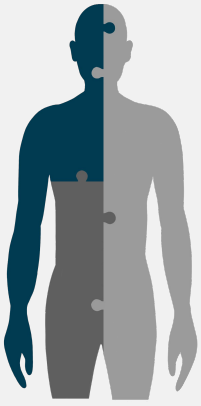
Physiology Team 439

MED439
KING SAUD UNIVERSITY



Physiology of the Pancreas and Pathophysiology of Diabetes Mellitus

Objectives:

- Identify the major hormones secreted from the endocrine pancreas, and their cells of origin.
- List the target organs for glucagon and describe its principal actions on each
- Describe the control of glucagon secretion
- Integrate the structure, synthesis, and secretion of glucagon with the levels of circulating fuels, insulin, and catecholamines.
- Identify insulin, its synthesis, receptor, and cellular effects at the molecular level.
- List the major target organs or cell types for insulin, the major effects of insulin on each, and the consequent changes in concentration of blood constituents.
- Understand the relationship between blood glucose concentrations and insulin secretion.
- Identify and describe the factors that modulate the secretory response.
- Map out and integrate the actions of insulin on the utilization and storage of glucose, free fatty acids (FFAs), and amino acids (AAs) by hepatocytes, skeletal muscle, and adipocytes during the digestive phase.
- Discuss the main types of diabetes mellitus, its symptoms and the role of insulin in its management.
- Explain the glucose tolerance test and its importance in medical practice.

Special Thanks to the Leader Aljoud Algazlan

Color index:

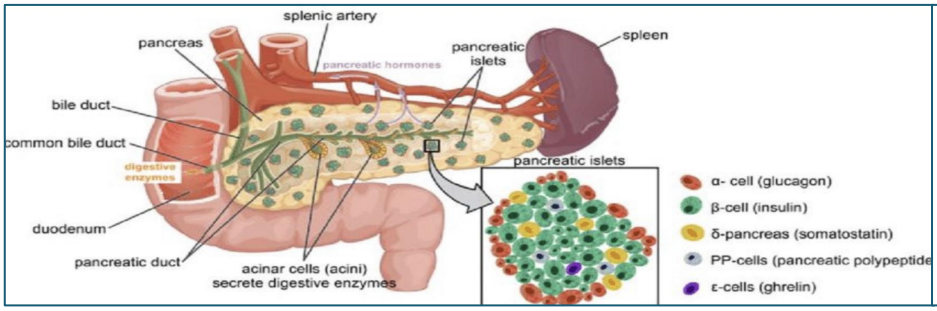
- Important.
- Girls slide only.
- Boys slide only.
- Dr's note.
- Extra information.

Editing File

Pancreas

- A triangular gland, which has both exocrine and endocrine cells, located behind the stomach.
- Strategic location.
- Divided into an endocrine part and an exocrine part:
  - Acinar cells produce an enzyme-rich juice used for digestion (exocrine product).
  - Pancreatic islets (islets of Langerhans) produce hormones involved in regulating fuel storage and use endocrine part , account for 1% of the pancreas

Extra



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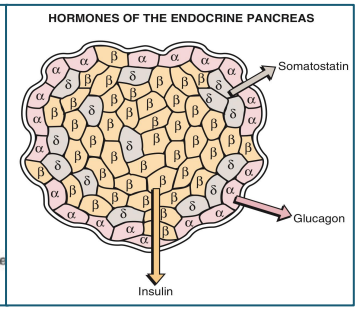


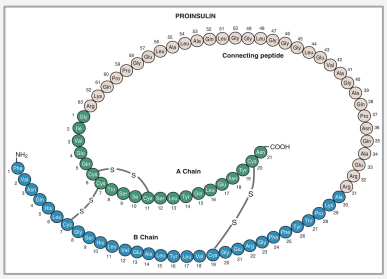
Cells of Islets of langerhans:

1-2 million islets, located at the periphery of the pancreas.

