Types of diabetes and specialist tests

1. Types of diabetes and specialist tests

This article was updated in June 2024.

Most – probably over 95% – of the diabetes we see will be type 1 or type 2, but there are other types.

The diagnosis of these other types is a matter for the specialist, but what are the different types and when might they be considered as a possibility?

Firstly, diabetes can be divided into polygenic or monogenic diabetes:

- **Polygenic diabetes:** several mutations in one individual which act together, resulting in diabetes. Most types of type 1 and type 2

diabetes are polygenic.

- **Monogenic diabetes:** the presence of a single gene defect causes diabetes (there are multiple genetic defects that can do this).

Polygenic diabetes (96% of all diabetes, almost all of which are T1 and T2, and very few are LADA)	
Type 1	• In basic terms, presents as insulin deficiency.
Type 2	• In basic terms, presents as insulin resistance. • Details on the different types of type 2 diabetes are outlined below.

LADA (latent autoimmune diabetes in adults)	• Sometimes called type 1.5 diabetes.
	• Probably a subgroup of type 1 diabetes.
	• Often not overweight (type 1 picture) but presenting at an older age (type 2 picture).
	• Often misdiagnosed and treated as type 2, and may initially respond to this treatment but then develop insulin deficiency quicker than would be expected.
	• Antibodies present, typically one or more of the following (although these can also be present in type 1 diabetes so presence is not confirmatory of LADA):
	  • Islet cell autoantibodies.
	  • GAD autoantibodies (glutamic acid decarboxylase).
	  • Tyrosine phosphatase-related islet antigen 2 (IA-2).
	  • Insulin autoantibodies (IAA).
	Diabetes Spectrum 2016;29(4):249-252

Monogenic diabetes	

(about 1–4% of all diabetes)	
MODY (maturity onset diabetes of the young)	• Classically presents as type 2 picture in younger person, but clinical features can vary depending on gene defect – some run with slightly high sugars but never need treatment, while others need insulin. • Most forms of MODY are autosomal dominant and so, typically, several successive generations have diabetes (type 2 diabetes tends to have a more sporadic picture than this). • Usually not overweight (although with increasing obesity in the population, obesity may be present). *National Institute of Diabetes and Digestive and Kidney Diseases – Monogenic Diabetes (Neonatal Diabetes Mellitus & MODY)*
Mitochondrial diabetes	• Looks like type 1 or type 2. • Strong family history (like MODY) but in MATERNAL line. • Most carriers have bilateral hearing impairment. • Genetic test for confirmation. *Diabetes 2004, 53(suppl 1):S103-S109*
Neonatal diabetes	• Rare (1 in 400 000). • Occurs in first 6–12 months of life (despite the name!). • Usually presents with DKA and usually misdiagnosed as type 1 diabetes. • Half are transitory (although may recur later in life). Half are permanent. • Genetic testing confirms diagnosis. *National Institute of Diabetes and Digestive and Kidney Diseases – Monogenic Diabetes (Neonatal Diabetes Mellitus & MODY)*
Steroid-induced diabetes	

Steroid-induced diabetes	Steroid-induced diabetes is not a separate genetic subtype of diabetes. However, it is a distinct type of diabetes we might see in primary care.
Rarer types	
This includes diabetes caused by diseases such as cystic fibrosis or pancreatitis.	

1.1. Autoantibodies

We would suggest these should only be tested on the advice of the diabetes specialists. We will therefore outline this only briefly (Diabetes Spectrum 2016 Nov;29(4):249-252).

- The presence of autoantibodies is seen in type 1 diabetes and LADA.
- There are a number of different autoantibodies that can be tested for:
    - Islet cell autoantibodies.
    - GAD autoantibodies (glutamic acid decarboxylase).
    - Tyrosine phosphatase-related islet antigen 2 (IA-2).
    - Insulin autoantibodies (IAA).

1.2. Understanding C-peptide

C-peptide can be used to distinguish between type 1 and type 2 diabetes, if there is doubt. However, C-peptide is not that helpful early after diagnosis; as time passes (years), it becomes a better discriminator.

