



Diabetes Mellitus Masterclass  
Chapter 2

# MAKING THE DIAGNOSIS



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# RISK FACTORS AND SCREENING

## *Risks for type 1 diabetes*

There are (as of yet) no screening tests that allow us to intervene and prevent the development of type 1 diabetes. Research continues to explore the possibility of type 1 diabetes prevention.

## *Risks for type 2 diabetes*

Screening for type 2 diabetes is important for early diagnosis. Currently, 25% of patients with type 2 diabetes are undiagnosed. This number is significantly higher, as high as 50%, for Asian and Hispanic populations.

### **Risk factors for developing type 2 diabetes**

- First degree relative with type 2 diabetes
- African American, Latino, Native American, Southeast Asian or Pacific Islander heritage
- History of gestational diabetes
- Conditions associated with insulin resistance (e.g., polycystic ovary syndrome or acanthosis nigricans)
- Cardiovascular disease, hypertension or hyperlipidemia
- Obesity (BMI of  $\geq 25$  kg / m<sup>2</sup> or for Asian patients  $\geq 23$  kg / m<sup>2</sup>)

### **Who should be screened for type 2 diabetes?**

Recommendations from different societies vary, but in general

- All overweight patients
- Adults aged 40–45 with at least one risk factor for type 2 diabetes

If results are normal, it is reasonable to repeat screening every three years.

# DIAGNOSING DIABETES

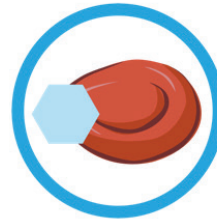
There are three tests used to diagnose diabetes



Fasting  
blood glucose



Oral glucose  
tolerance test



Hemoglobin  
A1c

## Fasting blood sugar

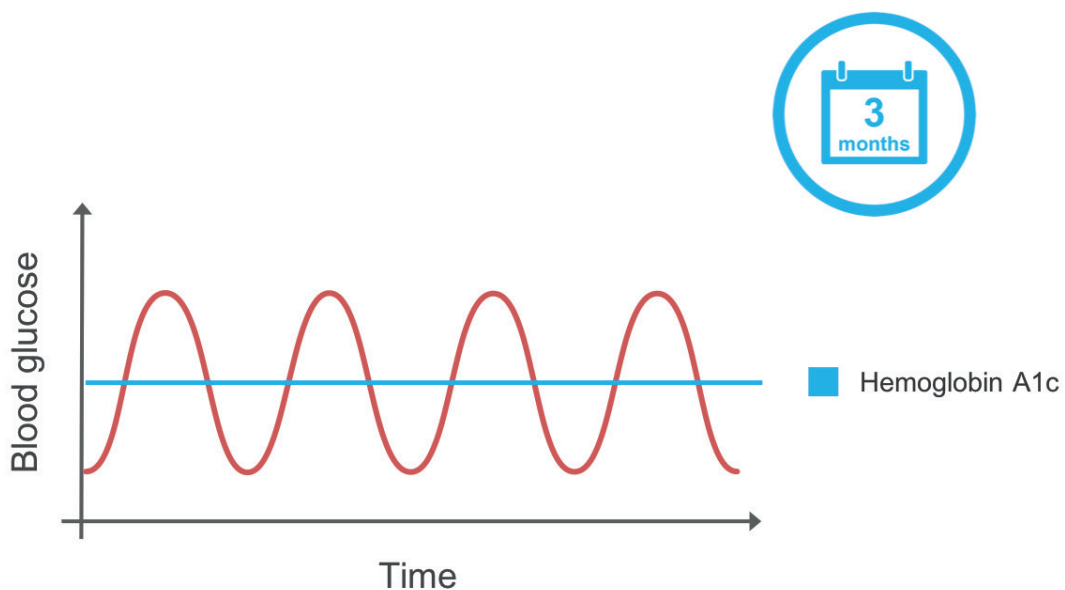
Blood sugar is measured on a blood draw after eight hours of fasting. Normal values are  $< 100 \text{ mg / dL}$  ( $5.6 \text{ mmol / L}$ ). Between  $100\text{--}125 \text{ mg / dL}$  ( $5.6\text{--}6.9 \text{ mmol / L}$ ) is considered pre-diabetes. Diabetes is diagnosed with values  $\geq 126 \text{ mg / dL}$  ( $7 \text{ mmol / L}$ ).

