

Glucose Homeostasis

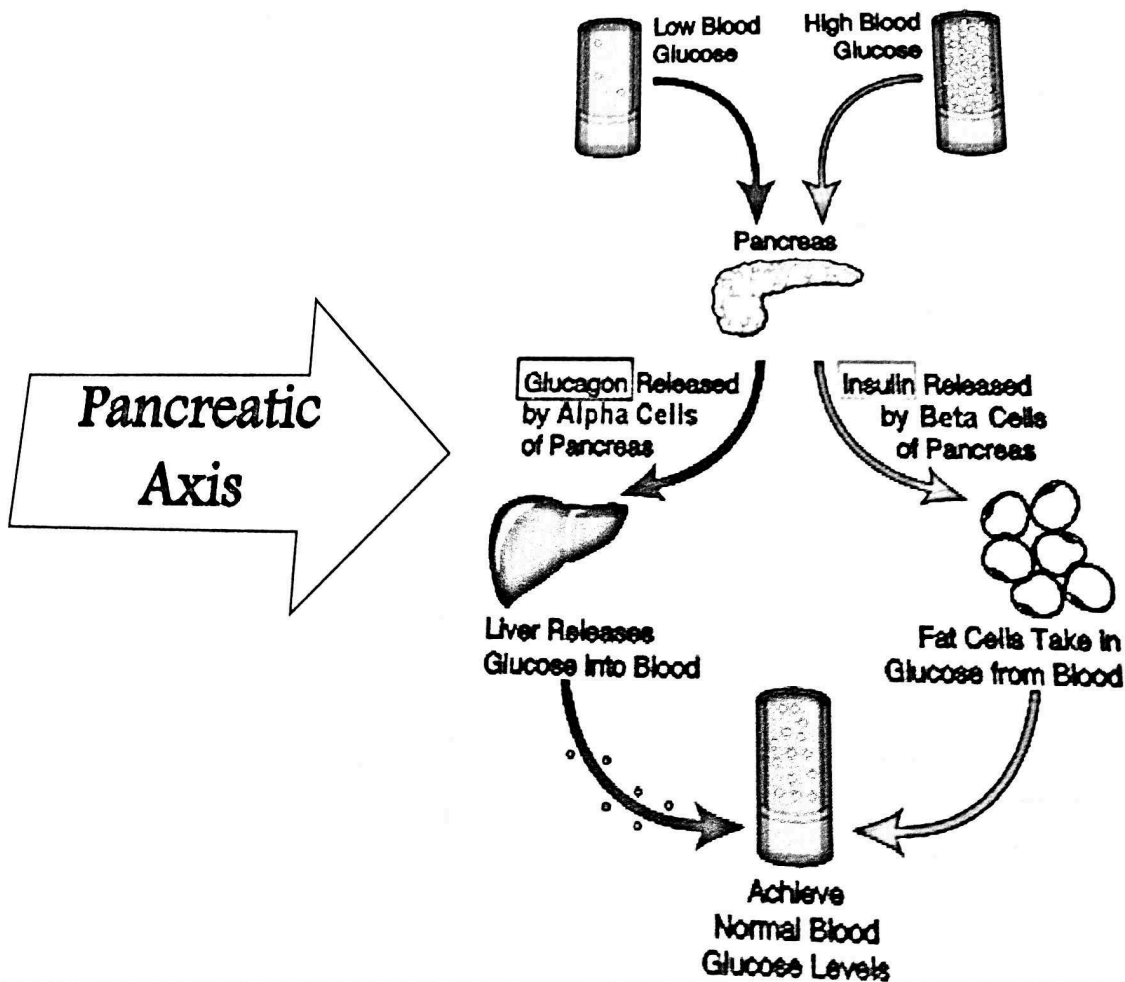
- **Glucose Homeostasis.** Is the balance of insulin and glucagon to maintain blood glucose levels within the normal range.
- **Insulin. Glucagon Ratio.** everything that happens to glucose, amino acids and fat in the well fed state depends upon a high insulin to glucagon ratio.

Insulin.