Cell	Action	Distribution	Notes
Beta (β) cells	Produce insulin, Amylin, C peptide & proinsulin.	70%	The most important and abundant one, lie **mainly in the middle of each islets**. any fuel (nutrients) will activate beta cells
Alpha (α) cells	Produce glucagon	20%	Located at the periphery of each islets,When there is no fuel (starvation) it will release glucose and fatty acids
Delta (δ) cells	Produce somatostatin	5%	Located at the center and periphery of each islets. Somatostatin inhibits the secretion of both insulin and glucagon (universal inhibitor)
F (PP) cells	Produce pancreatic polypeptide	5%	
G cells	Produce gastrin	1%	

Insulin

- Hormone of nutrient abundance.
- Has a plasma half-life of 6 minutes.
- A protein hormone consisting of two amino acid chains (α & β) linked by disulfide bond.
- Synthesized as: preproinsulin consisting of: signaling peptide & proinsulin (86 AA) and then excised by enzymes releasing functional insulin (51 AA) and C peptide (29 AA).



Insulin Synthesis:

- Insulin synthesis is stimulated by glucose or feeding and decreased by fasting.
- Threshold of glucose-stimulated insulin secretion is 100mg/dl.
- Glucose rapidly increase the translation of the insulin mRNA and slowly increases transcription of the insulin gene.

The Process of Insulin Synthesis:

DNA — Located at the short arm of chromosome 11 in β cells.

mRNA — The gene for the hormone is transcribed into an mRNA. mRNA goes to the ribosome to form *preproinsulin*.

Preproinsulin — Composed of:
- Signal peptide/sequence segment/initial segment
- A chain
- B chain

A chain + B chain — Peptide C (connects between A and B chains)

Proinsulin — Formed by:
1. Folding of the polypeptide In the RER.
2. Formation of disulfide bonds between A chain and B chain.
3. Removal of the initial segment.

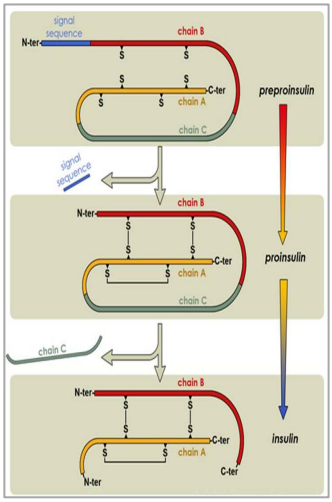
Insulin — In the Golgi apparatus C peptide is cleaved from the proinsulin to become Insulin.

Packaged — C peptide and insulin and a little zinc are packed into vesicles, some of the C peptides in the vesicles are not cleaved yet. Equal amounts of C peptide and insulin are packaged into vesicles.

This is important in the diagnosis of D.M. Measuring the C peptide will give us the natural insulin level when using exogenous insulin.

Released — Finally, release of insulin into the cytoplasm when needed (exocytosis).

Extra

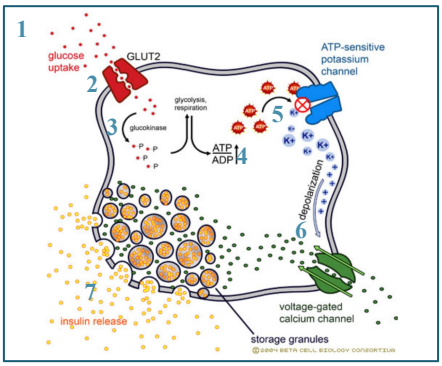


Extra, to summarize:

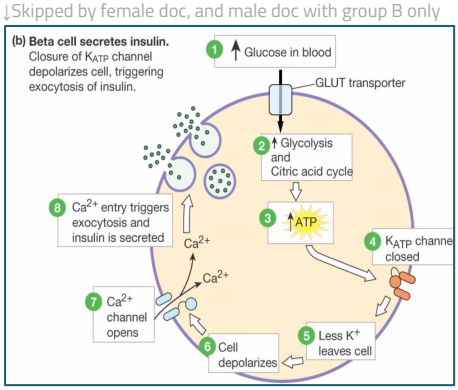
Preproinsulin = Signal peptide + Chain B + Chain A + Chain C
Proinsulin = Chain B + Chain A + Chain C + Disulfide bonds
Insulin = Chain B + Chain A + + Disulfide bonds

