The Diagnosis and Classification of Diabetes in Primary Care

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Primary Care Hacks

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	T1D	LADA	T2D	Monogenic Diabetes	GDM	T3cD (Pancreatogenic)
Pathophysiology	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 Diabetes UK's *Latent autoimmune diabetes in adults*	IR with relative insulin deficiency T2D is usually diagnosed when HbA_{1c} ≥48 mmol/mol. If use of HbA_{1c} is inappropriate (e.g. pregnant women, genetic variants [HbS or HbC trait], acute or chronic blood loss, end-stage kidney 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 one additional abnormal test is essential	Genetic mutation leading to diabetes. Most common is MODY See diabetesgenes.org for diagnosis guidance	Impaired glucose tolerance in pregnancy due to pancreatic beta-cell dysfunction on background of IR NICE NG3[1] diagnostic criteria: FPG ≥5.6 mmol/l or 2-hour PG post 75 g OGTT ≥7.8 mmol/l, i.e. much lower than the diagnostic criteria for non-pregnant individuals Some areas use FPG levels ≥5.1 mmol/l, as any degree of hyperglycaemia in pregnancy increases the risk of both adverse fetal and maternal outcomes	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 Pancreatic Cancer Action's information on T3cD Often misdiagnosed as T2D
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 TD2[2] Follow up after delivery: women require lifelong annual HbA_{1c} (NICE NG3)[1]	Both adults and children at any age Exclude pancreatic cancer in those >60 years with new-onset diabetes and weight loss (NICE NG12)[3]
Weight at Diagnosis	Usually underweight but can occur at any weight 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 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	Normal when treated	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 SGLT2i. See the *Guidelines* Primary Care Hack, *What Next After Metformin?*	Low	Low	Low but hypoglycaemia is common and can be prolonged

Commonly used drugs that can induce hyperglycaemia or cause diabetes:

- corticosteroids e.g. prednisolone, dexamethasone
- thiazide diuretics e.g. bendroflumethiazide, indapamide
- beta-blockers e.g. atenolol, propranolol
- antipsychotics e.g. olanzapine, quetiapine, risperidone
- statins (especially higher potency statins)

References

1. *NICE. Diabetes in pregnancy: management from preconception to the postnatal period.* NICE Guideline 3. NICE, 2015 (updated 2020). Available at: nice.org.uk/guidance/ng3
2. Vounzoulaki E, Khunti K, Abner SC et al. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. *BMJ* 2020: 369m:1361
3. NICE. *Suspected cancer: recognition and referral.* NICE Guideline 12. NICE, 2015 (updated 2021). Available at: nice.org.uk/guidance/ng12

Abbreviations

AD=autosomal dominant; **AR**=autosomal recessive; **CF**=cystic fibrosis; **DKA**=diabetic ketoacidosis; **FH**=family history; **FPG**=fasting plasma glucose; **GDM**=gestational diabetes mellitus; **HbA_{1c}**=haemoglobin A_{1c}; **HbC**=haemoglobin C; **HbS**=haemoglobin S; **IR**=insulin resistance; **LADA**=latent autoimmune diabetes in adults; **MODY**=maturity onset diabetes of the young; **NG**=NICE Guideline; **OGTT**=oral glucose tolerance test; **PEI**=pancreatic exocrine insufficiency; **PG**=plasma glucose; **RF**=risk factor(s); **SGLT2i**=sodium-glucose cotransporter-2 inhibitors; **T1D**=type 1 diabetes; **T2D**=type 2 diabetes; **T3cD**=type 3c diabetes.

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