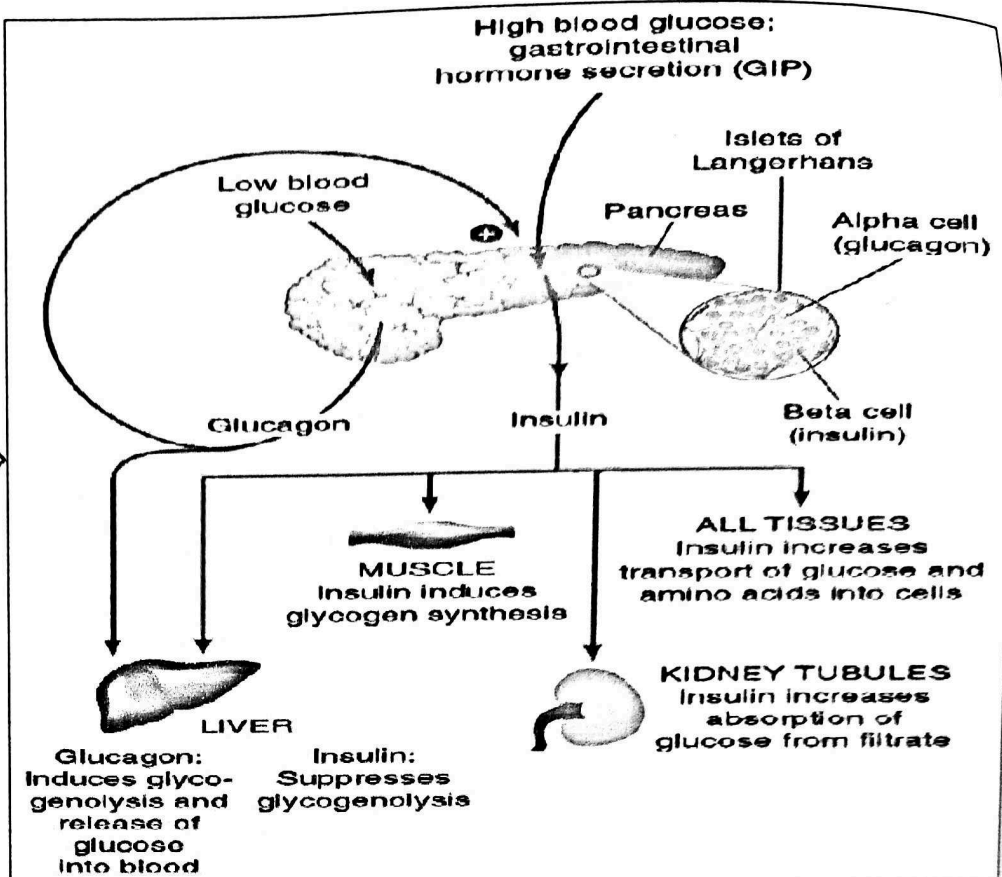
- **Insulin** is secreted by the beta cells (β cells, also called B cells) of the pancreas in response to elevated blood glucose following a meal.
- **Insulin** lowers blood glucose by **increasing glucose uptake** in muscle and adipose tissue and by promoting **glycolysis** and **glycogenesis** in the liver and muscles.

Glucagon.

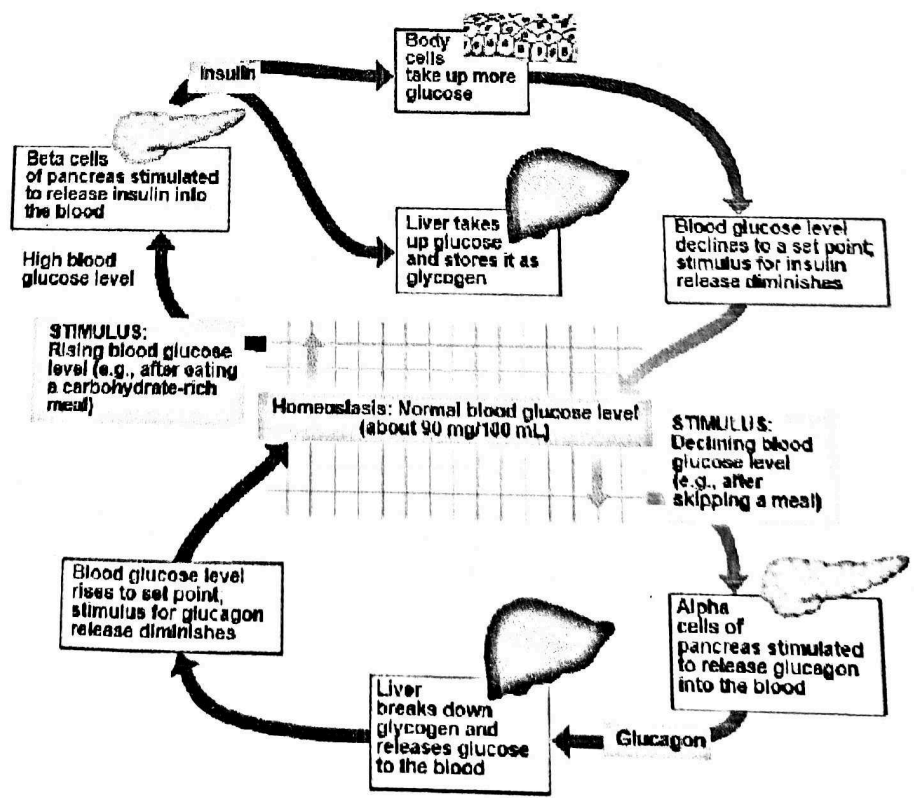
- A fall in blood glucose increases the release of **glucagon** from the alpha cells (α cells, also called A cells) of the pancreas to promote glucose production, and serves to keep blood glucose levels high enough for the body to function well.
- Glucagon generally elevates the concentration of glucose in the blood by promoting **gluconeogenesis** (the conversion of amino acids into glucose) and **glycogenolysis** (break down of glycogen in liver to be released into the blood as glucose).
- As these stores become depleted, glucagon then encourages the liver and kidney to synthesize additional glucose by gluconeogenesis.
- Glucagon turns off glycolysis in the liver.



