Test Definition: A1CJ

Hemoglobin A1c, Blood

Overview

Useful For

Diagnosis of diabetes

Evaluating the long-term control of blood glucose concentrations in patients with diabetes

Identifying patients at an increased risk for developing diabetes

This assay is **not useful** in determining day-to-day glucose control and should not be used to replace daily home testing of blood glucose.

Method Name

Ion-Exchange Chromatography Quantitative

NY State Available

No

Specimen

Specimen Type

Whole Blood EDTA

Specimen Required

Container/Tube: Lavender-top (EDTA)
Specimen Volume: 3 mL
Collection Instructions: Send specimen in original tube. Do **not** aliquot.

Specimen Minimum Volume

2 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood EDTA	Refrigerated (preferred)	7 days	
	Frozen	7 days	
	Ambient	24 hours	

Clinical & Interpretive

Clinical Information

Diabetes mellitus is a chronic disorder associated with disturbances in carbohydrate, fat, and protein metabolism characterized by hyperglycemia. It is one of the most prevalent diseases, affecting approximately 24 million individuals in the United States. Long-term treatment of the disease emphasizes control of blood glucose levels to prevent the acute complications of ketosis and hyperglycemia. In addition, long-term complications such as retinopathy, neuropathy, nephropathy, and cardiovascular disease can be minimized if blood glucose levels are effectively controlled.

Hemoglobin A1c (HbA1c) is a result of the nonenzymatic attachment of a hexose molecule to the N-terminal amino acid of the hemoglobin molecule. The attachment of the hexose molecule occurs continually over the entire life span of the erythrocyte and is dependent on blood glucose concentration and the duration of exposure of the erythrocyte to blood glucose. Therefore, the HbA1c level reflects the mean glucose concentration over the previous period (approximately 8-12 weeks, depending on the individual) and provides a much better indication of long-term glycemic control than blood and urinary glucose determinations. Diabetic patients with very high blood concentrations of glucose have from 2 to 3 times more HbA1c than normal individuals.

Diagnosis of diabetes includes 1 of the following:
-Fasting plasma glucose of 126 mg/dL or greater
-Symptoms of hyperglycemia and random plasma glucose of 200 mg/dL or greater
-Two-hour glucose of 200 mg/dL or greater during oral glucose tolerance test unless there is unequivocal hyperglycemia, confirmatory testing should be repeated on a different day

In addition, recommendations from the American Diabetes Association (ADA) include the use of HbA1c to diagnose diabetes, using a threshold of 6.5%. The threshold is based upon sensitivity and specificity data from several studies.

Advantages to using HbA1c for diagnosis include:
-Provides an assessment of chronic hyperglycemia
-Assay standardization efforts from the National Glycohemoglobin Standardization Program have been largely successful and the accuracy of HbA1c is closely monitored by manufacturers and laboratories
-No fasting is necessary
-Intraindividual variability is very low (critical value of <2%)
-A single test could be used for both diagnosing and monitoring diabetes

When using HbA1c to diagnose diabetes, an elevated HbA1c should be confirmed with a repeat measurement, except in those individuals who are symptomatic with a plasma glucose concentration above 200 mg/dL. Patients who have an HbA1c between 5.7 and 6.4 are considered at increased risk for developing diabetes in the future. (The terms prediabetes, impaired fasting glucose, and impaired glucose tolerance will eventually be phased out by the ADA to eliminate confusion.)

The ADA recommends measurement of HbA1c (typically 3-4 times per year for type 1 and poorly controlled type 2 diabetic patients, and 2 times per year for well-controlled type 2 diabetic patients) to determine whether a patient's metabolic control has remained continuously within the target range.

Reference Values

4.0-5.6%
<18 years: Hemoglobin A1c criteria for diagnosing diabetes have not been established for patients who are <18 years of age.
> or =18 years: Increased risk for diabetes (prediabetes): 5.7-6.4%
Diabetes: > or =6.5%

Interpretive information based on Diagnosis and Classification of Diabetes Mellitus, American Diabetes Association.

Estimated Average Glucose (eAG)
The range of eAG concentrations that correspond to hemoglobin A1c values of 4.0-5.6% is 68-114 mg/dL (> or =18 years).

Interpretation

Diagnosing diabetes: American Diabetes Association (ADA)
-Hemoglobin A1c (HbA1c): > or =6.5%

Therapeutic goals for glycemic control (ADA)
-Adults:
- Goal of therapy: <7.0% HbA1c
- Action suggested: >8.0% HbA1c

-Pediatric patients:
- Toddlers and preschoolers: <8.5% (but >7.5%)
- School age (6-12 years): <8%
- Adolescents and young adults (13-19 years): <7.5%

The ADA recommendations for clinical practice suggest maintaining a HbA1c value closer to normal yields improved microvascular outcomes for diabetics.(1) Target goals of below 7% may be beneficial in patients such as those with short duration of diabetes, long life expectancy, and no significant cardiovascular disease. However, in patients with significant complications of diabetes, limited life expectancy, or extensive comorbid conditions, targeting a goal of below 7% may not be appropriate.

