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# Glycated Haemoglobin (HbA1c)

*Synonym: glycosylated haemoglobin*

Glycated haemoglobin (HbA1c) laboratory tests are used to diagnose diabetes mellitus and to assess control in diabetes mellitus. For further information regarding HbA1c monitoring and targets, see the separate [Management of Type 1 Diabetes](#) and [Management of Type 2 Diabetes](#) articles.

## Haemoglobin A1 and haemoglobin A1c

Chromatography of normal adult blood divides into two parts:

- HbA (HbA0) 92-94%.
- HbA1 (6-8%) where the B chain has an additional glucose group.

HbA1 itself consists of three different glycation, the HbA1c subgroup being the most useful, usually measured by isoelectric focusing or electrophoresis.

The glycation of haemoglobin occurs at a variable (non-linear rate) over time, during the whole lifespan of the red blood cell (RBC), which is normally 120 days. This means the relative proportion of glycated haemoglobin at any one time depends on the mean glucose level over the previous 120 days.

Normal levels (laboratory normal 'range') will differ depending on whether HbA1 or HbA1c is measured, and on the method used - use your laboratory's reference range (EDTA (FBC) bottle).<sup>[1]</sup>

**HbA1c is usually a reliable indicator of diabetic control except in the following circumstances:**

- Situations where the average RBC lifespan is significantly less than 120 days will usually give rise to low HbA1c results because 50% of glycation occurs in days 90-120. Common causes include:<sup>[1]</sup>
  - Increased red cell turnover: blood loss, haemolysis, haemoglobinopathies and red cell disorders, myelodysplastic disease.
  - Interference with the test (this depends on the method used: persistent fetal haemoglobin and haemoglobin variants, carbamylated haemoglobin (uraemic patients)).
- In patients who fluctuate between very high and very low levels - HbA1c readings can be misleading (the clinician should compare with extra information obtained from home capillary blood glucose tests).
- HbA1c can be very useful in identifying patients who may be presenting an unrealistically good report of their home glucose tests.

## Normal ranges and values

HbA1c results in the UK have usually been aligned to the assay used in the Diabetes Control and Complications Trial (DCCT), expressed as a percentage (DCCT-HbA1c) - non-diabetic 'normal' range being 4-6%. Since 1st June 2009, HbA1c results in the UK have been standardised to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) which will allow global comparison of results, with the equivalent normal non-diabetic range of IFCC-HbA1c being 20-42 mmol/mol.<sup>[2]</sup>

### Comparing DCCT-HbA1c and IFCC-HbA1c Results<sup>[3]</sup>

DCCT-HbA1c (%)	IFCC-HbA1c (mmol/mol)
6.0	42
6.5	48
7.0	53
7.5	59
8.0	64
9.0	75

## Other important points to consider

- Any HbA1c target for the management of a person with diabetes should be individualised and agreed with the patient (considering comorbidity, life expectancy, hypoglycaemia frequency, etc).
- Do not test more frequently than every three months - and avoid over-interpreting results. Look for trends rather than the difference in two consecutive results - test imprecision varies with the method used and is typically 3-4%.
- Mean plasma glucose results are 10-15% higher than the equivalent HbA1c.<sup>[4]</sup>

## Diagnosing diabetes<sup>[5]</sup>

Although HbA1c testing is mainly used for monitoring blood sugar control in patients with diabetes, the World Health Organization (WHO) now recommends that HbA1c can be used as a diagnostic test for diabetes, provided that stringent quality assurance tests are in place and assays are standardised to criteria aligned to the international reference values. An HbA1c of 48 mmol/mol (6.5%) is recommended as the cut-off point for diagnosing diabetes. A value less than 48 mmol/mol (6.5%) does not exclude diabetes diagnosed using glucose tests. One advantage of using HbA1c for diagnosis is that the test does not require a fasting blood sample.

Situations where HbA1c is not appropriate for diagnosis of diabetes include:<sup>[6]</sup>

- Children and young people.
- Patients suspected of having type 1 diabetes.
- Pregnancy.
- 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.

- Presence of other factors that influence HbA1c and its measurement:
  - Erythropoiesis:
    - Increased HbA1c: **iron deficiency**, **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 vitamin 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.

## Fructosamine

Fructosamine is the glycated fraction of all plasma proteins (predominantly albumin) but considered less accurate because of the numerous factors affecting the half-lives of the many components. It generally reflects average glucose in the previous two weeks. If available, it may be useful in situations where there is reduced red cell survival time.

## Further reading & references

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