Actions of Insulin & Glucagon

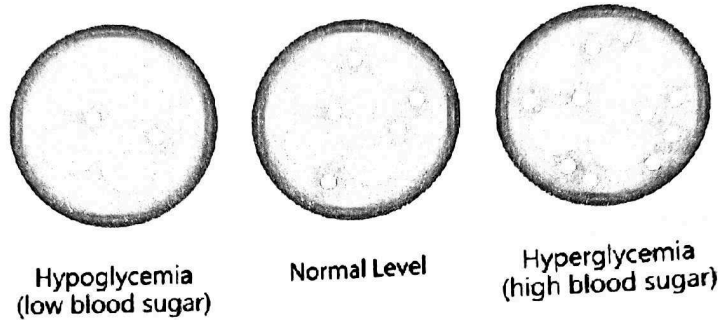


- Glucose homeostasis



Blood Glucose Levels

- A high or too much glucose in the blood is also called (high blood sugar or **hyperglycemia**).
- A low blood sugar level is called (**hypoglycemia**).



Diabetes Mellitus

Diabetes mellitus (DM) is the commonest endocrine disorder encountered in clinical practice. It may be defined as a syndrome characterized by **hyperglycaemia** due to:

- An absolute or relative lack of insulin.
- An insulin resistance

Criteria for the diagnosis of diabetes:

- The American Diabetes Association (ADA) diagnostic criteria for DM include any one of the following:
 - 1) Hemoglobin A1c (HbA1c) of 6.5% or more.
 - 2) Fasting (no caloric intake for at least 8 hrs.) plasma glucose of 126 mg/dL (7.0 mmol/L) or above.
 - 3) Random plasma glucose concentration of ≥ 200 mg/dL (11.1 mmol/L), with classic symptoms of hyperglycemia or hyperglycemic crisis (polyuria, polydipsia, polyphagia, weight loss and lethargy).
 - 4) Two-hour plasma glucose of 200 mg/dL (11.1 mmol/L) or more during an oral glucose tolerance test (OGTT).

Types of DM

Type 1 DM.

- Previously called insulin-dependent diabetes mellitus (IDDM)
- Accounts for approximately (5-10%) of cases, usually developed in childhood or early adulthood.
- It is the result of an autoimmune-mediated destruction of pancreatic beta cells.
- Resulting in absolute deficiency of insulin.

Types of DM

Type 2 DM.

- ▶ Previously called non-insulin dependent diabetes mellitus (NIDDM).
- ▶ Accounts for approximately 90% of cases.
- ▶ Results from a combination of **insulin resistance** and altered insulin secretion or **relative insulin deficiency**.

Types of DM

Gestational DM.