Since the HbA1c assay reflects long-term fluctuations in blood glucose concentration, a patient with diabetes who has come under good control in recent weeks may still have a high concentration of HbA1c. The converse is true for a patient with diabetes previously under good control who is now poorly controlled.

HbA1c results below 4.0% are reported with the comment: "Falsely low HbA1c results may be observed in patients with clinical conditions that shorten erythrocyte life span or decrease mean erythrocyte age. HbA1c may not accurately reflect glycemic control when clinical conditions that affect erythrocyte survival are present. Fructosamine may be used as an alternate measurement of glycemic control."

Cautions

Most common hemoglobin (Hb) variants (HbF <15%, heterozygous HbC, heterozygous HbS) do not interfere with this high-performance liquid chromatography (HPLC) method. Other variants of Hb may show interference with this method. The known variants that fall into this category are HbE, HbD, Hb Fukuoka, Hb Philadelphia, and Hb Raleigh.

If the specimen cannot be analyzed using the Biorad D-100 cation exchange HPLC method due to a hemoglobinopathy or other interference, a second-tier test will be performed on the Trinity Biotech ultra-2 HPLC method utilizing boronate-affinity chromatography, which is least affected by Hb variants. Most specimens from patients with hemoglobinopathies can be accurately monitored with the boronate-affinity method. If the specimen cannot be analyzed using either method due to a hemoglobinopathy or other interference, measurement of serum fructosamine may be helpful to monitor glycemic control. See FRUCT / Fructosamine, Serum.

In patients with rare homozygous forms of abnormal Hb (eg, CC, SS, EE, SC), there is no HbA present and, thus, no HbA1c value can be quantitated using this method. In these patients, the red blood cell lifespan is often variable and although an HbA1c could be reported using a boronate-affinity method, it is likely not providing a true measurement of the patient's glycemic control and could lead to misinterpretation. In such situations, fructosamine should be used as an alternate measurement of glycemia and is recommended for monitoring these patients. Fructosamine is a stable ketoamine that represents intermediate-term glycemic control (2-3 weeks). See FRUCT / Fructosamine, Serum.

In cases of hemolytic anemia, the lifetime of erythrocytes is shortened and will result in decreased HBA1c results. This effect will depend upon the severity of the anemia. Specimens from patients with polycythemia or postsplenectomy may exhibit increased HBA1c values due to a somewhat longer lifespan of the erythrocytes. Caution should be exercised when interpreting the HbA1c results from patients with these conditions.

Clinical Reference

1. Goldstein DE, Little RR, Lorenz RA, et al: Tests of glycemia in diabetes. Diabetes Care. 2003 Jan;26:S106-S108
2. Nathan DM, Kuenen J, Borg R, et al: Translating the A1c assay into estimated average glucose values. Diabetes Care. 2008 Aug;31:1473-1478
3. American Diabetes Association, Position Statement, Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2014 Jan;37:S14-S80
4. Little RR, Wiedmeyer HM, England JD, et al: Interlaboratory standardization of measurements of glycohemoglobins. Clin Chem. 1992;38:2472-2478
5. Hoelzel W, Weykamp C, Jeppsson JO, et al: IFCC reference system for measurement of hemoglobin A1c in human blood and the national standardization schemes in the United States, Japan, and Sweden: a method-comparison study. Clin Chem. 2004;50(1):166-174

Performance

Method Description

The D-100 hemoglobin (Hb) A1c test utilizes principles of ion-exchange high-performance liquid chromatography. The samples are automatically diluted on the D-100 and injected into the analytical cartridge. The D-100 delivers a programmed buffer gradient of increasing ionic strength to the cartridge, where the hemoglobin species are separated based on their ionic interactions with the cartridge material and the buffer gradient. The separated hemoglobin species then pass through the flow cell, where changes in the absorbance are measured at 415 nm. The D-100 software collects raw data from each analysis and calculates HbA1c values based on a bilevel calibration curve. The HbA1c area is calculated using an exponentially modified Gaussian algorithm. A sample report and a chromatogram are generated for each sample.(Instruction manual: D-100 Hemoglobin Testing System: Operation Manual, LB000341revB, 2015)

Estimated average glucose: eAg is calculated using the following formula: eAG, in mg/dL = 28.7 x HbA1c - 46.7.

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
Same day/1 to 3 days

Performing Laboratory Location
Jacksonville

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
83036

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
A1CJ	Hemoglobin A1c, B	55399-0

Result ID	Test Result Name	Result LOINC® Value
HBA1C	Hemoglobin A1c, B	4548-4
A1CE	Estimated Average Glucose	27353-2