Al Muthanna University College of Pharmacy

# Insulin Regulation of Blood Glucose

By

Dr. Sarah Zghair Hussein

Second Stage

# Introduction

Glucose is monosaccharide found in fruits and also derived from the breakdown of carbohydrates in the diet and the conversion of glycogen by liver. Glucose is the main source of energy used by the body cells.

The two hormones that directly regulate blood glucose are **Glucagon** and **Insulin**.

**Blood glucose levels decrease only slowly, by a balance between two sets of factors:**

- Rate of **glucose arrival** into the blood stream, and
- Rate of **its removal** from the blood stream.

# Normal range:

- Normal blood glucose level (fasting) is 70-110 mg/dl
- Post-prandial blood glucose level is 120-140 mg/dl
- Above and below these levels is considered as abnormal.

- **Hyperglycemia**: levels above the normal range
- **Hypoglycemia**: levels below the normal range

# Homeostasis of blood glucose

The ability of the body to maintain balance and regulate internal concentration of glucose is called **glucose homeostasis.**

1. Low blood glucose → Alpha cells release glucagon → Glycogenolysis in the liver; Glucose released to blood → Normal blood glucose.
2. High blood glucose → Beta cells release insulin →

Peripheral tissue cells take glucose from blood → Normal blood glucose.

# Insulin

**Insulin** is the most important hormone coordinating the use of fuels by tissues. Its metabolic effects are **anabolic**, favoring, for example, synthesis of **glycogen, triacyl- glycerol, and protein.**

The effects of **insulin** on **glucose metabolism** are most prominent in **three tissues**: **liver, muscle and adipose tissue.**

**How??**

In the case of excess carbohydrates, it causes them to be stored as glycogen mainly in the liver and muscles.

All the excess carbohydrates that cannot be stored as glycogen are converted under the stimulus of insulin into fats and stored in the adipose tissue.

Driving of insulin into the cell requires insulin receptors.

After meal the pancreas releases insulin for glucose metabolism provided there are enough insulin receptors.

Insulin bind to these receptors on the surface of target cells such as found in fat and muscle, this opens the channels so that glucose can pass into cells, where it can be converted to energy.

As cellular glucose metabolism occurs, blood glucose level falls.

# Notes:

Excretion of glucose in urine (**glycosuria**), when blood glucose level exceeds the renal threshold (180 mg/dl).

**Glucose tolerance test (GTT)** is also useful in the diagnosis of this renal tubular defect.

All the above processes are under **nervous** and **hormonal control**.

# Glucagon

- **Glucagon** is a **polypeptide hormone** secreted by the **α-cells** of the pancreatic islets of Langerhans. This hormone is released into the blood when blood glucose levels are **low.**
- **Glucagon**, along with **epinephrine, cortisol, and growth hormone (The "counter regulatory hormones"), opposes many of the actions of insulin.**

# Stimulation of glucagon secretion by:

- **Low blood glucose:** A **decrease** in plasma glucose concentration **stimulates glucagon release**.
- **During an overnight or prolonged fast**, elevated **glucagon** levels prevents **hypoglycemia.**
- **Amino acids:** stimulate the release of both **glucagon and insulin**.
- **Elevated levels of Epinephrine.**

# Mechanism:

- Insulin is carried to the cells. Place insulin onto each receptor on the liver, fat and muscle.
- The insulin/receptor combination activates a channel for the glucose to move into the cell in muscle and fat cells. In the liver, the channel is always active. The muscles are able to take up lots of glucose, so move more glucose into the muscles.
- Without insulin receptors, glucose can move freely into the brain. Give the brain one glucose.
- Continue moving glucose into organs until blood glucose is back to the normal level (glucose remain on the balance).
- Arrange the glucose in the muscle and liver into chains to represent stored glucose in the form of glycogen.
- Once glucose in the blood is decreased, insulin can be removed from the receptors.

**What happens when the blood glucose level below? How pancreas respond?**

1. Release glucagon into the blood stream.
2. Place a glucagon on its receptor on the liver. The glucagon/receptor combination results in glucose being released from the liver by breaking down glycogen.
3. Move glucose out of the liver into the blood stream. The brain needs energy again. Give it another glucose.

**What happens in overweight, especially around the middle?**

- The insulin receptors become changed and do not bind insulin as well. This is called **insulin resistance** and can lead to the development of type 2 diabetes.

**Insulin resistance** occurs because insulin receptors don't bind insulin as well. This causes the pancreas to work hard all the time to release enough insulin to bring down blood glucose levels. When the β-cells in the pancreas are working hard all the time, they gradually become damaged and cannot make enough insulin to overcome insulin resistance.

# Mechanism of insulin resistance

1. The resistant insulin receptors cannot bind insulin at this concentration. Muscle, liver and fat do not take up glucose.
2. The glucose levels are still high, so the pancreas releases more insulin. Release more insulin into the blood stream.
3. At this higher insulin level, some insulin receptors bind insulin.
4. Put insulin on some of the receptors.
5. Liver, fat and muscle can take up some of the glucose in the blood.
6. Put some of the blood glucose into these tissues.
7. Blood glucose is still high, so the pancreas releases more insulin.
8. Release  more insulin in the blood stream.