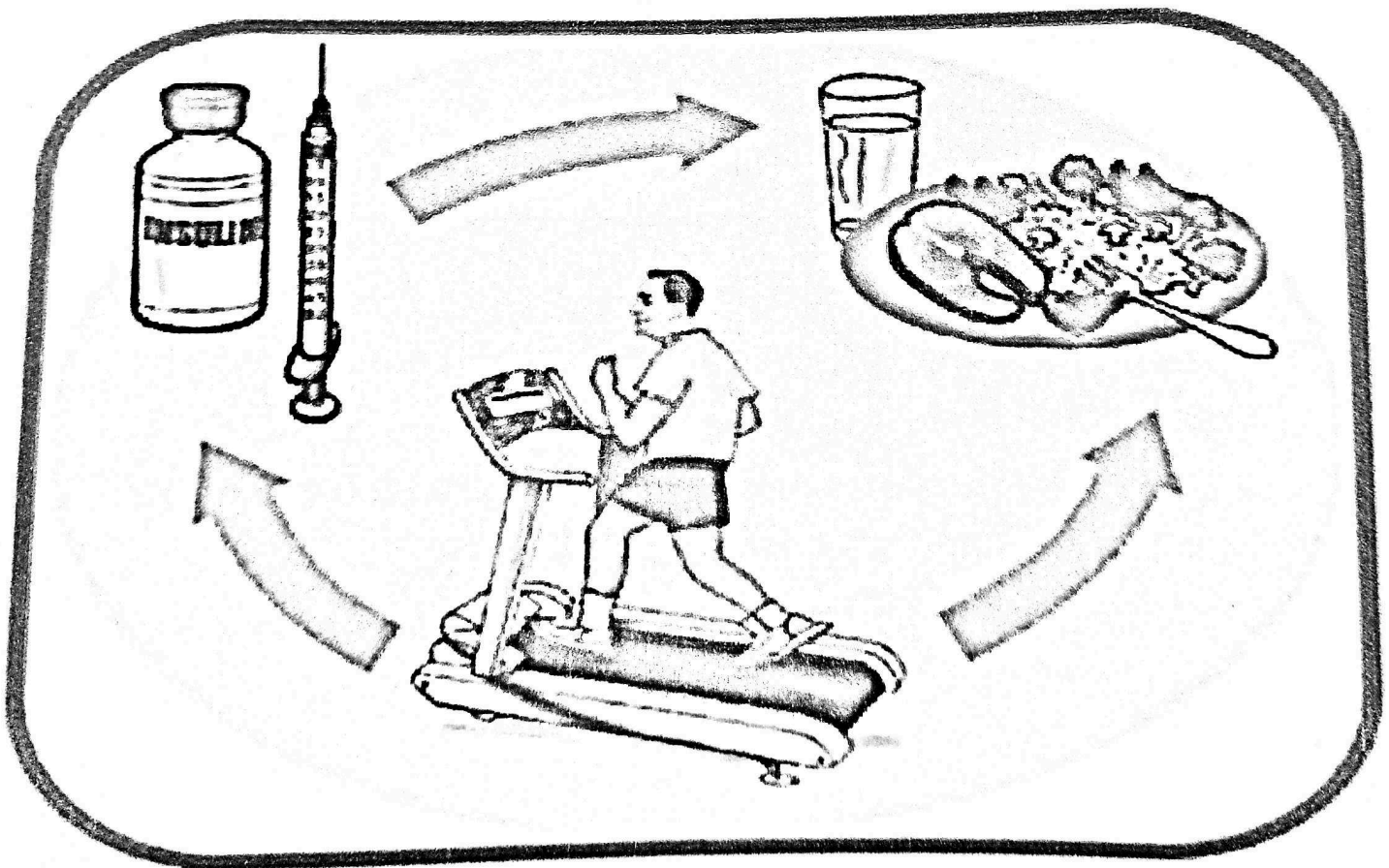
- ▶ Develops during pregnancy.
- ▶ About (4–5)% of pregnancies are complicated by gestational DM.
- ▶ Caused by the hormones of pregnancy, which can cause **insulin resistance** or a **shortage of insulin**.
- ▶ It is associated with increased fetal abnormalities (e.g.: high birthweight & cardiac defects).

Types of DM

Other specific types of DM,

Secondary diabetes is diabetes that results as a consequence of another medical condition, including:

- ▶ Pancreatic disease, e.g. Chronic pancreatitis and cystic fibrosis
- ▶ Endocrine disease, such as acromegaly (excessive growth hormone)
- ▶ Drugs, e.g. Thiazide diuretics, Interferon- α , and Glucocorticoids.



Prediabetes

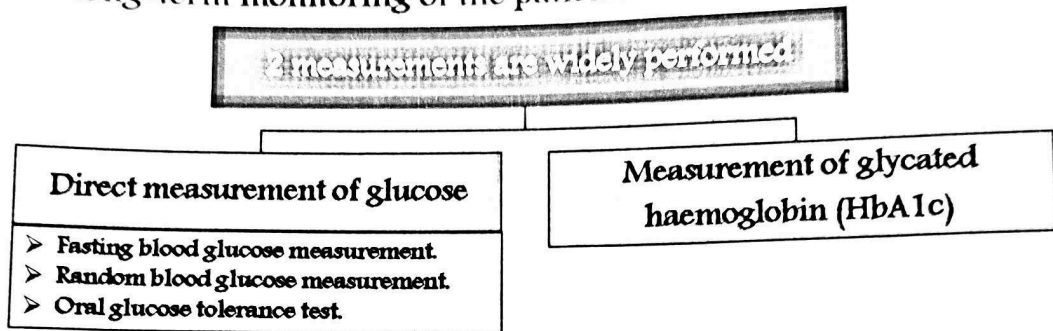
- ▶ People with glucose levels between normal and diabetic levels have the so-called **prediabetes** or **impaired glucose tolerance (IGT)**.
- ▶ The condition used to be called **borderline diabetes**.
- ▶ People with **prediabetes** have glucose levels that are higher than normal, but not high enough yet to indicate diabetes (they do not have diabetes).
- ▶ It is associated with insulin resistance.