Insulin Secretion (Very Important):

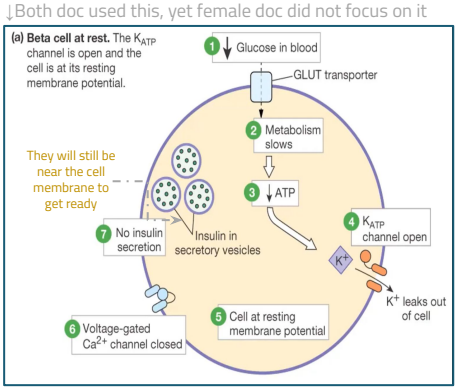
↓Both doctors used this image



↓Skipped by female doc, and male doc with group B only



↓Both doc used this, yet female doc did not focus on it



1	Increase in blood glucose level after eating. why is that the first step? Because Glucose is the primary stimulator of insulin secretion.
2	Glucose binds to GLUT2 and enters the cell. (The transporter is called GLUT**2** because it opens in **two** ways; if the glucose conc is high outside the cell glucose will enter the cell and the opposite (basically it follows the rule of "from high to low conc", no matter the direction)).
3	Since GLUT2 works in two ways, glucose can very easily escape from the cell. So the solution is an enzyme called: **Glucokinase**. It will add phosphate group to glucose at carbon number 6 to become glucose 6 phosphate now it is trapped and can't get out (polar and more big)
4	Glycolysis of glucose 6 phosphate gives energy, so ADP will be converted to ATP. The net result is decrease in ADP and increase in ATP.
5	Increase in ATP level will close the ATP - sensitive potassium channel (normally potassium goes out from high conc to low conc) when the channels are closed, an increase in potassium level inside the cell will decrease the negativity in the cell which will cause depolarization.
6	Depolarization will open the voltage gated calcium channel, Ca will move from outside (high conc) to inside the cell (low conc).
7	**Ca** will facilitate the vesicles which contain insulin to move near the cell membrane (docking), then exocytosis and release of insulin. (Please know that Ca is what triggers exocytosis).

The ATP sensitive K channel can be manipulated:

1. Closing the channel: A drug that closes the channel (mimics the action of ATP) will increase the release of insulin. Used in hyperglycemia in diabetes patients because they have insulin resistance, these drugs called sulfonylurea, and they were the most important drugs in treating diabetes in the past.
2. Facilitating the channel: Other drugs prevent the closure of the channel so insulin can't be released. This drug is used when there is insulin hypersecretion by a tumor in the beta cells, digoxin is an example.

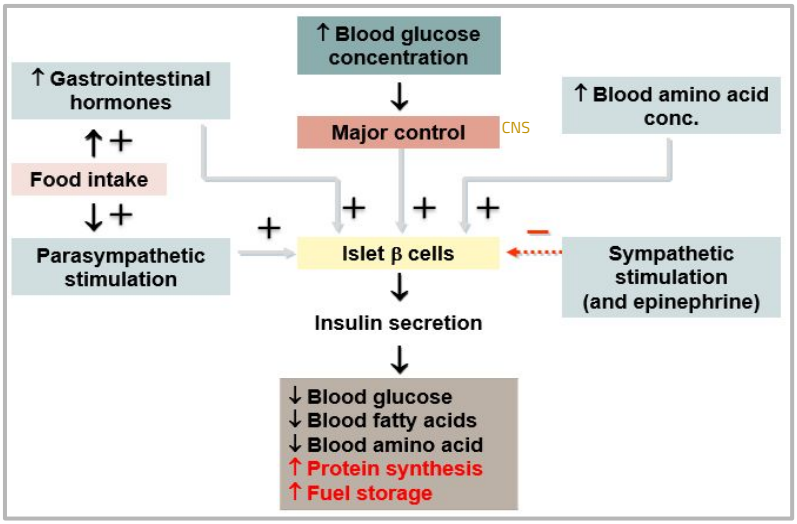
What is the most important step in releasing insulin?

