CLINICAL GUIDELINE

Diabetes Mellitus Diagnosis

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Diagnosis of Diabetes Mellitus

NHS Greater Glasgow and Clyde

Consider diagnosis of **diabetes mellitus** in **any** patient with one or more of these features:

- thirst and polydipsia
- polyuria and nocturia
- tiredness or lethargy
- recurrent infections (e.g. skin, urine)
- pruritus vulvae or balanitis
- blurred vision (usually an osmotic effect and not permanent)

Important features of undiagnosed diabetes in children and infants:

- bedwetting recurrence in a previously dry child
- failure to thrive in young children
- unexplained weight loss

Type 1 Diabetes

- causes total insulin deficiency leading to hyperglycaemia & diabetic ketoacidosis (DKA)
- likely if **Random Plasma Glucose >11 mmol/l** (after reasonable daily carb intake)
- is a **medical emergency** when first diagnosed, requiring same-day telephone referral & management

DO NOT carry out / request

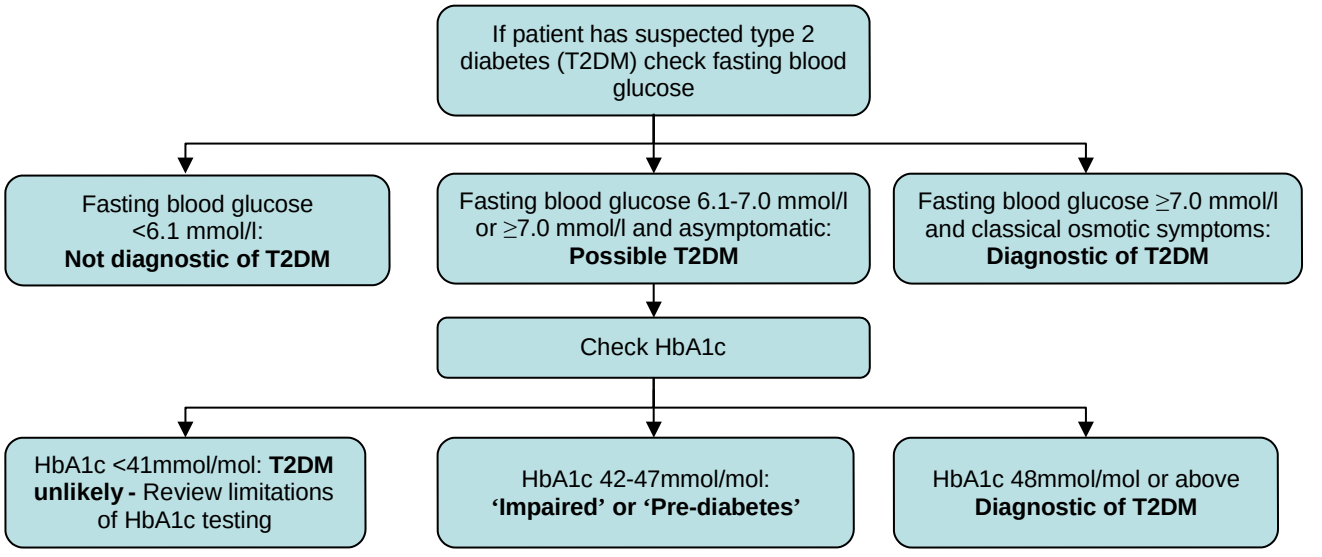
- *Fasting* Glucose,
- Oral Glucose Tolerance Test or
- HbA1c

DO

- immediately investigate (pref. random finger-prick blood glucose +/- urinalysis)
- make same-day telephone referral to specialist diabetes team even if patient ketone negative

Type 2 Diabetes

- is a multifactorial condition resulting in impaired insulin release, sensitivity, or both
- is nowadays being seen more frequently in younger patients than in the past
- initially causes sub-total insulin deficiency leading to hyperglycaemia and, more rarely, ketoacidosis



DEFINITION OF DIABETES MELLITUS

Diabetes mellitus is a group of conditions defined by the level of hyperglycaemia that gives rise to risk of microvascular complications (retinopathy, nephropathy and neuropathy). It is associated with reduced life expectancy, diminished quality of life, significant morbidity due to microvascular complications and also increased risk of macrovascular complications: ischaemic heart disease, stroke and peripheral vascular disease.

