PRIMEVIEW

TYPE 2 DIABETES MELLITUS

nature REVIEWS DISEASE PRIMERS

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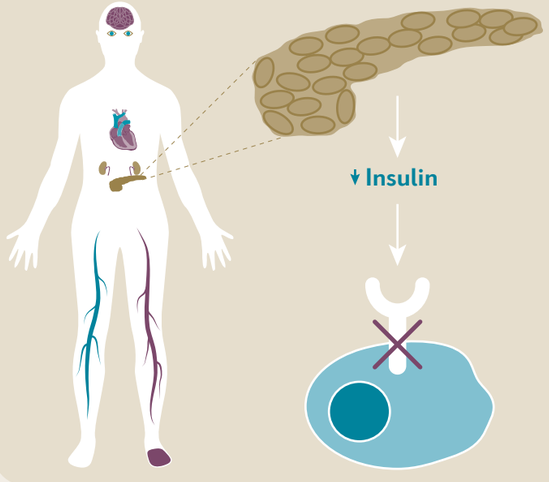
Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder associated with hyperglycaemia caused by impaired insulin secretion and insulin resistance.

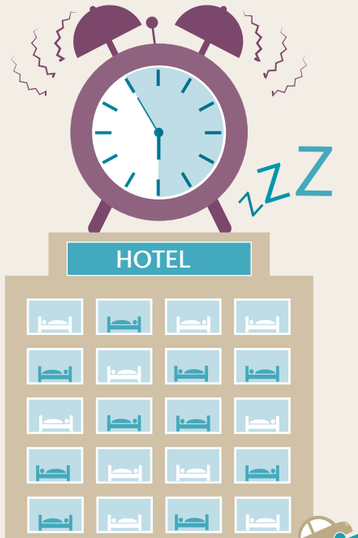
MECHANISMS

Impaired insulin secretion in T2DM is caused by pancreatic β-cell dysfunctioning owing to lipotoxicity, glucotoxicity and resistance to incretins (intestinal hormones that stimulate insulin secretion). Peripheral organs — including the liver, muscle and kidney — become insulin resistant, leading to reduced glucose uptake from blood, excessive glucose reabsorption by the kidney and increased gluconeogenesis, all of which contribute to hyperglycaemia. Insulin resistance is the result of impaired insulin receptor signalling. Causes of the insulin resistance include genetic abnormalities, ectopic lipid accumulation, mitochondrial dysfunction, inflammation and endoplasmic reticulum stress. The severity and duration of hyperglycaemia determine the risk of microvascular complications (retinopathy, nephropathy and neuropathy). Macrovascular complications (myocardial infarction, peripheral vascular disease and stroke) result from dyslipidaemia, hypertension, hyperglycaemia and inflammation.

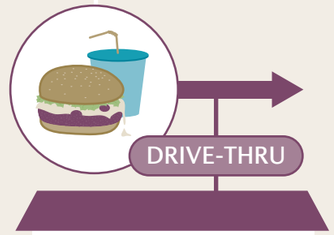


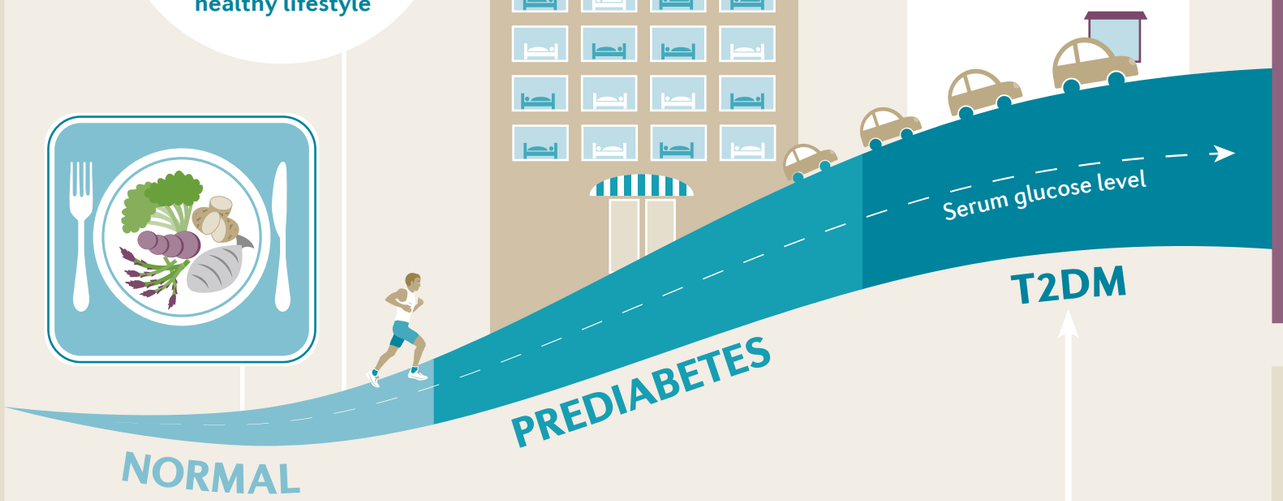
MANAGEMENT

Although T2DM has a strong genetic component, the vast majority of T2DM cases are potentially controllable by a healthy lifestyle



Weight management should always accompany T2DM therapy





Successful glycaemic control requires a multifactorial approach. Available drugs target hepatic glucose production (metformin), promote insulin secretion, increase sensitivity to insulin, act on the incretin axis or target intestinal and renal glucose absorption.

DIAGNOSIS

The clinical presentation, underlying pathophysiology and disease progression vary considerably between individuals, making a clear classification of T2DM difficult.

Diagnosis mainly depends on serum glucose levels. Cut-off values have been formulated based on the risk of complications. Fasting glucose levels of more than ~100 mg per dl are considered as prediabetes and of >126 mg per dl as T2DM. Glycated haemoglobin A1c (HbA1c) levels of ≥6.5% have been added as a diagnostic criteria.

EPIDEMIOLOGY

T2DM is the most common type of diabetes, (accounting for >90% of cases). T2DM has become a global health problem and parallels the obesity epidemic. BMI >25 is the single most important risk factor. However, the prevalence of T2DM has increased dramatically in China and India, despite the low prevalence of obesity. This observation might be explained by different fat-versus-muscle-mass ratios, different fat tissue distribution and a greater severity of the β-cell failure.

SCREENING

Screening for T2DM is recommended for adults who are ≥45 years of age, obese and/or have a family history, especially since randomized controlled clinical trials have shown that intensive lifestyle interventions, sometimes combined with medication, are effective in delaying and even preventing T2DM. However, pharmacological interventions to prevent T2DM have not been approved in most countries.

T2DM is preceded by prediabetes, in which patients have higher than normal glycaemic levels. Disease progression to overt T2DM is common, with an annual conversion rate of 3–11% per year.

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