The conversion of glucose to glucose 6 phosphate by **Glucokinase.** This is the rate limiting step which accelerate or decelerate the release of insulin.

- If there is a mutation in the glucokinase enzyme they will have MODY diabetes (Maturity Onset Diabetes of the Young), they will have the insulin (because the synthesis is normal) but it can't be released.

Regulation of Insulin Secretion (Very Important):

If the blood glucose concentration is high, Major control (CNS) will increase Beta-cell activity so insulin will be secreted as a negative feedback process. How does that happen? The body will detect high blood sugar and will send a report to the major control or the CNS. In this case, the CNS will influence the pancreas. Which will make it release insulin causing its different actions. Insulin will act also as a growth hormone by increasing hormone synthesis and storing fuel by storing glycogen in the liver. PNS is a "Rest and digest" system and the SNS is a "Fight or flight" system. PNS will increase insulin secretion because PNS is activated after meals. SNS will decrease insulin.



Stimulators	Inhibitors
- ↑ **Serum glucose** The most important one (Master regulator)	- ↓ Serum **glucose**
- ↑ **Serum amino acids**[1]	- ↓ Serum **amino acids**
- ↑ **Serum free fatty acids** [1]	- ↓ Serum **free fatty acids**
- ↑ **Serum ketone bodies**	- ↓ Serum ketone bodies
- **Parasympathetic nervous system** [2]	- **Sympathetic nervous system** [3]
Hormones	
1. Epinephrine (β-Receptor) 2. Gastric Inhibitory peptide (GIP).[4] 3. Glucagon. Glucagon will stimulate insulin release while insulin will inhibit the glucagon release 4. Gastrin. 5. Cholecystokinin (CCK). 6. Secretin. 7. Vasoactive intestinal peptide (VIP).	1. Epinephrine (α-Receptor) 2. Somatostatin

[1] Any fuel (nutrients) because they will cause glycolysis, an increase in ATP and close the ATP sensitive K channel... (same as glucose).

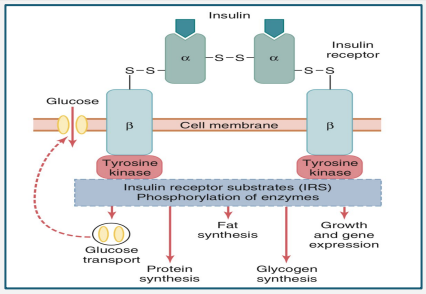
[2] In the rest situations when you are eating, increase in insulin release will cause glucose uptake by the cells and storage of glucose also it will be used for energy.

[3] we need high glucose in the blood. Why it will cause inhibition? Sympathetic stimulation on Beta 2 will increase the insulin secretion while in alpha 2 it will decrease the insulin secretion and because the beta cells have more alpha 2 receptors the net result is inhibition of insulin secretion.

[4] Which one will increase the blood insulin level more ? the oral glucose or I.V glucose? The oral glucose because of the GIT hormones (Incretin) .When you eat, the GIT hormones will stimulate the pancreas to release insulin.

- so, there are two stimuli of insulin release the glucose itself and the GIT hormones.
- GIT hormones reduce motility and increase the sense of satiety.
- Some drugs prevent the degradation of incretin, they are used in D.M type 2 to increase insulin secretion.

Insulin Receptors:



- The insulin receptor is a transmembrane receptor
- Belongs to the large class of tyrosine kinase receptors.
- Made of two α (extracellular) subunits and two β (intracellular) subunits, bound by disulfide bond.
- Found in liver ,adipose tissue,skeletal muscle.
- Mechanism:
    1. Insulin binds to α subunit, transformation of α subunits.
    2. Activation of β subunit (auto phosphorylation), it has tyrosine kinase activity.
    3. Activation of IRS this will lead to activation of any anabolic hormone and inhibition of any catabolic hormone.
- Binding of insulin to the receptor will move the transporter (GLUT 4) to the cell membrane for glucose uptake .
- 80% of cells will increase their glucose uptake within seconds.
- It is called insulin sensitive cells because glucose can't enter the cell without the presence of insulin.
- There is a synergistic effect of insulin and growth hormone on growth only.