The main forms of diabetes mellitus are type 1 diabetes, type 2 diabetes, secondary diabetes mellitus and gestational diabetes. The terms IDDM and NIDDM should now be avoided.

TYPE 1 DIABETES
Type 1 diabetes results from an absolute deficiency of insulin due to destruction of pancreatic beta-cells. It more commonly presents acutely before the age of 35 but can occur at any age. Patients are insulin-dependent and prone to ketoacidosis. Delay in diagnosis/referral can result in severe potentially life threatening DKA (diabetic ketoacidosis).

TYPE 2 DIABETES
Type 2 diabetes results from a relative deficiency of or insensitivity to insulin (insulin resistance) combined with impaired insulin secretion and is more commonly diagnosed over the age of 35, although this is now being seen increasingly in younger (especially obese) individuals. Although the onset of type 2 diabetes is less dramatic than that of type 1, the long-term complications are similar and equally devastating. Both type 1 and type 2 patients are at risk of developing the microvascular and macrovascular complications of the disease. For this reason, type 2 diabetes should never be referred to as 'mild diabetes'.

SECONDARY DIABETES
Secondary diabetes is diabetes resulting from pancreatic damage, hepatic cirrhosis, endocrine disease, or developing as a result of therapy (e.g. with steroids, anti-viral, or anti-psychotic drugs).

GESTATIONAL DIABETES (GDM)
Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. Since this does not exclude that glucose intolerance may have antedated pregnancy, a post-natal glucose tolerance test (OGTT) should be performed at 6 weeks post-natally (please see page 8 for detailed guidance on OGTT).

Women with a history of GDM have a 60% chance of developing diabetes (usually type 2) within the subsequent 20 years and this risk is increased by obesity. For this reason they should be given advise about weight management and have an annual fasting glucose measurement performed. For further details, see section Diabetes in Pregnancy. Women with a history of GDM should be screened for the condition in future pregnancies.

IMPAIRED GLUCOSE TOLERANCE (IGT) AND IMPAIRED FASTING GLYCAEMIA (IFG)

IGT and IFG are not illnesses. They are risk categories (risk factors) primarily for the future development of diabetes.

IMPAIRED GLUCOSE TOLERANCE (IGT)
IGT is a state of impaired glucose homeostasis, diagnosed on the basis of a glucose tolerance test (OGTT) (please see page 8 for detailed guidance on OGTT). IGT confers an increased risk of future diabetes of 2-5% per year. IGT is also (together with hypertension, obesity and dyslipidaemia) part of the metabolic syndrome, which is associated with an increased cardiovascular risk.

IMPAIRED FASTING GLYCAEMIA (IFG)
The term IFG denotes individuals with fasting glucose values of 6.1-6.9 mmol/l. Checking an HbA1c as detailed in the algorithm as detailed above may help identify those individuals with T2DM.

Individuals with impaired glucose tolerance or impaired fasting glycaemia should receive lifestyle advice including diet and exercise, especially if overweight, and should be reviewed periodically, since many will develop diabetes and are at increased cardiovascular risk. Appropriate lifestyle interventions can reduce or delay the development of diabetes by two thirds. Assessment of glycaemia using a fasting blood sugar or HbA1c, blood pressure and lipid profile should be checked annually. Weight loss and exercise should be encouraged if appropriate. Co-existing cardiovascular risk factors should be treated after risk assessment using an appropriate tool. Individuals with a CVD risk of 20% or more should receive suitable treatment in line with GGC cholesterol guidelines (available on StaffNet).