Prediabetes

- ▶ Most people with prediabetes don't have symptoms, but they are considered to be at **higher risk of developing cardiovascular pathology** (e.g.: heart disease and stroke) than those who does not have prediabetes.
- ▶ It is associated with an **increased risk of developing type 2 DM** (50% high risk).
- ▶ **Weight loss and exercise** may help people with IGT return their glucose levels to normal. In addition, some physicians advocate the use of medications, such as metformin (Glucophage), to help prevent/delay the onset of overt diabetes.

Methods for the Determination of Blood Glucose Levels

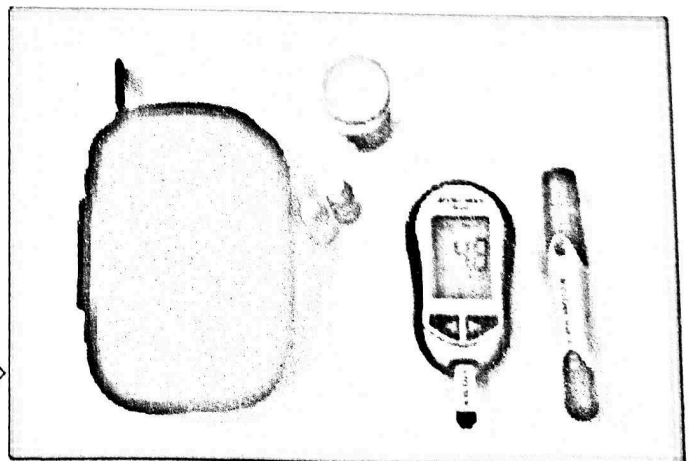
- A number of biochemical tests are used in association with clinical assessment for both the initial diagnosis of DM and long-term monitoring of the patients.



The fasting plasma glucose test (FPG):

- The fasting plasma glucose test can be done after an overnight fast (no caloric intake) or after an 8-hour fast during the day.
- It is a relatively easy, **inexpensive** test.
- After the fast, a simple blood test measures glucose levels before you eat again.

Blood glucose testing device



The fasting plasma glucose test (FPG):

- The test results indicate whether your blood glucose level is normal or whether you have prediabetes or diabetes.

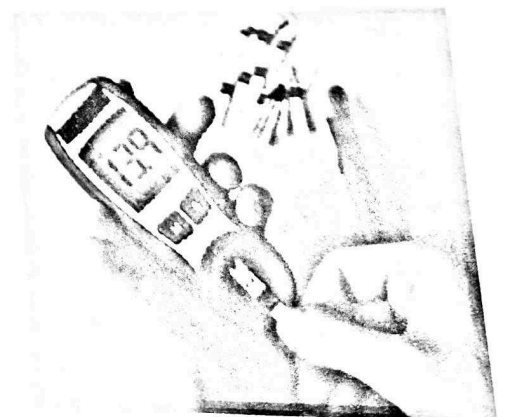
Normal	Prediabetes	Diabetes
<ul style="list-style-type: none">► Normal fasting blood glucose levels measure less than 100 mg/dL (70-100 mg/dL) after the fasting glucose test.	<ul style="list-style-type: none">► Blood glucose levels of 100-125 mg/dL after an overnight or eight-hour fast may indicate prediabetes.► People with these results are considered to have impaired fasting glucose (IFG).	<ul style="list-style-type: none">► Diabetes is diagnosed when the blood glucose is 126 mg/dL or above.

- In most cases, your doctor will repeat any abnormal test before confirming the diagnosis.

Random Blood Glucose Measurement (Casual Plasma Glucose):

- Performed at any time of the day without regard to the time since the last meal.
- **> 200 mg/dL (11.1 mmol/L)** plus symptoms of diabetes:

Polyuria, polydipsia, unexplained weight loss, requires confirmation with fasting blood glucose or oral glucose tolerance test.



Oral Glucose Tolerance Testing (OGTT):

- **Glucose Tolerance Test** evaluates how quickly an individual can restore their blood glucose to normal following ingestion of a large amount of glucose, i.e. measures an individual's ability to maintain glucose homeostasis.
- It is used to evaluate the ability to regulate glucose metabolism.
- The reference range of serum or plasma glucose is **less than 140 mg/dL** at 2 hours after a **75-g** glucose load.
- The OGTT is increasingly reserved for research purposes. OGTT using a **100-g** glucose load or a **50-g** load (the latter to screen for gestational diabetes) are no longer recommended by the ADA.

