GLUCOSE TOLERANCE TEST: FOR THE DIAGNOSIS OF DIABETES MELLITUS

Introduction

In most cases Diabetes mellitus can be diagnosed using either fasting glucose or HbA1c. Diagnosis of diabetes must be based on either glucose or HbA1c but not a combination of the two. Diagnostic algorithms for glucose based diagnosis of diabetes mellitus and glucose intolerance (WHO 2006) and for HbA1c based diagnosis of diabetes mellitus (WHO 2011) are shown in Appendix A and B of this document.

Note the cut-offs used locally are different to the WHO criteria applied to the non-pregnant population and are included, along with guidance on reporting by the duty biochemist in Appendix C.

Principle

Following the oral administration of a standard dose of glucose, the plasma glucose concentration normally rises but returns towards the fasting level within 2 hours. If insulin activity is reduced the plasma glucose concentration takes longer than 2 hours to return to normal.

Preparation

1) The patient should be on a normal carbohydrate diet (at least 150g per day) for at least 3 days before the test.
2) It is desirable to postpone the test if the patient is febrile, is within 6 weeks of a myocardial infarction or major surgery or is on short-term treatment with drugs which impair glucose tolerance, such as glucocorticoids, thiazide diuretics, beta blockers, loop diuretics, progesterone and oestrogen.
3) The patient should fast from 10 p.m. on the evening before the test with the exception of drinks of water and any drugs which he/she normally takes.
4) During the test the patient should be resting and should not smoke, eat or drink, except for glasses of water.

Procedure

1) At about 9 am take 2mls venous blood into a fluoride oxalate (grey top) bottle. Note the time of the specimen on the bottle and the request form/electronic request.
2) Give the patient 75 g of glucose. This can be given in 3 different ways:

a) Polycal liquid (Nutricia Clinical).
This is available on prescription. The instructions below should be followed:
• 113ml Polycal liquid made up to a volume of 200ml in a beaker with water, shaken thoroughly and consumed over a 5 minute period followed by a further 100ml plain water
b) Rapilose:
- Adults (including the elderly): 300ml to be consumed over a period of 5-10 minutes
- Children: for children weighing less than 43kg the dosage should be reduced based on child’s body mass; the dose is 7ml of solution per kg of body weight up to a maximum 300ml

c) Anhydrous glucose
- 75 g dissolved in 300 ml water

3) The patient needs to rest and not smoke for 2 hours until the post glucose samples are taken.
4) Take one further 2mls venous blood sample into a fluoride oxalate bottle 120 minutes after the glucose was given. Note the time of the specimen on the bottle and the request form/electronic request.
5) The test is now complete and the patient may eat. If the patient vomits during the test, stop the test.
6) Send both blood specimens with the request form (if applicable).

**Interpretation (Non pregnancy)**

If the above procedure is followed, venous plasma glucose is measured and the WHO criteria are as follows:

<table>
<thead>
<tr>
<th>Classification</th>
<th>Fasting</th>
<th>2 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;6.1</td>
<td>&lt;7.8</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>≥7.0</td>
<td>≥11.1</td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td>&lt;7.0</td>
<td>7.8 - 11.0</td>
</tr>
<tr>
<td>Impaired fasting glucose</td>
<td>6.1-6.9</td>
<td>&lt;7.8</td>
</tr>
</tbody>
</table>

**NB.** The above criteria apply to venous plasma. If venous whole blood or capillary blood is used, different criteria apply. Please contact laboratory.

**Local diagnostic criteria in pregnancy**

The local maternity guidelines use a venous fasting range of 5.5 – 7.0 mmol/L and a 2 hour range of 7.8 – 11 mmol/L to define impaired glucose tolerance. There is no separate category for impaired fasting glucose and the fasting cut-off used to define normal results is lower than the WHO guidelines. A flow chart outlining the protocol is included at the end of this document.

**GTT comment**

An automatic comment will be put on all GTT results:

- Diabetes: Fasting glucose >7.0 mmol/L or 2hr glucose >11.0mmol/L
- Impaired glucose tolerance: 2hr glucose 7.8-11.0mmol/L
- Impaired fasting glucose: Fasting glucose 6.1-6.9mmol/L (>5.5mmol/L in pregnancy)
In pregnancy, all abnormal results, including impaired fasting glucose, should be referred to the antenatal clinic within 72hrs (telephone No. 0117 3235310). Please see local maternity guidelines for referral pathways.

**References**
Definition and diagnosis of Diabetes Mellitus and intermediate hyperglycaemia. Geneva WHO 2006
Use of Glycated Haemoglobin (HbA1c) in the diagnosis of Diabetes Mellitus WHO 2011
Appendix A.

Diagnostic algorithm for glucose based diagnosis of diabetes mellitus and glucose intolerance (WHO 2006)

- Fasting glucose is recommended as the initial diagnostic test where feasible.
- In the absence of classical symptoms, (thirst, polyuria and unexplained weight loss) at least two diagnostic glucose results on different days are essential.
- If discordant results are obtained, either fasting (if reliable) or 2h OGTT value may be diagnostic, but re-testing after an interval is recommended.
- Tests should not be carried out during intercurrent illness or periods of stress as this may result in false positive results.
- Impaired Glucose Tolerance and Impaired Fasting Glycaemia carry increased risk of progression to diabetes – recommended re-assess in one year.
Appendix B.

Diagnostic algorithm for HbA1c based diagnosis of diabetes mellitus (WHO 2011)

- **Diabetes unlikely**
  - ≤42 mmol/mol
  - Reassess in 3 years if high risk

- **Measure HbA1c**
  - ≥48 mmol/mol
  - Probable diabetes

- **42 - 47 mmol/mol**
  - Increased diabetes and CV risk
  - Reassess in 1 year

- **High diabetes and CV risk**
  - Reassess in 6 months

- **<48 mmol/mol**
  - Repeat HbA1c within 2 weeks

- **≥48 mmol/mol**
  - Diabetes Confirmed

**HbA1c must not** be used if hyperglycaemia has developed rapidly, for example:
- Possible Type 1 diabetes
- Symptomatic children and young adults
- Symptoms less than three months
- Acutely ill patients
- Medication that may cause rapid rise in glucose e.g. corticosteroids, antipsychotics
- Acute pancreatic damage or pancreatic surgery

**HbA1c must not** be used in the presence of factors affecting HbA1c formation or measurement. These include:
- Iron and vitamin B₁₂ deficiency
- Haemolytic anaemias
- Administration of iron, vitamin B₁₂ or erythropoietin
- Chronic liver disease
- Chronic renal failure (CKD 4 and 5)
- Alcoholism
- Rheumatoid arthritis
- Splenomagaly or splenectomy
- Haemoglobinopathies
- Drugs that may affect erythrocyte lifespan e.g. antiretrovirals, ribavarin, dapsone

**HbA1c must not** be used to diagnose diabetes in pregnancy
Appendix C

Screening for Diabetes in Pregnancy (local protocol)

+++ Glycosuria
at any routine AN visit

TIMED GLUCOSE

Within 2 hours of eating
- Glucose <7
  - Normal
  - No further action

> 2 hours after eating
- Glucose <5.5
  - Normal

> 2 hours after eating
- Glucose >7
  - Abnormal
  - GTT

Fasting >7 or 2hr >11.0
  - Diabetic
  - Urgent referral to Med ANC. Telephone 35310

Fasting 5.5-7.0 or 2hr 7.8-11.0
  - Impaired
  - Referral within 72 hours to Med ANC

Fasting <5.5 or 2hr <7.8
  - Normal
  - No action required