DIAGNOSIS OF DIABETES

Type 1 Diabetes Mellitus

- results from progressive autoimmune destruction of pancreatic beta cells
- causes total insulin deficiency leading to hyperglycaemia & diabetic ketoacidosis (DKA)
- presents in life-threatening DKA in over 25% of cases under 15 years old
    - *30% in DKA have prior HCP encounter when diagnosis delayed or not made*
- likely if **Random Plasma Glucose over 11 mmol/l** (after reasonable daily carb intake)
- is a **medical emergency** and requires
    - immediate investigation (pref. random finger-prick blood glucose +/- urinalysis)
    - same-day referral to a specialist diabetes team even if patient ketone negative
- diagnosis does **not** require *Fasting* Glucose, Oral Glucose Tolerance Test or HbA1c

Consider diagnosis of **Type 1 diabetes** in **any** patient with one or more of these features:

- thirst and polydipsia
- polyuria and nocturia
- recurrence of bedwetting in a previously dry child
- failure to thrive in young children
- unexplained weight loss
- tiredness or lethargy
- recurrent infections (e.g. skin, urine)
- pruritus vulvae or balanitis
- blurred vision (usually an osmotic effect and not permanent)

NB: the diagnosis of diabetes has important medical and legal implications for the patient.

Type 2 Diabetes Mellitus

- is a multifactorial condition resulting in impaired insulin release, sensitivity, or both
- initially causes sub-total insulin deficiency leading to hyperglycaemia and, more rarely, ketoacidosis

Consider diagnosis of **Type 2 diabetes** in **any** patient with one or more of these features:

- thirst and polydipsia
- polyuria and nocturia
- tiredness and lethargy
- recurrent infections (e.g. skin, urine)
- pruritus vulvae or balanitis
- blurred vision (usually an osmotic effect and not permanent)
- discoloured or ulcerated feet
- hypertension, ischaemic heart disease or stroke
- obesity, with diagnosis of arterial disease or family history of diabetes.

In such patients, it is useful to perform preliminary screening investigations i.e. random plasma glucose result and urinalysis or blood for presence of glucose and ketones.

A diagnosis of diabetes should **not** be based solely on the finding of:

- glycosuria
- raised blood glucose (finger prick sample) on a 'stick' reading

NB: the diagnosis of diabetes has important medical and legal implications for the patient.

Patients with Ketonuria

If ketonuria is present with:

- **Severe symptoms** i.e. vomiting and dehydration, **urgent hospital admission** required
- **Milder symptoms** and weight loss, **discuss patient urgently (same day) with the diabetes team** for consideration of insulin therapy.
- **It is important to note that SGLT2 inhibitors are an increasingly recognised cause of diabetic ketoacidosis in people with Type 2 diabetes**

ONLY use the algorithm below for those with suspected Type 2 Diabetes Mellitus

CRITERIA FOR DIAGNOSIS OF TYPE 2 DIABETES

Diabetes may be diagnosed on any of the following criteria (WHO 2006, John 2012).