Indications/Applications for the OGTT

The test is usually used to test for:

1. Diabetes. Equivocal FPG or random plasma glucose results.

The OGTT is seldom used as a confirmatory test in the diagnosis of DM, but it may be helpful when fasting or random glucose results are equivocal.

2. Insulin resistance and pre-diabetic state. OGTT is required for diagnosing **Impaired glucose tolerance (IGT)**.

3. To screen for GDM at **(24-28) weeks** of gestation in all pregnant women not known to have diabetes.

Indications/Applications for the OGTT

4. To screen for DM at (6-12) weeks postpartum in women with a history of GDM, using non pregnant OGTT criteria.
5. Reactive hypoglycemia or (postprandial hypoglycemia), which is a medical term describing recurrent episodes of symptomatic hypoglycemia occurring within 4 hours after a high carbohydrate meal in people who do not have diabetes.
6. Acromegaly, or rarer disorders of carbohydrate metabolism.

The preparation for OGTT:

The preparation for the OGTT involves:

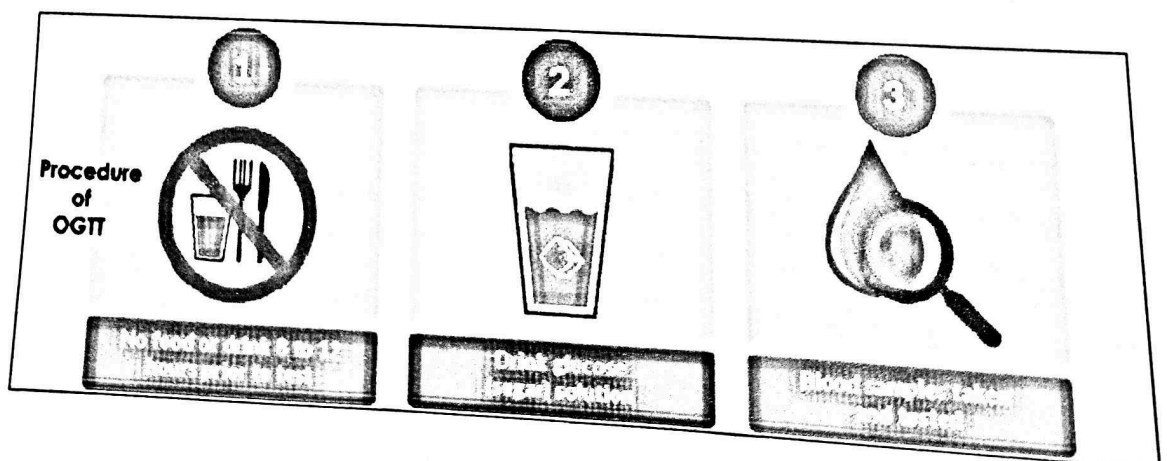
- The individual should eat and drink as they normally do prior to the test.
- On the day before the test: Fasting overnight (from 8 to 16 hours) is required (except for water) and participating normally in activities of daily living.
- At the morning of the test, the person should not consume caffeine or smoke.
- As there is a risk of later-onset hypoglycaemia in some individuals, it is advisable to suggest that the patient has something to eat immediately upon completion of the test, especially if he/she is planning to drive.

Procedure of OGTT:

- 1) The OGTT usually requires performing a baseline FPG test first.
- 2) Then, a dose of high-sugar solution (glucose load, prepared by dissolving 75 g anhydrous glucose in water) is administered to challenge the body to clear the glucose from the blood. The glucose load is administered—either **intravenously** or, more commonly, **orally**—over a 5-min period and plasma glucose is measured at specified intervals thereafter.
- 3) The venous serum glucose sample is then taken 2 h after the drink. The patient should be seated and is not permitted to smoke, eat or drink anything other than water until the test is complete.
 - In the standard OGTT, plasma glucose concentration is measured **2 hours** after a 75-g oral glucose load; for **GDM**, an additional measurement may be made at **1 hour**.

Procedure of OGTT:

- 4) The final test results indicate whether you have a normal level of blood glucose or may have prediabetes or diabetes.

