

Regulation of blood glucose is classified into:-

- 1) regulation by organs
- 2) hormonal regulations

1)organs is responsible for regulation are:-

a)liver

(as mentioned before in glycogenesis, gluconeogenesis and glycogenolysis)

b)pancreas:

it secretes 2 important hormones:

- 1) **insulin**: secreted after meals when blood glucose level is high, to decrease it (hypoglycemia)
- 2) **glucagon**: secreted due to hypoglycemia, to increase glucose level (hyperglycemia)

ويفضلو الاثنتين يشتغلو مع بعض علشان يخلوه في النص لا hyper ولا hypo

c)kidney:

when blood glucose levels **exceeds 180** mg% (renal threshold), it will pass in urine resulting in glucosuria (will be explained later) in order to protect the body against excessive glucose in blood

2)hormonal regulation:

1)hypoglycemic hormones:

- ❖ **Insulin** only
- ❖ Secreted by Beta cells of islets of langerhans in pancreas
- ❖ Glucose stimulates secretion and release of insulin from pancreas in 30 to 60 seconds
- ❖ It stimulates glycogenesis in liver and muscle as well as all oxidative pathways of glucose, and inhibits glycogenolysis
- ❖ It stimulates glucokinase in the liver, so it stimulates glycolysis (oxidation of glucose), and it's **antagonist in this process is the growth hormone** (it inhibits glucokinase)
- ❖ It stimulates lipogenesis (تصنيع الدهون) and protein synthesis (anabolic hormone). It inhibits lipolysis
- ❖ It acts on genetic level to induce synthesis of some enzymes (بتشجع علي تصنيع بعض الأنزيمات)

(the rest are explained before)

Mode of action of insulin (water soluble hormone):

#Helper_Team

- 1) binds to receptors present on the plasma membrane of target organs of insulin (muscle cells, adipose tissue and liver cells) الخاليا اللي الهدف بتاع الانسولين انه يروح لها
- 2) then activated

2)Hyperglycemic hormones: (anti-insulin hormones)

1)Catecholamines: (adrenaline and noradrenaline = epinephrine and norepinephrine)

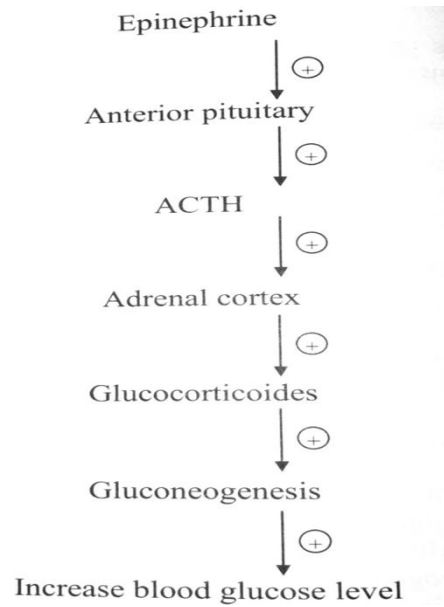
(we will talk about epinephrine)

- It is secreted by **adrenal** (suprarenal) **medulla** when there is hypoglycemia, it's the hormone of rapid physiologic response (ex: **fear** (as mentioned in sympathetic nervous system), **hypoglycemia** and **hypotension** انخفاض ضغط الدم))

- **It has two mechanisms:**

1) Stimulation of glycogenolysis in liver and muscle by activation of **phosphorylase enzyme** by cAMP (as mentioned before), which leads to release of free glucose and increase blood glucose level

2) It stimulates the **anterior lobe of pituitary gland** to secrete ACTH (adrenocorticotrophic hormone), which will stimulate the adrenal cortex to secrete glucocorticoids (**ex:cortisone**), which will stimulate gluconeogenesis, which will increase blood glucose level
(will be explained in point 3)



- It inhibits insulin secretion and Glycogenesis in liver and muscles to increase blood glucose level

2) Glucagon:

- It's secreted by alpha cells of islets of Langerhans of pancreas due to hypoglycemia
- It stimulates glycogenolysis in **liver only** by activating phosphorylase enzyme same as epinephrine
- It stimulates gluconeogenesis and inhibits glycogenesis to increase blood glucose level

3) Glucocorticoids:

- They are secreted by adrenal cortex ex: Cortisone
- They stimulate gluconeogenesis from amino acids by activating transaminases (will be studied in protein metabolism)
- Prolonged treatment with Cortisone may lead to **persistent** (دائمة) **hyperglycemia** and **diabetes mellitus**
- It stimulates lipolysis in adipose tissues (تفتيت الدهون) (hydrolysis of triacylglycerol into glycerol and fatty acids)
- It decreases glucose utilisation in extrahepatic tissues

بتقلل استهلاك الجلوكوز في أي خلايا غير الكبد
*ييزود الجلوكوز على حساب أي حاجة ثانية

4)Anterior pituitary gland secretes:

a)ACTH as discussed before

b)Growth hormone:

- It inhibits glucokinase and so inhibits glycolysis (the antagonist of insulin)
- It stimulates gluconeogenesis and lipolysis in adipose tissue

5)Thyroid hormone (thyroxine):

- Thyroxine is a **mild** hyperglycemic hormone يعني شغله ضعيف اوي في إنه يعلي السكر في الدم
- It increases absorption of glucose from the small intestine to the blood
- It accelerates insulin catabolism بتسرع تكسير الأنسولين
- It stimulates glucose oxidation by the tissues دلوقتي الهورمونات دي دورها أنها تزود الطاقة في الجسم باي شكل فبتكسر في الجلوكوز عشان تطلع طاقة بس دا لحد معين عشان ما يحصلش hypoglycemia و بيكسر الإنسولين عشان ما يحصلش hypoglycemia
- increases lipolysis in adipose tissue

Glucagon > epinephrine > cortisone > growth hormone > thyroxine in increasing blood glucose level

Abnormalities in blood glucose level:

- 1)Glucosuria
- 2)Hypoglycemia

1)Glucosuria

- Def: Appearance of glucose in urine

Types:

1)Normoglycemic glucosuria:

- It's the presence of glucose in urine but blood glucose level is normal

Causes:

- **Physiologically: as in pregnancy**, due to decreased carbohydrate tolerance in late months
الجسم مش بيبيقي قادر يستحمل الجلوكوز فبيخلص منه في ال urine
- In **renal disorders as renal diabetes**: due to congenital low renal threshold
يعني بدل ما اعلى حاجة 180 تبقى 120 مثلا
- **Injection of phlorhizin** which causes inhibition of the reabsorption of glucose in renal tubules

2)Hyperglycemic glucosuria:

- It occurs when blood glucose level is **above the renal threshold** (180 mg%)

Causes:

- **Diabetes mellitus** due to insulin deficiency
- **Emotional**: due to over secretion of epinephrine
كثر الضغط النفسي او العصبية حتطلع أدرينايين كثير فا هايخلي نسبة السكر في الدم جامد فا هيعمل hyperglycemic glucosuria
- **Alimentary (GIT)** :by increasing carbohydrate feeding
الناس اللي بتاكل سكريات كثير
- **Experimental pancreatectomy**
استئصال ال pancreas هاييسبب في عدم افراز ال insulin

Diabetes mellitus

- It is a medical disorders characterized by varying متغير or persistent مستمر hyperglycemia especially after eating
- All types of diabetic patients share similar symptoms and complications at advanced stages في المراحل المتأخرة
- It may lead to **dehydration** and **ketoacidosis** which takes place due to:-

- 1) excessive metabolism of lipids (to compensate the un-utilized glucose)
- 2) this leads to excessive production of acetyl CoA
- 3) which leads to excessive formation of ketone bodies (ketosis)
- 4) which are acidic (ketosis+acidosis = ketoacidosis)

Types:

Name	Type 1 diabetes mellitus or Insulin dependent diabetes mellitus (IDDM)	Type 2 diabetes or Non insulin dependent diabetes (NIDDM)
age	Most common in children and adolescents (less than 30 years old), but may occur in adults	Most common in age above 30
causes	<ul style="list-style-type: none"> •It is an autoimmune disease in which the body attacks the Beta cells in pancreas so they are destroyed and insulin production is reduced. •and this may take place due to: <ol style="list-style-type: none"> 1)virus infection called coxsackie 2)trauma 3)tumors 4)pancreatitis التهاب البنكرياس <p>So,It is due to insulin deficiency</p>	<ul style="list-style-type: none"> •due to insulin resistance, there is a defect in insulin receptors, so the body doesn't respond when insulin is present •and this resistance may be caused by some diseases and long term steroid use زي في بعض المسكنات و ادوية بناء العضلات <p>So,It's due to impaired insulin receptors and insulin resistance</p>
Other names	"Juvenile" or "childhood" onset diabetes	"mature" or "adult" onset diabetes or "insulin resistance diabetes"

Obesity (السمنة))	Mainly not present	Present and it leads to increased insulin resistance
treatment	by insulin injection	First: by changes in diet and weight loss Then: by oral antidiabetic drugs (hypoglycemic drugs) to decrease the insulin resistance and increase sensitivity to insulin Ex of drugs: sulphonylureas and metformin Finally: if both failed, insulin injection as type 1 is necessary

Complications: المضاعفات التي ما اتعالجش

- 1) **cardiovascular diseases** specially microcirculation (small arterioles), this disease is called **micro angiopathy**, and this will lead to the following 3 complications:
- 2) **chronic renal failure** (nephropathy) فشل كلوي
- 3) **retinal damage** and may lead to blindness (retinopathy)
- 4) **peripheral nerve damage** (peripheral neuritis) with risk of amputation
of toes, feet and even legs
- 5) and if ketosis is extremely increased without treatment this will lead to **ketoacidonic coma** (diabetic coma)

Symptoms:

- 1) **polyurea** (excessive urination)
في حاجة اسمها osmotic diuresis و هي ان الجلوكوز و هو نازل في ال urine بيسحب معاه مياه فا يزود ال dehydration فا يعمل polydipsia يعني يشرب مياه كتير و عطلول عطشان

- 2) increased **thirst** sensation
- 3) weight loss due to metabolism of fats and protein
الجسم بيكسر فيهم عشان ياخذ منهم الطاقة اللي مش عارف ياخوها من بالجلوكوز
- 4) **hunger** (because body energy is very low) انه بياكل و رغم انه جعان و فا بيتهيأله انه جعان و رغم انه بياكل
كثير بيخس برده
- 5) **fatigue** (due to metabolism of muscle proteins), **nausea**, and **vomiting** when untreated
- 6) **infections** (the non oxidized glucose will be the perfect source of energy to any virus or bacteria and immune defenses will not be able to overcome it)
- 7) **Blurred vision, renal failure, peripheral neuritis** (burning in hands and feet)
- 8) **Diabetic coma**

Criteria for diagnosis of diabetes mellitus:

It can be diagnosed by demonstrating anyone of these: يعني

لما نشوف حاجة منهم نعرف ان عنده السكر

- 1) 2-3 fasting blood glucose levels **above (126 mg%)** on different days
يعني يعمل تحليل مرتين أو ثلاث مرات في أيام مختلفة ولو النتيجة فوق 126 يبقى مريض سكر
- 2) 2 to 3 times blood glucose **above 200 mg%** ,two hours after drinking a 75 g glucose (postprandial) (will be explained in glucose tolerance test)
- 3) Symptoms of diabetes, and a random glucose level test above 200mg%
- 4) High amount of glucose bound to haemoglobin HbA1c **"glycosylated hemoglobin"** which is 6% or higher (studied in 201), this is a follow up

test showing average blood glucose level approximately 90 days before

2) Hypoglycemia: (second abnormality)

- It is the decrease of blood glucose level **below its normal fasting level** (starts below 60 and is **marked below 50 mg%**)
- **Maternal and Fetal hypoglycemia** may take place during pregnancy especially if there are long intervals between meals at night (**because fetal glucose consumption increases**)
- **Premature babies are more subjected to hypoglycemia** (due to **impaired gluconeogenesis**) (when born in the 7th or 8th month of pregnancy)
- Diabetic patients on insulin or oral antidiabetic medication are liable to **drug-induced hypoglycemia** (when they take overdose of insulin or antidiabetic drug)
- **Hypoglycemic coma** in diabetic occurs when blood sugar level is less than 40 mg% **due to over dosage of insulin , or normal dosage but without eating any carbohydrates**

Oral glucose tolerance test (GTT)

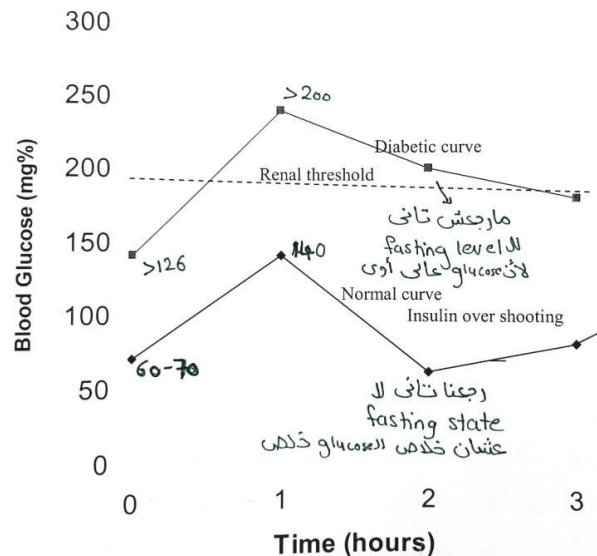
- **Glucose tolerance** is the ability of the body to regulate the blood glucose level after administration of a dose of glucose for the test
- **Diabetes mellitus** is characterized by **decreased** glucose tolerance **due to decreased secretion of insulin or insulin resistance**, so no regulation can occur

How to perform this test:

- 1) The patient comes to the lab **fasting for 8-10 hours**, and drugs are **avoided for 2-3 days** before the test
- 2) The test takes 2-3 hours

- 3) **Blood** and **urine** samples are collected from the patient in the fasting state (this indicates the zero time of the test (the starting time of the 2 or 3 hours))
- 4) Then after taking the first sample, the patient drinks a cup of water with a specific dose of glucose which is **70-75 gm if adult**, and **1-1.5 gm per each kilogram of the body weight in children** (1-1.5 X his body weight in kg)
- 5) After administration of the glucose dose , blood and urine samples are collected **each half an hour**
- 6) Write down the results (**estimation of blood glucose in all samples**)
- 7) Draw a curve for blood glucose (mg) on x-axis and time (hours) on y-axis
- 8) Detection of glucose in urine is done in all samples

Observations on the curve in diabetic patients:



- the blood glucose level in fasting state (first sample before administration) **is above 126**
- the level in postprandial state (second sample) **is above 200**