PRIMEVIEW

# TYPE 1 DIABETES MELLITUS

nature REVIEWS DISEASE PRIMERS

For the Primer, visit doi:10.1038/nrdp.2017.16

**Type 1 diabetes mellitus (T1DM) is a chronic disease characterized by hyperglycaemia owing to insulin deficiency as a consequence of pancreatic β-cell loss. The most common type of T1DM — autoimmune T1DM — is marked by immune-mediated β-cell loss.**

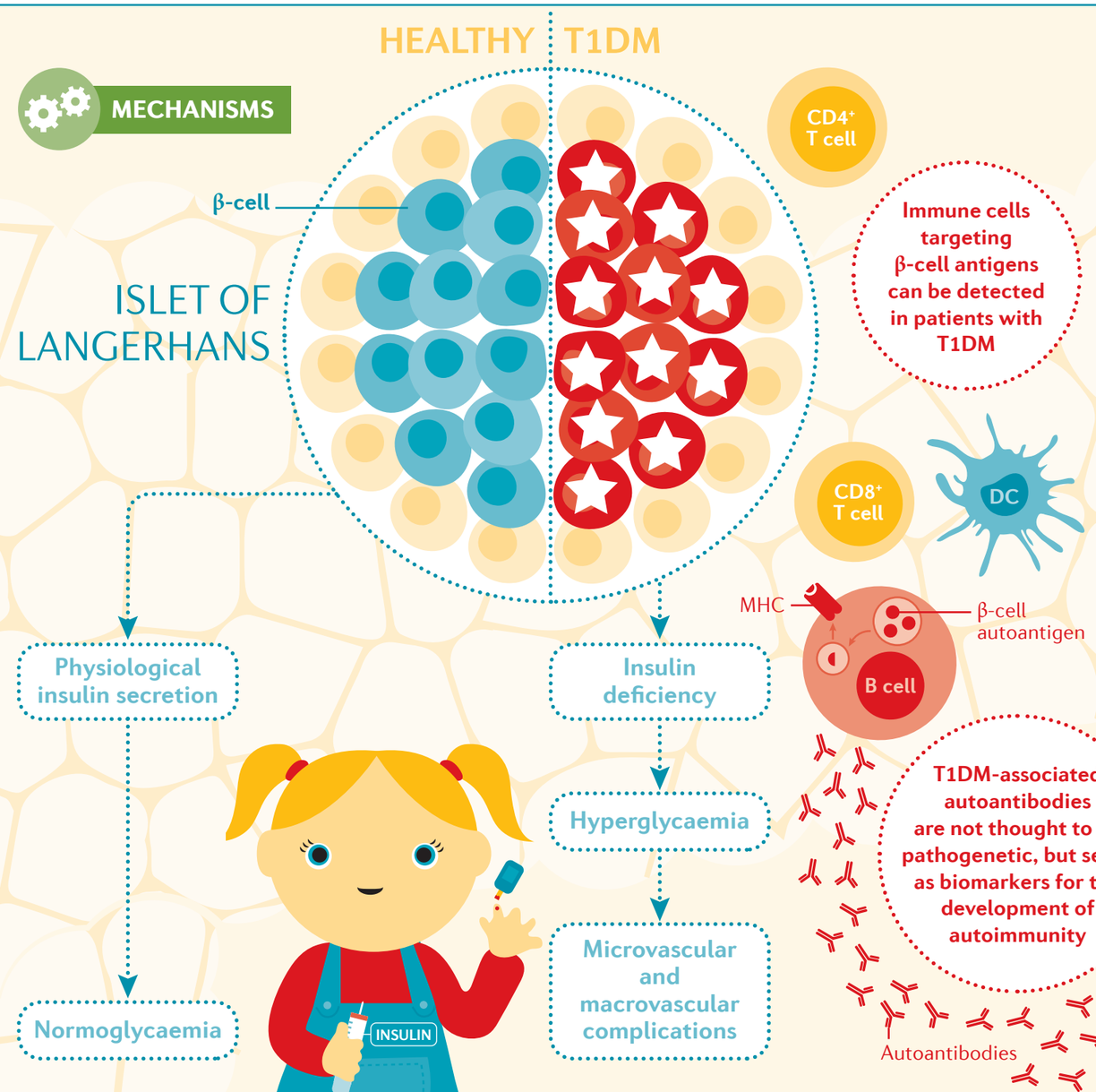
## EPIDEMIOLOGY

T1DM is the most common cause of diabetes in children, with >500,000 children currently living with this condition globally — making it one of the most common endocrine and metabolic conditions in childhood. Incidence peaks around 12–14 years of age, although children are increasingly being diagnosed at younger ages. The number of new patients of <5 years of age is expected to increase between 2005 and 2020.

**Autoantibodies targeted against insulin, 65 kDa glutamic acid decarboxylase (GAD65), insulinoma-associated protein 2 or zinc transporter 8 can be detected months to years before symptom onset. The majority of individuals with two or more autoantibodies will progress to symptomatic disease. Autoantibodies against insulin and GAD65 are usually detected first; the order of appearance is associated with age, environmental factors and genetics, and might determine disease progression.**

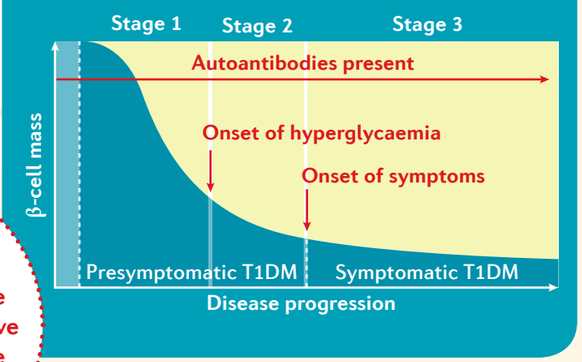
**T1DM is a polygenic disease. The major genetic risk factors are the *HLA-DR3-DQ2* and *HLA-DR4-DQ8* haplotypes, but several non-HLA risk factors have been identified as well.**

## MECHANISMS




## DIAGNOSIS

**Most patients present with classic symptoms of hyperglycaemia, such as rapid onset of polyuria (large volume of urine), polydipsia (abnormal thirst), weight loss, abdominal symptoms, headaches and ketoacidosis (a metabolic state associated with high levels of ketones owing to the breakdown of fatty acids and amino acids). Few patients are diagnosed via routine glucose testing or enrolment in autoantibody screening programmes. Diagnostic criteria classify T1DM based on the presence of hyperglycaemia, insulin deficiency and autoantibodies. With the advent of autoantibody testing, T1DM can now be divided into three stages.**




## MANAGEMENT

**A cure for T1DM is not available; patients depend on lifelong insulin injections. Although rigorous glucose control with intensive insulin therapy has reduced the risk of life-threatening ketoacidosis, patients still experience substantial morbidity and mortality due to chronic complications.**

## OUTLOOK

Investigation of individuals at risk (based on genetic or autoantibody tests) will bring about a better understanding of aetiology, pathophysiology and disease progression. Immunosuppressive therapy — aimed at slowing down immune-mediated β-cell loss — either as secondary prevention (stage 1 or stage 2) or as treatment (stage 3) has not proven to be successful alone; combination therapy might be required. Novel approaches to insulin treatment (such as insulin pumps and an artificial pancreas) and continuous glucose monitoring are in development.

Written by Liesbet Lieben; designed by Laura Marshall

Article number: 17017; doi:10.1038/nrdp.2017.17; published online 30 Mar 2017

© 2017 Macmillan Publishers Limited, part of Springer Nature. All rights reserved.