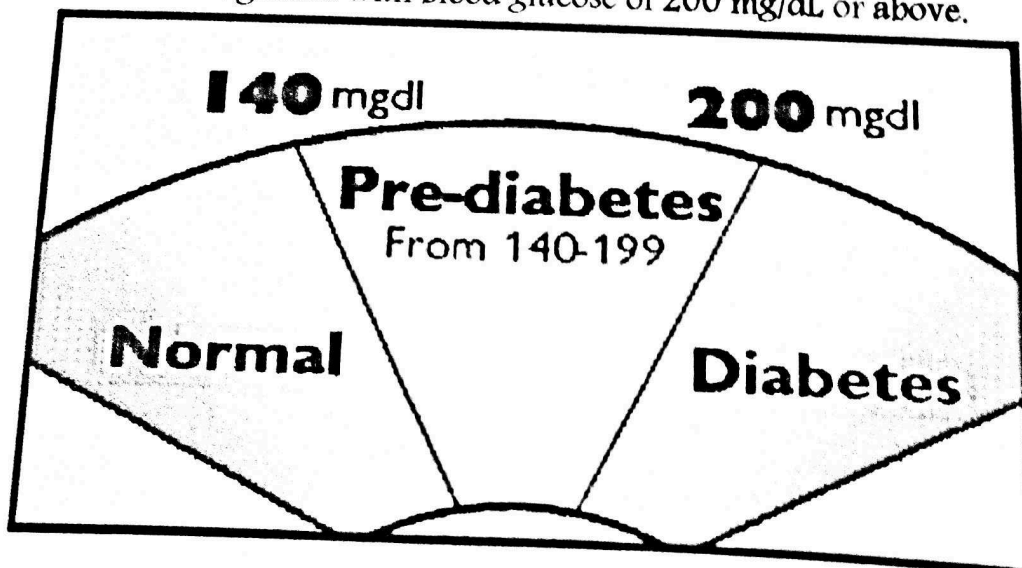


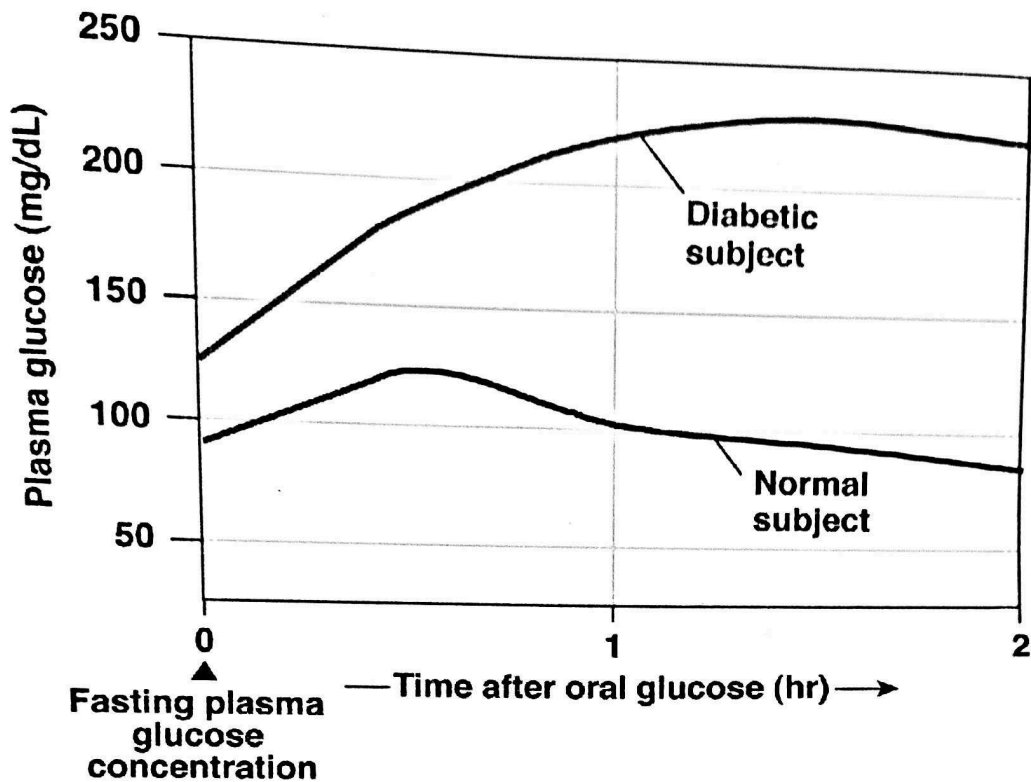
Sampling Method

Is for venous samples only (i.e. a blood sample taken from a vein in the arm). An increasingly popular method for measuring blood glucose is from a **capillary** or **finger-prick** sample. This is less invasive, more convenient for the patient and requires minimal training to conduct.

Interpretation of OGTT Results:

- **Normal** blood sugar levels measure less than 140 mg/dL after the OGTT.
- **Prediabetes (IGT)**. Blood glucose levels of 140-199 mg/dL after the OGTT is diagnosed as prediabetes.
- **Diabetes** is diagnosed with blood glucose of 200 mg/dL or above.