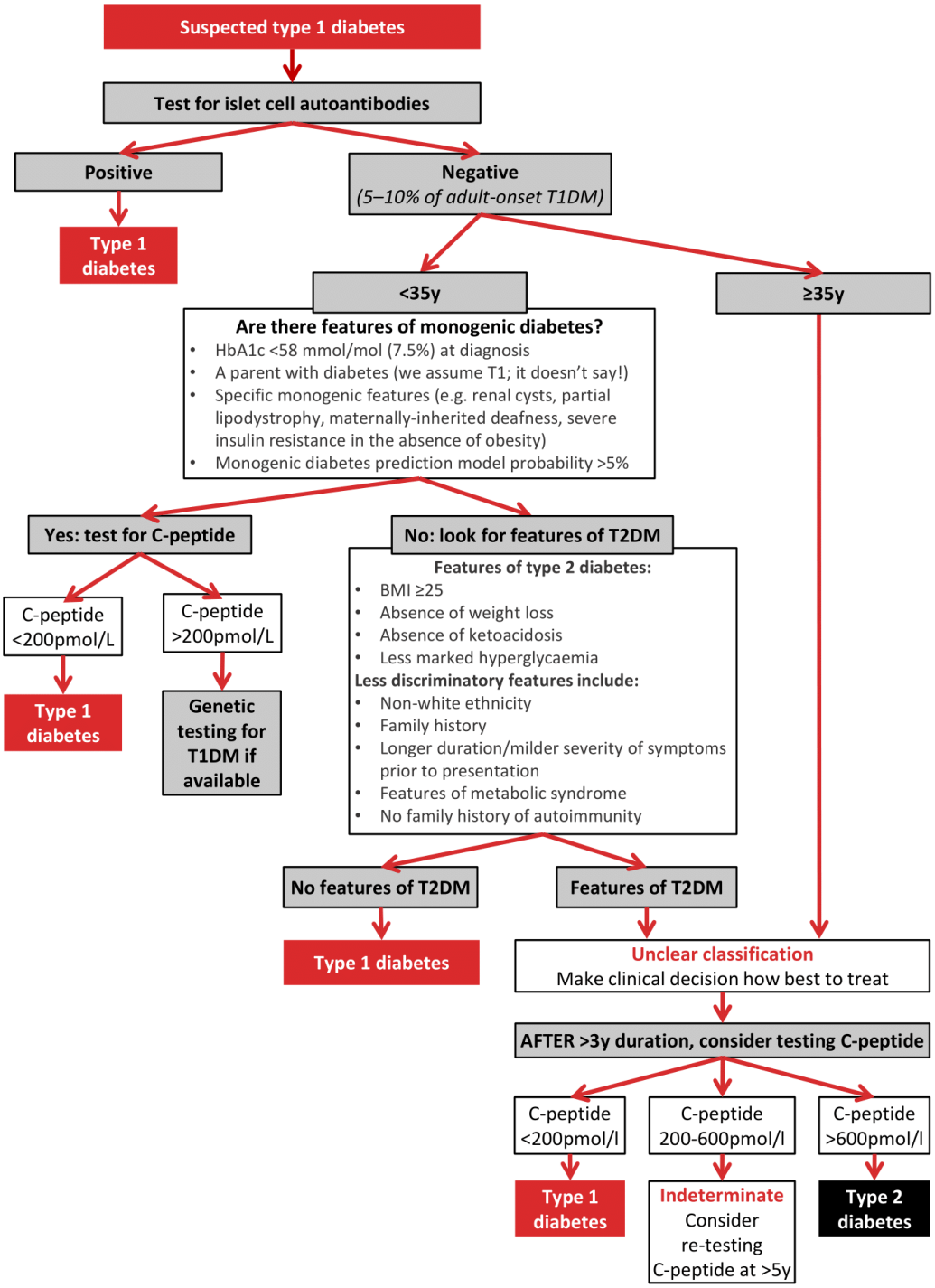
In primary care, we would only test this on the advice of a specialist.

Type of diabetes	**C-peptide level (often, not always!)** Normal range is usually 0.51–2.72ng/ml or 0.17–0.90nmol/l *(Diabetes Spectrum 2016 Nov; 29(4): 249-252)*
Type 1	Low (although can be high in honeymoon period).
Type 2	Normal to high.
MODY	May have intermediate or higher levels.
LADA	Often low to normal initially.

- Low levels of C-peptide are also seen in liver disease, Addison's or severe infection.
- Higher levels can also occur with an insulinoma or Cushing's.

1.3. Interpreting testing for type 1 diabetes

This will be the remit of the diabetes service, but it may be helpful to understand what they are doing. This is summarised from Diabetes Care 2021;44:2589 and BMJ 2024;384:e075681.



1.4. Subtypes of type 2 diabetes

Different types of type 2 diabetes are also described (Lancet 2022;400:1803):

Severe insulin-resistant diabetes	• Late onset (compared with type 1). • Obesity. • Insulin resistance. • Increased risk of renal disease and fatty liver.
Mild obesity-related diabetes	• Early onset. • Obesity. • Lack of insulin resistance.
Mild age-related diabetes	• Late onset. • Low risk of complications.
Severe insulin-deficient diabetes	Similar to type 1 diabetes (but, unlike type 1 diabetes, GAD antibodies are negative): • Low insulin secretion. • High HbA1c and early insulin requirement. • High prevalence of retinopathy and nephropathy.

In primary care, not much is discussed about the different subtypes of type 2 diabetes, but it can be helpful to think about this – for example:

- A person developing diabetes in their 80s – possibly mild age-related type 2 diabetes – may not warrant intensive interventions (glycaemic control/statins/antihypertensives) because their lifetime risk of complications is low.
- For a younger person with type 2 diabetes who has poor control early in the disease, consider whether this might be severe-insulin deficient diabetes: early insulin may be more beneficial than other options.

	**Types of diabetes** • The vast majority of diabetes we see is type 1 or 2, but there are some rare types that we need to be aware of. • Diagnosis of these types is for the specialist, but we have highlighted the things that may point them towards one diagnosis over another. • Specialist tests may be helpful but, again, are not something to be undertaken without specialist advice.
	Does your local diabetes team have guidance on when specialist tests are indicated?

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