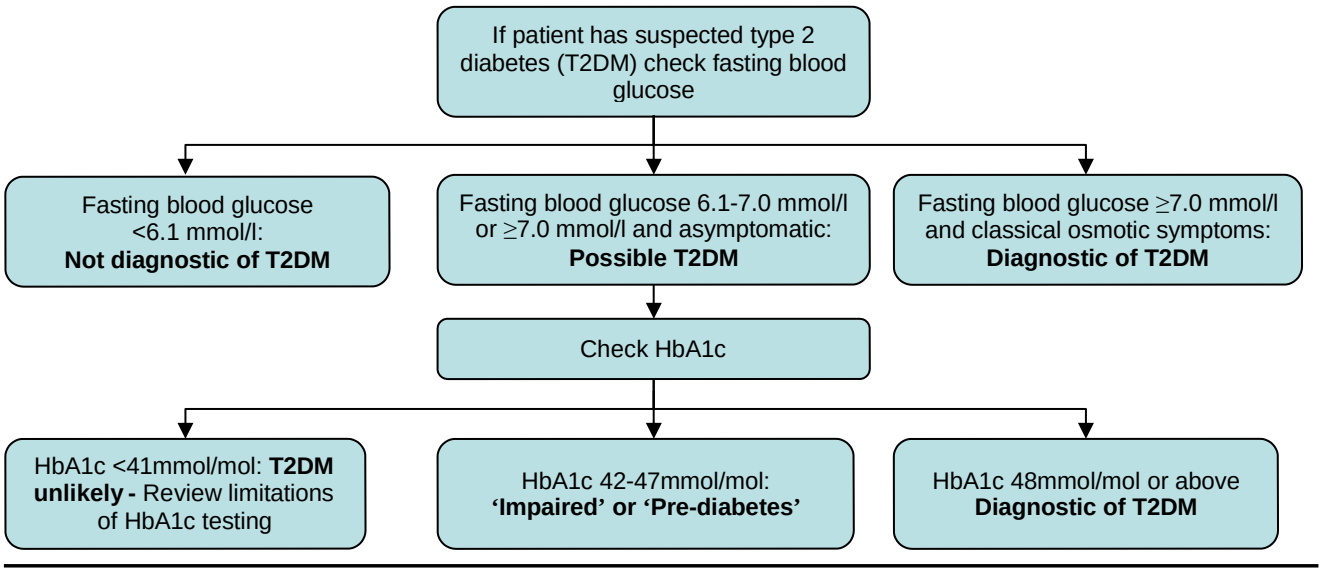
	Diabetes	**"Impaired" or "Pre-diabetes"**	**Normal**
HbA1c	48 mmol/mol and above	42 – 47 mmol/mol	41 mmol/mol and below
Fasting glucose	7.0 mmol/L and above	6.1 – 6.9 mmol/L	6.0 mmol/L and below
2-hr glucose in OGTT	11.1 mmol/L and above	7.8 – 11.0 mmol/L	7.7 mmol/L and below
Random glucose	11.1 mmol/L and above		

<u>Which test is best?</u>

National and international expert groups have not reached consensus. Relevant groups (WHO, ADA) simply advise that HbA1c is now an option for diagnosing diabetes.

Benefits of using HbA1c for diagnosis	**Disadvantages of using HbA1c**
1. *No need for patient to fast* 2. *More reproducible* than glucose. 3. *Continuity with diabetes* (once diagnosed, we switch attention from glucose to Hb1A1c, so it makes sense to use HbA1c for diagnosis)	1. *Inappropriate for some patients* (see below). 2. *Relatively high cost (£1.12 v 3p for glucose)* 3. *Will define a slightly different population to using glucose values.*

Pragmatic Approach to Testing



When to further investigate a raised random glucose

Again, there is no national consensus on when to further investigate a raised random blood glucose. In general we would suggest further investigation (either a fasting blood glucose or HbA1C) when random blood glucose is ≥ 7 mmol/l.

When not to use HbA1c to diagnose Type 2 diabetes

The following are the most common situations where HbA1c is not suitable. In these situations, except pregnancy, diagnose diabetes by fasting glucose ≥7.0 mmol/L twice, or once with symptoms. In pregnancy, follow NICE guidelines.

1. **Rapid onset of diabetes** – an increase in HbA1c may not be detected until a few weeks later.
    a. *Suspected type 1 diabetes* – rapid onset of symptoms, weight loss, ketosis.
    b. *Children* – because most will have type 1 diabetes.
    *****Both these conditions require urgent (same day input) from specialist diabetes teams*****
    c. *Steroids*. Antipsychotics & immunosuppressants can raise blood glucose, rarely precipitously.
    d. After *pancreatitis* or *pancreatic surgery***.**

