

Diagnosis and Classification of Diabetes for Primary Care

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	T1D	LADA	T2D	Monogenic diabetes	GDM	Type 3c diabetes (pancreatogenic)
Pathophysiology and diagnosis	Autoimmune destruction of pancreatic beta-cells. Clinical diagnosis ± PG and ketone levels. Urgent specialist discussion required. It is increasingly challenging to differentiate T1D from T2D, partly due to the obesity epidemic. Often the safest strategy is to presume T1D until proven otherwise	LADA is essentially "slow-onset" T1D. Gradual autoimmune destruction of pancreatic beta cells. Diagnosis and management similar to T1D. See: https://www.diabetes.org.uk/diabetes-the-basics/other-types-of-diabetes/latent-autoimmune-diabetes	IR with relative insulin deficiency. T2D is usually diagnosed when HbA _{1c} ≥48mmol/mol. If use of HbA _{1c} is inappropriate (e.g. pregnant women, women who are 2 months postpartum, end-stage renal disease) then T2D is diagnosed by an FPG ≥7 mmol/L. If asymptomatic, the diagnosis should never be based on a single abnormal HbA _{1c} or PG level; at least 1 additional abnormal test is essential	Genetic mutation leading to diabetes. Most common is MODY. See: www.diabetesgenes.org for diagnosis guidance	Impaired glucose tolerance in pregnancy due to pancreatic beta-cell dysfunction on background of IR. NICE guideline NG3 (last updated December 2020) diagnostic criteria: FPG ≥5.6 mmol/L or 2-hour PG post 75 g OGTT ≥7.8 mmol/L	Diabetes associated with disease, trauma or surgery of the exocrine pancreas. Causes include acute and chronic pancreatitis, pancreatic surgery, cystic fibrosis, haemochromatosis and pancreatic cancer. See: https://pancreaticcanceraction.org/help-and-support/living-with-pancreatic-cancer/type-3c-diabetes/
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 during 2nd to 5th decades and usually <45 years	Can occur in any women of child-bearing age. Women with GDM have a nearly 10-fold higher risk of developing T2D (<i>BMJ</i> 2020;369:m1361). Follow-up after delivery: women require lifelong annual HbA _{1c} (NICE guideline NG3 [last updated December 2020])	Both adults and children at any age. Exclude pancreatic cancer in those >60 years with new-onset diabetes and weight loss (NICE guideline NG12 [last updated September 2020])
Weight at diagnosis	Usually thin but can be overweight. Marked weight loss common	Variable	Usually overweight	Variable	RF for GDM include overweight/obesity but baseline weight can be variable	Variable
Family history of diabetes	Infrequent (5–10%)	Variable	Frequent (75–90%)	Multi-generational. MODY is AD. A strong FH of diabetes (any type) involving two or three consecutive generations may point towards a diagnosis of MODY	FH of diabetes is an important RF for GDM	Variable. Haemochromatosis and CF are AR
History of autoimmune disease	Often personal or FH, e.g. thyroid and coeliac disease	Variable	Variable	Variable	Variable	Variable but often PEI present, e.g. diarrhoea and steatorrhoea, abdominal discomfort, flatulence and bloating. Check stool sample for faecal elastase-1. Low levels suggestive of PEI
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 IR	Reduced	Normal (maybe 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. Much more likely to need insulin within 5 years of diagnosis
Risk of DKA	High	Low initially but high once insulin-deficient	Low but euglycaemic DKA is a rare side-effect of SGLT2 inhibitors. See GPnotebook Shortcut What next after metformin?	Low	Low	Low but hypoglycaemia is common and can be prolonged

Table based on author's clinical experience and appraisal of the literature.

Abbreviations

AD: autosomal dominant; **AR:** autosomal recessive; **CF:** cystic fibrosis; **DKA:** diabetic ketoacidosis; **FH:** family history; **FPG:** fasting plasma glucose; **GDM:** gestational diabetes mellitus; **IR:** insulin resistance; **LADA:** latent autoimmune diabetes in adults; **MODY:** maturity onset diabetes of the young; **OGTT:** oral glucose tolerance test; **PEI:** pancreatic exocrine insufficiency; **PG:** plasma glucose; **RF:** risk factor(s); **SGLT2:** sodium-glucose cotransporter-2; **T1D:** type 1 diabetes; **T2D:** type 2 diabetes