## Methods of analysis

1- In the past, the majority of the quantitative test for glucose determination depended upon the oxidation of glucose by hot, alkaline copper solutions or solutions of potassium ferricyanide.

2- Reduction methods: These methods depend on the reductive property of glucose (aldose)

3- A glucose meter (or glucometer) is a medical device for determining the approximate concentration of glucose in the blood.

# How it the glucose meter working?

1. In each test strip, there is a chemical called glucose oxidase.
2. This glucose oxidase reacts with the glucose in the blood sample and is created into a acid called gluconic acid.
3. This current is then able to read and determine how much glucose is in the sample of blood on the testing strip.
4. The number is then relayed on the screen of the glucose testing meter.

**Materials:**

1. Lancets
2. Glucose strips
3. A digital glucose-meter.

## There are several different types of blood glucose tests:

A. **Fasting blood sugar (FBS):** This test measures blood glucose after you have not eaten for at least 8 hours. It is often the first test done to check for pre-diabetes and diabetes.
B. **hour postprandial blood sugar:** This test measures blood glucose exactly 2 hours after you start eating a meal. This is not a test used to diagnose diabetes. This test is used to see if someone with diabetes is taking the right amount of insulin with meals.
C. **Random blood sugar (RBS):** It measures blood glucose regardless of when you last ate. Several random measurements may be taken throughout the day. Random testing is useful because glucose levels in healthy people do not vary widely throughout the day. Blood glucose levels that vary widely may mean a problem.
D. **Oral glucose tolerance test (OGTT):**The patient is placed on a diet which includes 200-300 g of carbohydrates per day for 3 days prior to the test (starvation produces a diabetic type of response).

## Objective of OGTT:

The test usually used to diagnosis for diabetes, insulin resistance, Impaired glucose tolerance, gestational diabetes and reactive hypoglycemia.

## Preparation

1. Patient is instructed to eat a normal diet during the days leading up to the test.
2. Patient is instructed to fast (no eating or drinking) for 8 to 10 hours prior to the test (usually overnight).
3. The test should not be done during an illness, as results may not reflect the patient's glucose metabolism when healthy.
4. Usually the OGTT is performed in the morning as glucose tolerance can exhibit a diurnal rhythm with a significant decrease in the afternoon.

# Procedure

- A zero time (baseline) blood sample is drawn.
- The patient is then given a 75g of glucose in a 300 ml solution and drink within a 5-minute time frame.
- Blood is drawn every 30 min for 2 hour to measure of glucose (blood sugar). For simple diabetes screening, the most important sample is the 2 hour sample and the 0 and 2 hour samples may be the only ones collected.

# Results

A- Fasting plasma glucose should be **(60-110mg/dL)** in normal person.

- ✓Fasting levels between **(110 and 125mg/dL)** indicate prediabetes (Impaired glucose tolerance).
- ✓Fasting levels repeatedly at or above **(126mg/dL)** are diagnostic of diabetes.

B- One hour GTT (Glucose Tolerance Test) glucose level below **(180mg/dL)** is considered normal.

- ✓C- Two hour GTT glucose level below **(140mg/dL)** is normal. Blood plasma glucose between **(140mg/dL)** and **(200mg/dL)** indicate "pre-diabetes.
- ✓Blood plasma levels above **(200mg/dL)** at 2 hours confirm a diagnosis of diabetes.

# E. Glycated Hemoglobin(HbA1c)

- Hb: hemoglobin
- HbA1: is a series of glycated variants resulting from attachment of various carbohydrates to N terminal valine of Hb.
- **Glycosylation: enzymatic addition of any sugar (glucose)to a protein molecule.**
- **Glycated hemoglobin** is a form of hemoglobin that is measured primarily to identify the three month average plasma glucose concentration.

**Note: The test is limited to a three month average because the lifespan of a red blood cell is three months (120 days).**

- When blood glucose levels are high, glucose molecules attach to the hemoglobin in red blood cells. The longer hyperglycemia occurs in blood, the more glucose binds to hemoglobin in the red blood cells and the higher the glycated hemoglobin.
- Once a hemoglobin molecule is glycated, it remains that way. A build-up of glycated hemoglobin within the red cell, therefore, reflects the average level of glucose to which the cell has been exposed during its life-cycle.

- Measuring glycated hemoglobin assesses the effectiveness of therapy by monitoring long-term serum glucose regulation.

**Reference values of HbA1c:**

- Normal 4.5 -5.6%
- Pre-diabetics 5.7-6.4%
- Diabetics more than 6.5%
- Adequate control 6.6-7%
- Inadequate control 7-8%
- Very poor control more than 9%

# Any questions ??
# Please ask