Glucose tolerance tests

See also the separate Diabetes in Pregnancy, Metabolic Syndrome, Managing Impaired Glucose Tolerance In Primary Care and Gestational Diabetes articles.

What is a glucose tolerance test?

The oral glucose tolerance test (OGTT) evaluates the efficiency of the body to metabolise glucose. For many years the OGTT was used as the 'gold standard' for diagnosis of diabetes. An increase in postprandial glucose concentration usually occurs before fasting glucose increases. Therefore, postprandial glucose is a sensitive indicator of the risk for developing diabetes and an early marker of impaired glucose tolerance. Evidence has suggested that, when compared with fasting blood glucose, an increased two-hour plasma glucose during an OGTT is a better predictor of both all-cause mortality and cardiovascular mortality or morbidity. However extensive patient preparation is necessary to perform an OGTT. Important conditions include, among others, ingestion of at least 150 g of dietary carbohydrate per day for three days prior to the test, a 10- to 16-hour fast, and commencement of the test between 7:00 am and 9:00 am. In addition, numerous conditions other than diabetes can influence the OGTT. Evidence also indicates a high degree of individual patient variability in the OGTT, with greater variability than fasting blood glucose. The lack of reproducibility, the inconvenience and the cost of the OGTT led to the removal of the OGTT for the routine diagnosis of diabetes, which is now usually done by measuring HbA1c, although it can also be done by measuring fasting or random glucose.[1]

Definitions of diabetes

The information in this article is mainly concerned with the diagnosis of type 2 diabetes, where a lack of symptoms, and insidious onset to the illness, mean that diagnostic tests may be needed to confirm a clinical suspicion of the disease, or investigate significant risk factors for the illness. Those with type 1 diabetes are much more likely to present with symptoms and a fairly rapid onset of illness, glycosuria and significant random hyperglycaemia.

There are a variety of definitions and diagnostic criteria for concepts such as impaired fasting glucose (IFG), impaired glucose tolerance (IGT), the metabolic syndrome and 'pre-diabetes', now known as non-diabetic hyperglycaemia. The most important concern for primary care practitioners is that they can identify those patients with frank type 1 or type 2 diabetes and be able to advise and monitor patients with indicators of impaired glucose metabolism who are at risk of developing type 2 diabetes.

Diagnosing diabetes

- Diabetes may be diagnosed on the basis of one abnormal plasma glucose (random ≥11.1 mmol/L or fasting ≥7 mmol/L) in the presence of diabetic symptoms such as thirst, increased urination, recurrent infections, weight loss, drowsiness and coma.
- In asymptomatic people with an abnormal random plasma glucose, two fasting venous plasma glucose samples in the abnormal range (≥7 mmol/L) are recommended for diagnosis.
- More usually in clinical practice, diabetes is diagnosed with an HbA1c of 48 mmol/mol or more - a single test if there are symptoms, or two results if the patient is asymptomatic.[1]
- OGTT is not recommended as a screening test for diabetes mellitus.

Glycated haemoglobin[2]

HbA1c testing is used for both monitoring blood sugar control in patients with diabetes and as a diagnostic test for diabetes. An HbA1c of 48 mmol/mol is recommended as the cut-off point for diagnosing diabetes. A value less than 48 mmol/mol does not exclude diabetes diagnosed using glucose tests.

Situations where HbA1c is not appropriate for diagnosis of diabetes include:

- Children and young people.
- Patients suspected of having type 1 diabetes.
- Patients with symptoms of diabetes for less than two months.
- Patients at high diabetes risk who are acutely ill.
- Patients taking medication that may cause rapid glucose rise - eg, steroids, antipsychotics.
- Patients with acute pancreatic damage, including pancreatic surgery.
- Pregnancy.

- Presence of other factors that influence HbA1c and its measurement:
    - Erythropoiesis:
        - Increased HbA1c: iron, vitamin B12 deficiency, decreased erythropoiesis.
        - Decreased HbA1c: administration of erythropoietin, iron, vitamin B12, reticulocytosis, chronic liver disease.
    - Altered haemoglobin:
        - Genetic or chemical alterations in haemoglobin: haemoglobinopathies, HbF and methaemoglobin may increase or decrease HbA1c.
    - Glycation:
        - Increased HbA1c: alcoholism, chronic kidney disease.
        - Decreased HbA1c: aspirin, vitamin C and E, certain haemoglobinopathies.
    - Erythrocyte destruction:
        - Increased HbA1c: increased erythrocyte lifespan - eg, splenectomy.
        - Decreased HbA1c: decreased erythrocyte lifespan - eg, haemoglobinopathies, splenomegaly, rheumatoid arthritis or drugs such as antiretrovirals, ribavirin and dapsone.
    - Other factors:
        - Increased HbA1c: hyperbilirubinaemia, alcoholism, large doses of aspirin, chronic opiate use.
        - Variable HbA1c: haemoglobinopathies.
        - Decreased HbA1c: hypertriglyceridaemia.

