains important for managing overall health and blood glucose control.

### Type 2 Diabetes

Type 2 diabetes primarily involves insulin resistance, where the body's tissues do not respond properly to insulin, despite its normal or increased production. Over time, the beta cells attempt to compensate by producing more insulin, leading to hyperinsulinemia. Eventually, these cells become exhausted and fail to produce sufficient insulin, resulting in dysregulated blood glucose levels similar to type 1 diabetes. Unlike type 1, type 2 is often preventable through lifestyle modifications such as diet and exercise, although it is not curable.

### Differences in Treatment Approaches

In type 1 diabetes, insulin injections are necessary immediately because of the absence of beta cells. In contrast, type 2 diabetes may initially be managed with oral medications and lifestyle changes, with insulin therapy introduced later if needed. The goal of these drugs is to improve insulin sensitivity and control blood glucose levels. Specific mechanisms of action of these drugs are outside the scope of this module, but they generally aim to enhance the body's response to insulin or reduce glucose production.

### Prevention and Management

Type 2 diabetes can often be prevented through healthy lifestyle choices, including balanced diet and regular exercise. Conversely, type 1 diabetes cannot be prevented because it stems from autoimmune destruction of beta cells. Nonetheless, individuals with type 1 diabetes require ongoing insulin management and a healthy diet to maintain blood glucose control and prevent complications.

## Stages of Type 1 Diabetes Development

### Stage 1: Risk Factors and Autoimmunity Initiation

Genetic and environmental factors increase the risk of developing type 1 diabetes. The initial event, likely an autoimmune response, triggers the destruction of beta cells. Detection at this stage involves identifying autoantibodies against beta cell antigens in the blood, with individuals still maintaining normal blood glucose levels due to sufficient functional beta cells.

### Stage 2: Early Autoimmune Activity and Blood Glucose Changes

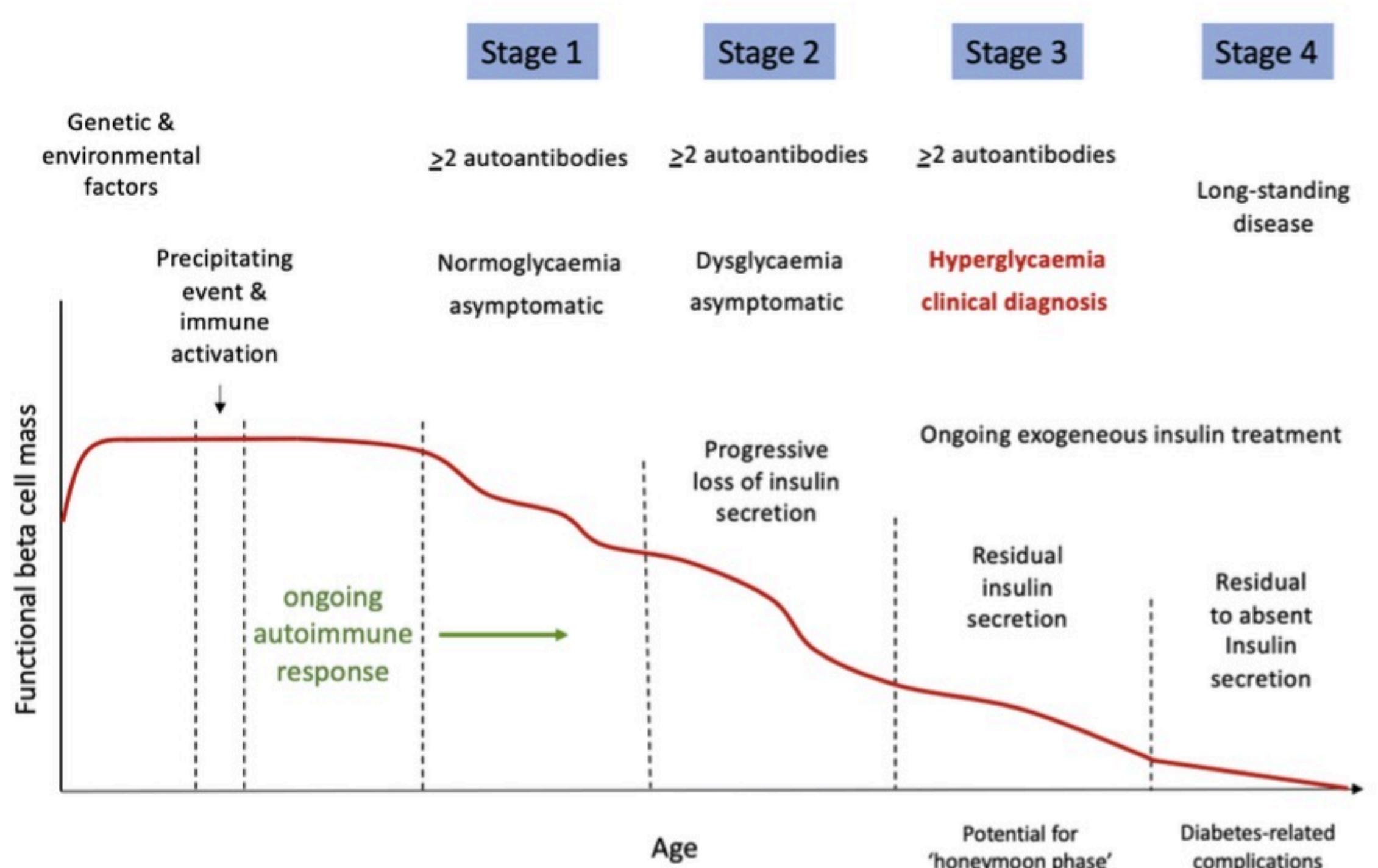
At this stage, individuals have more than two autoantibodies, and blood tests reveal abnormal or elevated blood glucose levels, especially after carbohydrate intake. There is also a decline in insulin production and beta cell mass, although symptoms are not yet apparent. Special tests, such as glucose tolerance tests, can detect these early changes.