2. **Pregnancy**. Multiple factors make HbA1c lower in pregnancy. The diagnosis of gestational diabetes should be made by using glucose measurements in line with SIGN guidance: https://www.sign.ac.uk/media/1054/sign116.pdf
    For the diagnosis of Gestational Diabetes, the following glucose levels should be used
    Fasting glucose - 5.1 mmol/l or above
    2 hr glucose in GTT - 8.5 mmol/l or above

3. **Conditions with reduced red cell survival may lower HbA1c markedly:**
    a. *Haemoglobinopathy* which will normally be detected by the lab, but should be suspected in racial groups where there is a high prevalence of sickle trait, sickle disease or thalassaemia.
    b. Haemolytic anaemia
    c. Severe blood loss
    d. Splenomegaly
    e. Antiretroviral drugs

4. **Increased red cell survival** may increase HbA1c e.g. Splenectomy.

5. **Renal dialysis patients** have a markedly reduced HbA1c especially if treated with erythropoietin.

6. **Iron and B12 deficiency and their treatment**. May raise or lower HbA1c, but the effect is small.

What if you have glucose values and an HbA1c on a single patient that are incongrous?

The WHO guidance is to diagnose diabetes if either result is high.

How should we manage the patient with "pre-diabetes" or "impaired glucose tolerance"?

Treat as high diabetes risk:

- Discuss dietary and lifestyle factors that may help to reduce risk of progression to T2DM.
- If appropriate discussion about weight management and if necessary in accordance with current GGC weight management guidelines

Monitoring can be appropriate for individuals at high risk of diabetes such as strong family history, ethnicity, previous gestational diabetes or transient elevated blood glucose after acute illness.

We do not advise measuring blood glucose after an HbA1c of 42-47 mmol/mol. You may be tempted to try another test in pursuit of a "clear diagnosis", but it is likely to create diagnostic confusion. As detailed above it is appropriate to introduce lifestyle measures and re-assess glycaemic status, blood pressure and lipids annually.

What if a patient lowers their HbA1c below 48 mmol/mol through lifestyle change?

If someone is diagnosed with diabetes, and then drops their HbA1c below 48 mmol/mol without drugs – we consider that they have excellently controlled diabetes on diet alone, and recommend that they continue to receive care appropriate for people with diabetes.

References

WHO 2006 – http://whqlibdoc.who.int/publications/2006/9241594934_eng.pdf
John et al 2012 - http://onlinelibrary.wiley.com/doi/10.1111/j.1464-5491.2012.03762.x/pdf

Secondary Diabetes Mellitus

Clinicians should be aware of rare causes of hyperglycaemia such as inflammatory or neoplastic pancreatic disease. People who present with non-ketotic hyperglycaemia whose phenotype and clinical history are not classical of type 2 diabetes, for example thin patients with no family history of diabetes, should also be considered for referral to secondary care to clarify the diagnosis. All patients with persistent ketonuria should be referred for a secondary care assessment.

ORAL GLUCOSE TOLERANCE TEST (OGTT)

INDICATIONS FOR OGTT

The need to perform an OGTT will be limited if the above advice is followed. An OGTT is not necessary if the diagnostic criteria for diabetes are present.

PERFORMING OGTT

- Perform OGTT after at least 3 days of unrestricted diet (> 150g carbohydrate daily).
- Fast patient overnight (8-14 hours, water allowed) and rest during the test. Patient should not smoke on the day of the test.
- Take a sample for fasting blood glucose.
- Give Rapilose oral glucose tolerance test solution 75g/300ml. Or alternatively, give 75g of anhydrous glucose in 250-350 ml of water over a 5-minute period. Previously lucozade was used for OGTT. Since the reduction in sugar content in 2017, using lucozade would now require 950mls to be consumed within 5 minutes, which is not felt to be a realistic volume over such a short space of time.
- Check blood glucose after 2 hours. Samples at times other than 0 and 2 hours are not necessary for diagnosis.
- Diagnostic interpretation of OGTT is different in pregnancy.