## Oral glucose tolerance test

For this test, the patient consumes a standardized dose of  $75 \text{ g}$  glucose (usually in the form of an orange-flavored soda). Blood sugar is measured two hours later. Normal values are  $< 140 \text{ mg / dL}$  ( $7.8 \text{ mmol / L}$ ). Between  $140\text{--}200 \text{ mg / dL}$  ( $7.8\text{--}11.1 \text{ mmol / L}$ ) is considered pre-diabetes and any value  $\geq 200 \text{ mg / dL}$  ( $11.1 \text{ mmol / L}$ ) is diagnostic of diabetes.

## Hemoglobin A1c

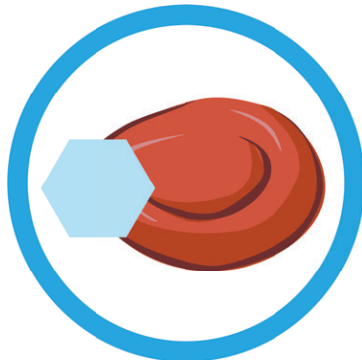
This is a measure of the average blood sugar over the last three months. While there are some limitations to this test, it is considered a tool for use in diagnosing diabetes. Normal values are  $< 5.7\%$ , values between  $5.7\text{--}6.4\%$  indicate pre-diabetes, with values  $\geq 6.5\%$  diagnostic of diabetes.



For all of these tests, the abnormal result must be confirmed on repeat testing using either the same test or one of the other testing options.

In addition to these tests, if the patient has classic symptoms of hyperglycemia, such as frequent urination, increased thirst, or unexplained weight loss, a **random glucose** of  $\geq 200$  mg / dL (11.1 mmol / L) is diagnostic of diabetes.

# HEMOGLOBIN A1C



Hemoglobin A1c is a hemoglobin molecule that has been glycosylated, or modified, by exposure to glucose. Once modified, the hemoglobin remains this way until the red cell turns over (usually 120 days).

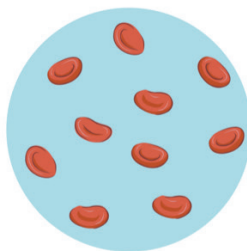
The higher the glucose levels, the more hemoglobin molecules are modified, thus hyperglycemia results in a higher % of A1c

There are some issues with the hemoglobin A1c, however, which have caused some people to question whether this lab marker is an appropriate tool for diagnosing diabetes:

- A1c is an estimate of average blood sugar, but ranges of blood glucose levels overlap for the different A1c values. So a patient with an average blood sugar of 180 mg / dL can have an A1c of 7%, while a patient with better blood sugar control, and an average of 150 mg / dL, can have a higher A1c (8%).

Hemoglobin A1c (%)	Estimated average glucose (mg / dL)
5	100
6	125
7	150 (120–185)
8	180 (150–220)
9	210
10	240
11	270
12	300

- The A1c measurement assumes a normal red blood cell life span of approximately 3–4 months (120 days), so anything that alters the red blood cell life span will cause the A1c to be inaccurate.