### Stage 3: Onset of Clinical Diabetes

Individuals continue to have multiple autoantibodies, but now exhibit hyperglycemia and clinical symptoms of diabetes. Insulin production is insufficient, necessitating treatment with exogenous insulin. This stage marks the transition from preclinical to clinical diabetes, with the disease becoming more apparent and requiring medical intervention.

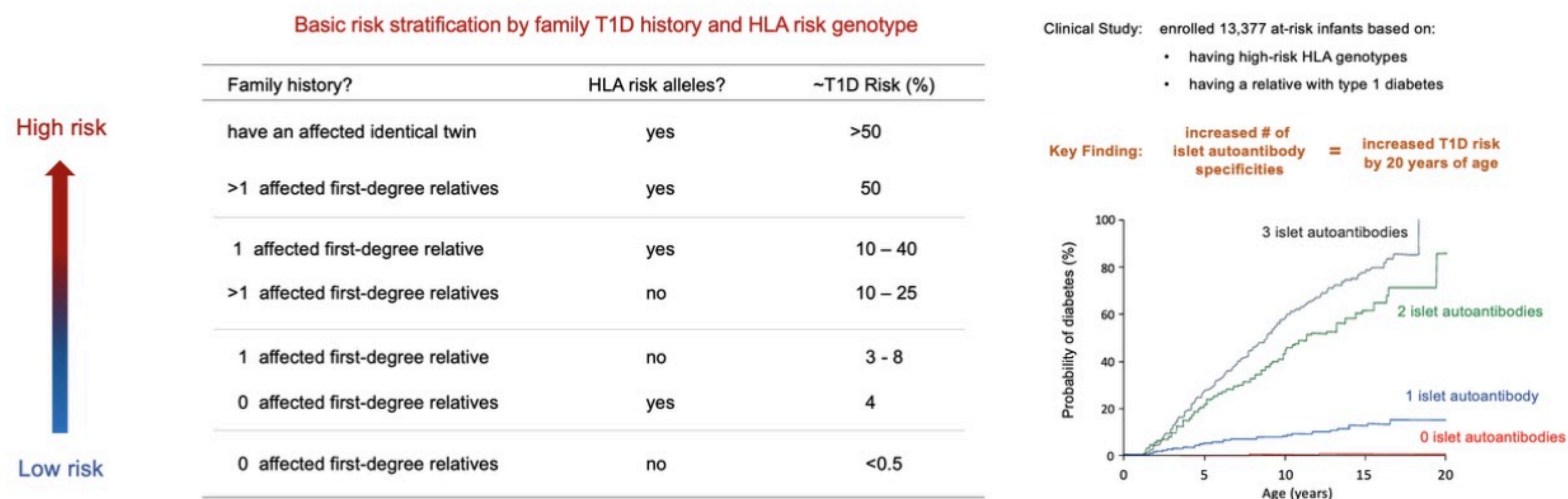
### Stage 4: Long-term Complications

This stage involves the development of long-term diabetes complications, especially if blood glucose levels have been poorly managed. These complications include neuropathy, retinopathy, nephropathy, and cardiovascular issues. The progression from stage 1 to stage 3 varies among individuals, influenced by genetic predisposition and environmental exposures.



## Predicting and Diagnosing Type 1 Diabetes: Genetic and Immunological Markers

Family history and specific HLA alleles are key genetic risk factors. The presence of certain HLA risk alleles, especially in individuals with a family history, significantly increases the likelihood of developing type 1 diabetes. Risk assessment involves analyzing these genetic markers and autoantibodies in the blood.



## Autoantibodies as Predictive Biomarkers

Autoantibodies targeting beta cell antigens serve as important biomarkers. The number and specificity of these autoantibodies correlate with the risk of developing diabetes. For example, having three or more autoantibodies against different islet cell antigens strongly predicts the development of type 1 diabetes by age 20. The presence of fewer autoantibodies indicates a lower risk.

## Risk Stratification and Disease Progression

Combining family history, HLA genotypes, and autoantibody profiles allows clinicians to stratify risk levels. Individuals with multiple autoantibodies are almost certain to develop diabetes, with the timing varying based on individual factors. However, predicting the exact age of onset remains challenging due to variability in disease progression.

## Assessing Beta Cell Function and Disease Monitoring: Indirect Measurement of Beta Cell Mass

Direct measurement of pancreatic beta cell mass in living individuals is currently not feasible. Instead, indirect methods are used to assess beta cell function, such as measuring insulin or C-peptide levels in the blood. These indicators reflect the ability of remaining beta cells to produce insulin in response to glucose.