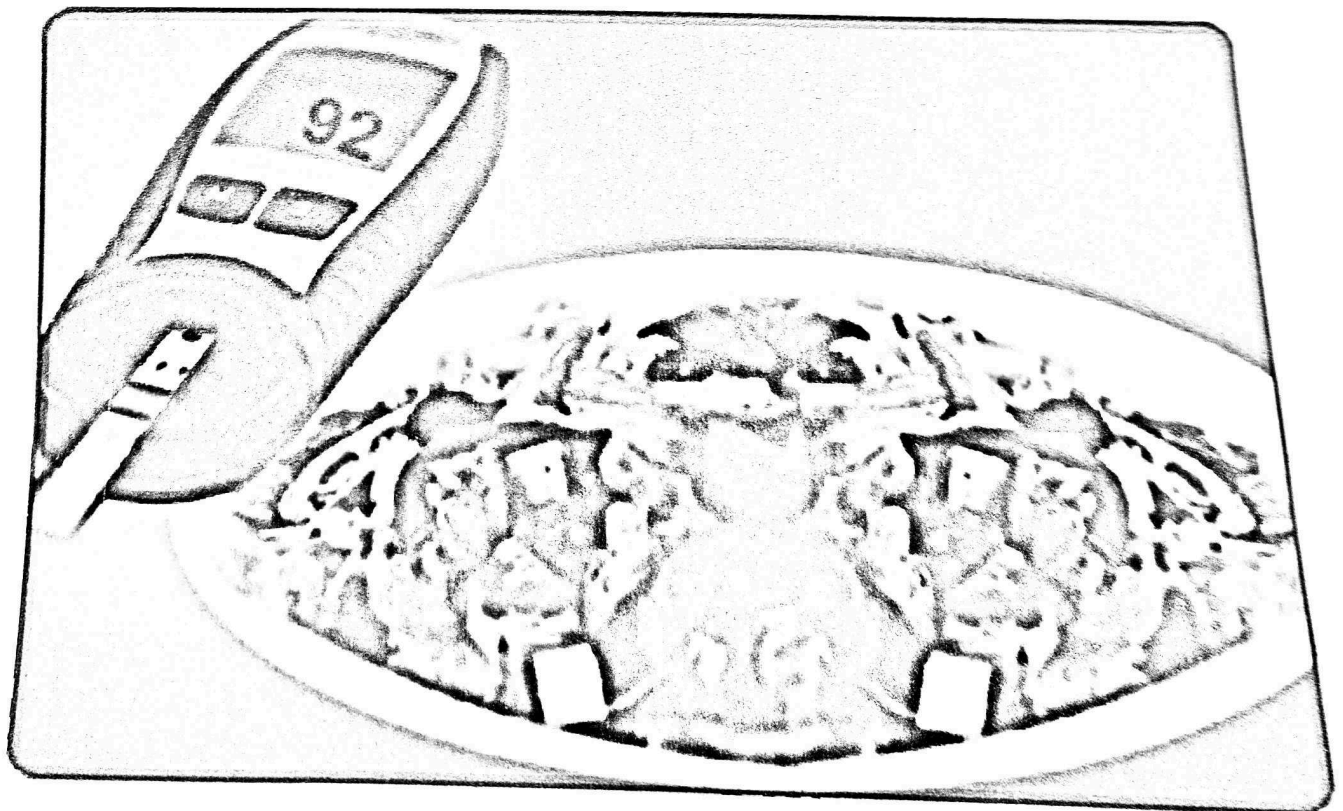


Factors affecting the result of OGTT:

- Previous diet
- Time of day
- Drugs: steroids, oral contraceptive and thiazide diuretics may impair glucose tolerance.
- And others as, smoking, alcohol, recent surgery, illnesses, and infectious diseases, weight loss through dieting, and long periods of bed rest (such as from a hospitalization or illness).

What is the hemoglobin A1c Test ?

- The hemoglobin A1c (HbA1c) test is a simple blood test that reflects the average blood sugar for the past **2 to 3 months**. It can be used to diagnose prediabetes or diabetes. It can also be used to check if your diabetes is under control.
- Normal: 5.6% or less
- Prediabetes: (5.7 - 6.4)%
- Diabetes: 6.5 % or above



Diagnostic Cut Points

Category	FPG (mg/dL)	Random plasma glucose (mg/dL)	2h 75g OGTT (2 h postprandial) (mg/dL)	HbA1c (%)
Normal	< 100	< 200	< 140	< 5.7
Prediabetes	100-125	N/A	140-199	5.7-6.4
Diabetes	≥ 126	≥ 200 (with classic hyperglycemic symptoms.)	≥ 200	≥ 6.5

Gestational Diabetes (GDM)

- ✓ Fasting blood glucose: >92 mg/dL
 - ✓ 1 h post glucose: >180 mg/dL
 - ✓ 2 h post glucose: >153 mg/dL
 - ✓ 3 h post glucose: >140 mg/dL
- Any one abnormal value is adequate.