

Late-onset type 1 diabetes: More common than you think? A GPnotebook Shortcut

Evidence suggests that type 1 diabetes develops after the age of 30 years in at least 40% of cases; however, it is frequently misdiagnosed in this age group as it is considered to have its onset predominantly in younger people. This GPnotebook Shortcut is a handy guide to the different classifications of diabetes to help readers establish the right diagnosis.

Type 1 diabetes is characterised by insulin deficiency brought about by autoimmune-mediated destruction of the pancreatic beta-cells. Although type 1 diabetes is commonly thought to first develop predominantly in younger people, genetic stratification analysis suggests that at least 40% of cases occur after the age of 30 years (Thomas et al, 2018). Most of these cases are characterised by severe insulin deficiency, with 89% needing insulin therapy after 1 year.

Type 1 diabetes can easily be misdiagnosed if it develops outside of childhood, as a recent study from the University of Exeter demonstrates (Thomas et al, 2019). The authors reviewed 583 people who were diagnosed with any type of diabetes after 30 years of age and who received insulin therapy. Overall, 21% of these had severe insulin deficiency and met the criteria for type 1 diabetes. They had similar clinical characteristics to a comparison cohort of 220 people with young-onset type 1 diabetes.

Overall, 38% of those with late-onset type 1 diabetes did not receive insulin at diagnosis; half of these were misdiagnosed as having type 2 diabetes. Early progression to insulin was a strong predictor of type 1 diabetes, with 85% of the type 1 cohort receiving insulin within 1 year; furthermore, 47% of those who required insulin within 3 years of diagnosis had type 1 diabetes. BMI was not a robust identifier of late-onset type 1 diabetes: only 41% had

a BMI <25 kg/m², and 28% of those with type 2 diabetes had a BMI <25 kg/m².

Classification of diabetes: A GPnotebook Shortcut

If misdiagnosed, people with late-onset type 1 diabetes will not receive appropriate education and may not be eligible for interventions such as carbohydrate counting courses, continuous glucose monitoring and insulin pump therapy; therefore, it is vital to correctly identify the condition. Anyone who is diagnosed with type 2 diabetes but progresses to insulin therapy within 3 years should strongly consider a C-peptide test to confirm the diagnosis – even if this requires referral or liaison with secondary care colleagues if the test cannot be ordered in primary care.

The diagnosis and classification of diabetes in primary care is increasingly challenging. The GPnotebook Shortcut overleaf will help in establishing the right diagnosis and ultimately to avoid any harm. ■

NICE (2015a) *Diabetes in pregnancy: management from preconception to the postnatal period* [NG3]. NICE, London. Available at: www.nice.org.uk/guidance/ng3

NICE (2015b) *Suspected cancer: recognition and referral* [NG12]. NICE, London. Available at: www.nice.org.uk/guidance/ng12

Thomas NJ, Jones SE, Weedon MN et al (2018) Frequency and phenotype of type 1 diabetes in the first six decades of life: a cross-sectional, genetically stratified survival analysis from UK Biobank. *Lancet Diabetes Endocrinol* **6**: 122–9

Thomas NJ, Lynam AL, Hill AV et al (2019) Type 1 diabetes defined by severe insulin deficiency occurs after 30 years of age and is commonly treated as type 2 diabetes. *Diabetologia* **62**: 1167–72

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Classification of Diabetes

	Type 1 diabetes (T1D)	Latent autoimmune diabetes in adults (LADA)	Type 2 diabetes (T2D)	Monogenic diabetes	Gestational diabetes (GDM)	Type 3c diabetes
Pathophysiology and diagnosis	Autoimmune destruction of pancreatic beta-cells. Clinical diagnosis +/- BG and ketone levels. Urgent specialist discussion required	LADA is essentially "slow-onset" T1D. Gradual autoimmune destruction of pancreatic beta-cells. Diagnosis and management similar to T1D	Insulin resistance with relative insulin deficiency. Diagnose if HbA _{1c} >48 mmol/mol (6.5%)	Genetic mutation leading to diabetes. MODY is most common. www.diabetesgenes.org for diagnosis guidance	Impaired glucose tolerance in pregnancy due to pancreatic beta-cell dysfunction on background of insulin resistance. NICE (2015a) NG3 diagnostic criteria: FBG ≥5.6 mmol/L or 2-hour BG ≥7.8 mmol/L (2 hours post-75 g OGTT)	Pancreatic function disrupted by disease; e.g. pancreatitis, cystic fibrosis, haemochromatosis (check ferritin) and pancreatic cancer
Age at diagnosis	Usually <25 years but can occur at any age	Can occur at any adult age. Often initially mistaken for T2D	Both adults and children at any age	MODY onset often second to fifth decades and usually <45 years	Can occur in any women of child-bearing age. Follow-up after delivery: lifelong annual HbA _{1c} checks required (NICE, 2015a [NG3])	Both adults and children at any age. Exclude pancreatic cancer in those aged >60 years with new-onset diabetes and weight loss (NICE, 2015b [NG12])
Weight at diagnosis	Usually thin but can be overweight. Marked weight loss common	Variable	Usually overweight	Variable	Risk factors for GDM include excess weight/obesity but baseline weight can be variable	Variable
Family history of diabetes	Infrequent (5–10%)	Variable	Frequent (75–90%)	Multigenerational. MODY is autosomal dominant. A strong family history of diabetes (any type) involving two or three consecutive generations may point towards MODY	Family history of diabetes is an important risk factor for GDM	Variable. Haemochromatosis and cystic fibrosis are autosomal recessive
History of autoimmune disease	Often personal or family history; e.g. thyroid and coeliac disease	Variable	Variable	Variable	Variable	Variable but pancreatic exocrine insufficiency often present; e.g. diarrhoea, steatorrhea or abdominal pain. Check faecal elastase-1 levels
Pancreatic autoantibodies	Present	Present	Absent	Absent	Absent	Absent
C-peptide levels	Low/absent	Initially normal then low/absent	Normal to high	Normal	Normal to high	Low
Insulin sensitivity	Normal when treated	Some insulin resistance	Reduced	Normal (may be reduced if obese)	Reduced	Compensatory increase in peripheral insulin sensitivity
Insulin requirements	Immediate: specialist input urgently required	Latent; months to years	Variable	Variable	Variable	Variable
Risk of diabetic ketoacidosis (DKA)	High	Low initially but high once insulin-deficient	Low, but euglycaemic DKA rare side effect of SGLT2 inhibitors	Low	Low	Low but hypoglycaemia is common and can be prolonged

BG=blood glucose; FBG=fasting blood glucose; MODY=maturity-onset diabetes of the young; OGTT=oral glucose tolerance test; SGLT2=sodium-glucose cotransporter 2. www.gpnotebookeducation.co.uk