Screening for diabetes

Screening for diabetes is now included in the NHS Health Check for adults in England between the ages of 40 and 74 years.[3]

- It is estimated that one million people people have undiagnosed type 2 diabetes in the UK and that 7% of the UK population have type 2 diabetes. One third of people have microvascular complications at the time of diagnosis of type 2 diabetes.[4]
- There is good evidence that an appropriately designed and targeted screening strategy is effective at detecting undiagnosed type 2 diabetics in a UK-based primary care setting. Screening is more cost-effective for people in the hypertensive and obese subgroups and the costs of screening are offset in many groups by lower future treatment costs.
- The National Institute for Health and Care Excellence (NICE) recommends that the following groups of people have a risk-assessment for type 2 diabetes:[5]
    - All non-pregnant adults aged 40 and above.
    - People aged 25-39 from certain ethnicities which are at a higher risk of having diabetes (South Asian, Chinese, African-Caribbean, black African).
    - Adults with conditions that can increase the risk of type 2 diabetes, such as cardiovascular disease, hypertension, obesity, stroke, polycystic ovary syndrome or a history of gestational diabetes.

Indications for the oral glucose tolerance test

- The OGTT is no longer used for the routine diagnosis of diabetes.
- It is used in pregnancy to diagnose gestational diabetes.[6]

The oral glucose tolerance test and pregnancy

The most appropriate strategies for screening and diagnosing gestational diabetes mellitus remain controversial. There is a continuous relationship between maternal glucose level at 24-28 weeks and pregnancy outcomes (macrosomia, fetal insulin, clinical neonatal hypoglycaemia and caesarean section). Women should be screened for glycosuria at each antenatal visit. NICE recommends:[6]

- Assess risk of gestational diabetes using the following risk factors for gestational diabetes:
    - BMI above 30 kg/m^2.
    - Previous macrosomic baby weighing 4.5 kg or above.
    - Previous gestational diabetes.
    - Family history of diabetes (first-degree relative with diabetes).
    - Minority ethnic family origin with a high prevalence of diabetes.
- Offer women with any one of these risk factors testing for gestational diabetes. Do not use fasting plasma glucose, random blood glucose, HbA1c, glucose challenge test or urinalysis for glucose to assess risk of developing gestational diabetes.
- Use the two-hour 75 g OGTT to test for gestational diabetes in women with any of the above risk factors.
- Offer women who have had gestational diabetes in a previous pregnancy:
    - Early self-monitoring of blood glucose; **or**
    - A 75 g two-hour OGTT as soon as possible after booking (whether in the first or second trimester) and a further 75 g two-hour OGTT at 24-28 weeks if the results of the first OGTT are normal.
- Offer women with any of the other risk factors for gestational diabetes a 75 g two-hour OGTT at 24-28 weeks.

- Diagnose gestational diabetes if the woman has either:
    - Fasting plasma glucose level of 5.6 mmol/L or above; **or**
    - Two-hour plasma glucose level of 7.8 mmol/L or above.

Conducting the oral glucose tolerance test[7]

- The test should be preceded by ≥3 days of normal, unrestricted diet (>150 g carbohydrate daily) with normal physical activity. There should be a carbohydrate-rich meal (30-50 g) on the night before the test. There should then be an overnight fast of 8-14 hours; drink only water.
- Record any factors that may affect interpretation of the test, such as medication, inactivity, infection, gestation of pregnancy, acute psychological stress, etc. The patient should not smoke during the test.
- Collect fasting (and all other) samples in a tube that permits measurement of plasma glucose (eg, a sodium fluoride tube). Timing of test (0 hours) starts at the beginning of the glucose drink.
- Adults ingest 75 g glucose in 250-300 ml water over five minutes. Children ingest 1.75 g/kg body weight in a similar volume of water by ratio (max 75 g as for adults).
- Take a blood sample at two hours; some schema suggest taking a one-hour sample but this is not strictly necessary in terms of diagnosing diabetes. Ideally, take the sample from a warmed vein on the back of the patient's hand (antecubital fossa samples may be artificially lower).
- An indwelling 'butterfly' or conventional cannula can be left in situ throughout the test (affix in place and dress); flush with saline after taking a fasting sample, then draw at least 10 ml and discard before drawing a sample for the assay tube.
- Glucose should be measured immediately after collection by near-patient testing or, if a blood sample for a laboratory is collected, plasma should be immediately separated, or the sample should be collected into a container with glycolytic inhibitors and placed in ice-water until separated prior to analysis.

- An extended glucose tolerance test may be conducted to detect cases of reactive hypoglycaemia or other abnormalities of glucose metabolism with samples taken at 0, 30, 60, 90, 120, 150 and 180 minutes. The extended test may also be used to diagnose acromegaly when samples are also taken for growth hormone levels.

If the test is conducted correctly and blood sampling performed appropriately, there are no causes of false-positive results other than factors that can provoke hyperglycaemia that should be checked for before performing the test:

- Undisclosed medication changes (eg, steroids).
- Inactivity.
- Infection.
- Other acute illness.
- Pregnancy.
- Acute psychological stress.
- Failure to comply with the pre-test feeding/fasting regimen.

References

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