Oral Glucose Tolerance Testing

Background[1,2]

Diabetes mellitus is a chronic illness that has significant acute and chronic implications for patients. Some of the most common classifications for diabetes include type 1, type 2, and gestational. Type 1 diabetes is caused by an autoimmune-mediated destruction of pancreatic β cells. These cells are insulin producing, and their destruction leads to subsequent insulin deficiency. Type 2 diabetes is a progressive loss of insulin secretion in association with insulin resistance. Gestational diabetes refers to diabetes diagnosed during pregnancy.

All of the disease classifications for diabetes produce increased blood glucose levels. If diabetes is left untreated, the patient may exhibit complications that could be acute (e.g., diabetic ketoacidosis) or chronic (e.g., heart and peripheral vascular disease). Early diagnosis and appropriate treatment can help decrease these deleterious effects.

Clinical Indications

Oral glucose tolerance testing is used for the following purposes:

- Screening for common types of diabetes (especially in high-risk groups) in which clinical intervention could lead to preventing complications.
- Confirming the diagnosis of diabetes or impaired glucose tolerance when clinically suspected and a definitive answer is not obvious based on fasting glucose and hemoglobin A1c (commonly for type 2 diabetes and pre-diabetes).

Non-Gestational

Diabetes is a major cause of death and illness worldwide, and its global prevalence continues to rise. Treatments for type 2 diabetes are well established and its complications can be prevented. Moreover, decisive intervention when pre-diabetes is discovered can prevent or delay the onset of diabetes.

Currently, the American Diabetes Association (ADA) recommends testing for diabetes at 3-year intervals using fasting plasma glucose, hemoglobin A1c, or the 2-hour oral glucose tolerance test. Screening with a fasting glucose or hemoglobin A1c is convenient because of a single blood draw and no need for glucose administration. However, fasting glucose alone could miss a large number of patients with impaired glucose tolerance and early diabetes. Hemoglobin A1c testing is associated with significant false-positive and false-negative results when compared to oral glucose tolerance testing. The 2-hour glucose tolerance test could be used in higher risk groups to clarify diagnosis (e.g., normal fasting glucose and elevated hemoglobin A1c), and to verify diagnosis when there is high clinical suspicion (e.g., normal fasting glucose and hemoglobin A1c in association with neuropathy).

Testing is recommended for all adults with a body mass index (BMI) ≥25 kg/m^2 and 1 or more additional risk factors for diabetes. Alternatively, testing is recommended starting at age 35 years if no risk factors are present.

Pertinent risk factors for diabetes might include: age >45 years old, BMI >25 kg/m^2, sedentary lifestyle, dyslipidemia, possible history of gestational diabetes, hypertension (>140/90 mmHg), and diagnosis of diabetes in a first degree relative. The presence of symptomatology associated with diabetes (e.g., polyuria or polydipsia) may also indicate a need for testing.

Gestational

The American College of Obstetricians and Gynecologists (ACOG) recommends all pregnant women be screened for gestational diabetes. Typically the test is accomplished between 24 and 28 weeks or earlier if risk factors are present. Women with gestational diabetes are more prone to macrosomia, preeclampsia, shoulder dystocia, and stillbirth, and their children have increased risks for respiratory complications, hypoglycemia, and jaundice.

Methodology

Non-Gestational

A fasting (at least 8 hours) plasma glucose specimen is first collected. After its collection, the patient is orally administered 75 grams of anhydrous glucose dissolved in

water. Two subsequent plasma glucose samples are then collected at 1 and 2 hours.

Gestational Two-Step Approach
Gestational screening: The patient (non-fasting) is orally administered 50 grams of anhydrous glucose dissolved in water. A 1-hour plasma glucose specimen is then collected.

Gestational confirmation: A fasting (at least 8 hours) plasma glucose specimen is first collected. After its collection, the patient is orally administered 100 grams of anhydrous glucose dissolved in water. Three subsequent plasma glucose specimens are then collected at 1, 2, and 3 hours.

Analytical Method
Glucose is phosphorylated to glucose-6-phosphate by hexokinase in the presence of ATP. Glucose-6-phosphate is then oxidized to gluconate-6-phosphate by glucose-6-phosphate dehydrogenase in the presence of NADP. The subsequent NADPH formation is measured photometrically. The rate of NADPH formation is directly proportional to the glucose concentration.

Interpretation

Non-Gestational
Prediabetes: ADA guidelines state patients are at increased risk for diabetes mellitus when the fasting plasma glucose result is 100-125 mg/dL or the 2-hour glucose tolerance is 140-199 mg/dL.

The ADA criteria do not specify the importance of glucose measurements at 1 hour after glucose ingestion. It has been suggested that a glucose level >155 mg/dL at 1 hour after glucose ingestion is associated with a higher risk for developing diabetes.[3]

Diabetes: ADA guidelines state a diabetes mellitus diagnosis is preliminarily made when the fasting plasma glucose is ≥126 mg/dL and/or the 2-hour glucose tolerance is ≥200 mg/dL. In the absence of unequivocal hyperglycemia, results should be confirmed with repeat testing.

A diagnostic cutoff for the 1-hour time point is not established and should be clinically determined.

Gestational Two-Step Approach[4-6]
Gestational screening: ACOG guidelines state that, in women not previously diagnosed with overt diabetes, a gestational diabetes mellitus positive screen is made when the 1-hour plasma glucose level is ≥140 mg/dL. The Cleveland Clinic Ob/Gyn & Women's Health Institute recommends a 135 mg/dL cut-off.

Gestational confirmation: ACOG guidelines indicate gestational diabetes mellitus is present when 2 or more of the plasma glucose concentrations meet or exceed the following levels:
- Fasting: 95 mg/dL
- 1-hour: 180 mg/dL
- 2-hour: 155 mg/dL
- 3-hour: 140 mg/dL

References

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3. Abdul-Ghani MA, Abdul-Ghani T, Ali N, Defronzo RA. One-hour plasma glucose concentration and the metabolic syndrome identify subjects at high risk for future type 2 diabetes. *Diabetes Care*. 2008;31(8):1650-1655.
4. Coustan DR, Nelson C, Carpenter MW, Carr SR, Rotondo L, Widness JA. Maternal age and screening for gestational diabetes: a population-based study. *Obstet Gynecol*. 1989; 73:557-561.
5. Committee on Practice Bulletins-Obstetrics. Practice Bulletin No. 137: Gestational diabetes mellitus. *Obstet Gynecol*. 2013;122(2 Pt 1):406-416.

6. Van Dorsten JP, Dodson WC, Espeland MA, Guise JM, Mercer BM, et al. Diagnosing gestational diabetes mellitus. National Institutes of Health Consensus Development Conference Statement. *NIH Consense State Sci Statements*. 2013;29(1):1-30.

Test Overview

Test Name	50 gram, non-fasting, 1-hour, gestational glucose screen	100 gram, fasting, 3-hour, gestational glucose tolerance confirmation	75 gram, fasting, 2-hour, non-gestational glucose tolerance	75 gram, fasting, 5-hour, non-gestational glucose tolerance
Methodology	Glucose hexokinase			
Specimen Requirements	Potassium oxalate/sodium fluoride (gray-top) tube			
Specimen Stability	24 hours at ambient (15-25˚C) and refrigerated (2-8˚C) conditions 72 hours at refrigerated (2-8˚C) conditions if removed from cells			
Ordering Mnemonic	GLTGST	GTGST3	GTNG2	GTNG5
CPT Code	82950	82951, 82952	82951	82951, 82952

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