

HbA1c Test : Physiology and Interpretation of Results

The **Hemoglobin A1c (HbA1c)** test measures the average blood glucose concentration over the preceding 2 to 3 months by quantifying the percentage of glycated hemoglobin in the blood. It is an essential tool for assessing long-term glycemic control in diabetic patients and is increasingly used for diabetes diagnosis.

Physiology and Biochemistry

- **Hemoglobin (Hb)** is the oxygen-carrying protein in red blood cells (RBCs). About 90% of adult hemoglobin is HbA (α₂β₂).
- HbA consists of minor components, including **HbA1a, HbA1b, and HbA1c**.
- **HbA1c** forms by the non-enzymatic attachment (glycation) of glucose to the N-terminal valine of the β-globin chain.
- The degree of glycation correlates directly with plasma glucose concentration.
- Since RBC lifespan is approximately **120 days**, HbA1c reflects average glucose levels over the previous 8-12 weeks, weighted toward more recent weeks.
- HbA1c is **stable and unaffected by short-term glucose fluctuations**, unlike plasma glucose.

Test Methodology

- **Specimen collection:** Venipuncture or fingerstick blood sample.
- **Analysis:** Most commonly performed using **High-Performance Liquid Chromatography (HPLC)**, which separates hemoglobin variants based on charge differences.
- Other methods include immunoassays and capillary electrophoresis.
- **No fasting required** prior to the test.

Indications

- Monitoring glycemic control in patients with **diabetes mellitus (type 1 and type 2)**.
- **Diagnostic tool** for diabetes and prediabetes.
- Assessing risk and guiding therapeutic interventions.

Interpretation of Results

HbA1c (%)	mmol/mol (IFCC units)	Clinical Interpretation
<5.7	<39	Normal
5.7-6.4	39-47	Prediabetes (increased risk of diabetes)
≥6.5	≥48	Diabetes mellitus (diagnostic cutoff)
≥7.0	≥53	Poor glycemic control in known diabetics

- Target HbA1c for most adults with diabetes is **<7.0%** (American Diabetes Association)

guidelines), individualized per patient.

- HbA1c correlates with risk of microvascular and macrovascular complications:
 - **Higher HbA1c ? increased risk** of diabetic retinopathy, nephropathy, neuropathy, cardiovascular disease, and stroke.

Limitations and Factors Affecting Accuracy

Conditions causing falsely **low HbA1c**:

- Hemolytic anemia (shortened RBC lifespan)
- Recent blood loss or transfusion
- Sickle cell disease and other hemoglobinopathies
- Chronic kidney disease
- Pregnancy
- Use of high doses of vitamin C or E (antioxidants interfering with glycation)

Conditions causing falsely **high HbA1c**:

- Iron deficiency anemia (due to prolonged RBC lifespan)
- Certain hemoglobin variants (may interfere with assay methods)
- Chronic alcoholism

Clinical Pearls (High-Yield Notes)

- **HbA1c reflects long-term control**; daily self-monitoring of blood glucose is still necessary.
- **Fasting is NOT required** for HbA1c testing.
- HbA1c is **not a substitute** for diagnosing acute hyperglycemia or hypoglycemia.
- Certain ethnic groups and genetic variants may affect HbA1c levels independently of glucose.
- **HbA1c variability may affect medication decisions**, especially with drugs metabolized differently depending on glycemic control.

Clinical Use and Monitoring

- Used to guide **treatment adjustments** in diabetes management.
- Regular testing every **3 months** in patients with uncontrolled diabetes or therapy changes; every **6 months** for stable patients.
- Can predict the **risk of diabetic complications** and help in early intervention.

Diagnostic Procedure & Patient Care

1. Preparation:

- No fasting required.
- Review medications that may affect results.
- Inform patient about the blood draw procedure.

2. Collection:

- Perform standard venipuncture or fingerstick.
- Collect blood in appropriate tubes (usually EDTA or heparinized).

3. Post-procedure:

- Apply pressure to prevent hematoma.
- Educate patient on test purpose and implications.

4. **Precautions:**

- Maintain sterile technique.
- Monitor for complications such as bleeding, infection, or light-headedness.