Hemolytic anemia

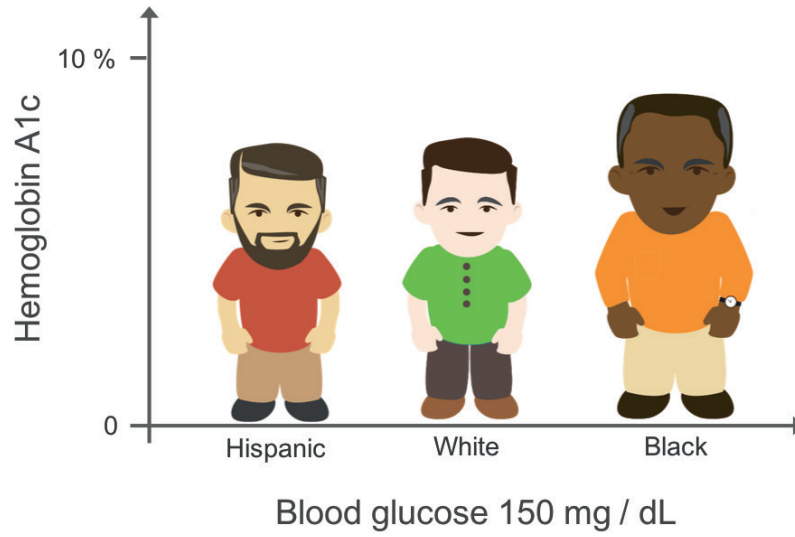


Blood loss



Pregnancy

- A1c values tend to be higher for African American patients at the same glucose level compared to other ethnicities. If we use the A1c for diagnosis of diabetes, we may be overdiagnosing in these populations. This may not accurately reflect their true risk of diabetes complications.



# PRE-DIABETES

When screening shows values that are abnormal but do not meet the criteria for a diagnosis of diabetes, patients are diagnosed with pre-diabetes.

- Impaired fasting glucose
  - fasting glucose = 100–125 mg / dL (5.6–6.9 mmol / L)
- Impaired glucose tolerance
  - glucose level two hours after oral glucose tolerance test = 140–200 mg / dL (7.8–11.1 mmol / L)
- Pre-diabetes
  - hemoglobin A1c = 5.6–6.5%

Patients with pre-diabetes are at high risk of developing overt type 2 diabetes. If pre-diabetes is identified when screening patients for diabetes, there are some interventions that have been shown to prevent progression to type 2 diabetes.

- Intensive lifestyle intervention
  - 7% weight loss and 150 minutes physical activity weekly leads to a 58% decline in progression to diabetes after five years
- Metformin
  - 850 mg twice daily, reduced progression by 31%; 58% decrease for patients with a BMI > 35
- Acarbose
  - reduced progression by 25%, but is poorly tolerated
- Pioglitazone
  - reduced progression by 72%, but with significant weight gain

# READING LIST

## **American Diabetes Association Guidelines for Diabetes Screening**

American Diabetes Association. 2017. 2. Classification and Diagnosis of Diabetes. *Diabetes Care*. **40**: S11–S24.  
<https://www.ncbi.nlm.nih.gov/pubmed/27979889>

## **Diagnostic tests for diabetes**

American Diabetes Association. 2017. 2. Classification and Diagnosis of Diabetes. *Diabetes Care*. **40**: S11–S24.  
<https://www.ncbi.nlm.nih.gov/pubmed/27979889>

## **Review of the limitations of A1c**

Radin, MS. 2014. Pitfalls in Hemoglobin A1c Measurement: When Results may be Misleading. *J Gen Intern Med*. **29**: 388–394.  
<https://www.ncbi.nlm.nih.gov/pubmed/24002631>

## **Prevention of type 2 diabetes**

Chiasson, JL, Josse, RG, Gomis, R, et al. 2002. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet*. **359**: 2072–2077.  
<https://www.ncbi.nlm.nih.gov/pubmed/12086760>

DeFronzo, RA, Tripathy, D, Schwenke, DC, et al. 2011. Pioglitazone for diabetes prevention in impaired glucose tolerance. *N Engl J Med*. **364**: 1104–1115.  
<https://www.ncbi.nlm.nih.gov/pubmed/21428766>

Knowler, WC, Barrett-Connor, E, Fowler, SE, et al. 2002. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. **346**: 393–403.  
<https://www.ncbi.nlm.nih.gov/pubmed/11832527>