Glucose Metabolism Terms:

- **Gluconeogenesis**: Synthesis of glucose from noncarbohydrate precursors, Lactic acid, glycerol, amino acids, liver cells synthesis glucose when carbohydrates are depleted.
- **Glycogenesis**: Formation of glycogen, glucose stored in liver and skeletal muscle as glycogen, important energy reserve.
- **Glycogenolysis**: breakdown of glycogen (polysaccharide) into glucose molecules (monosaccharide).
- **Glycolysis**: the breakdown of glucose into pyruvate by cells for the production of ATP.

Glucose Transporters:

Transporters	Present in
GLUT-1	Placenta, Blood brain barrier, RBCs, Kidneys and Colon.
GLUT-2	β cells of Pancreas, Liver, Epithelial cells of small intestines and Kidneys. Mnemonic: GLUT 2 LIKes Beta cells. Present in: L:liver , I: intestine, K:kidney , beta cell
GLUT-3	Brain, Placenta and Kidneys.
GLUT-4 Insulin sensitive	Skeletal Muscles, Cardiac muscles and Adipose tissue.
GLUT-5	Jejunum and sperm.

Actions of Insulin (Important):

Rapid (Seconds)	Intermediate (Minutes)		Delayed (Hours)
↑ Transport of glucose, amino acids, K+ into insulin sensitive cells K will enter with glucose if there is GLUT4	↑ Protein synthesis	↓ Protein degradation	↑ mRNAs for lipogenic and other enzymes to enhance growth
	↑ Of glycolytic enzymes and glycogen synthase glycogen synthesis	↓ Phosphorylase[1] and gluconeogenic enzymes (they inhibit gluconeogenesis and glycogenolysis)	

Any nutrient enter the body, it will be used as energy if there is more than what we need 1/ it will be stored as glycogen 2/ it will be stored as fat 3/ in protein synthesis (anabolism and inhibit catabolism) 4/finally ,it's important in growth

[1] Phosphorylase will remove phosphate from glucose and glucose will not be trapped, so inhibition of Phosphorylase will trap the glucose.

General: ↑ cell growth Same as GH

Adipose tissue	Muscle	Liver The most important site for glucose storage
↑ Glucose use		
↑ Glycolysis		↑ Glycolysis[2]
↑ Glucose uptake by increasing GLUT-4 availability		↑Glucose uptake (if blood glucose level is high)
	↑ Glycogen synthesis (Glycogenesis)	
	↑ Protein synthesis in ribosomes[3]	
↑ K uptake		
↑Fatty acid synthesis (Lipogenesis) ↑ Synthesis of α-glycerol phosphate ↑ Triglyceride deposition glycerol and the fatty acid ↑ Lipoprotein lipase [4] ↑ Esterification of fats	↑ Amino acid uptake (particularly branched-chain amino acid). ↑ Ketone uptake[5]	↑ Lipid and fatty acid synthesis released through VLDL in the blood, so you'll have ↑ VLDL formation
	↓Glycogenolysis	
↓ Of hormone-sensitive lipase (Guyton loves this enzyme) & ↓lipolysis[6]	↓ Release of gluconeogenic amino acids A.A that help in glucose synthesis ↓Protein catabolism (proteolysis)	↓ Gluconeogenesis ↓ Urea cycle activity ↓ Ketogenesis

[2] In the liver we will have an increase in glucose level indirectly. There is no glucose uptake as in muscles and adipose tissue (no GLUT4) . We can't say increase uptake, here the glucose will enter the cell from high conc to low conc not because of the insulin

[3] Diabetes patients can't synthesize protein, which will lead to muscle wasting

[4] Located in the wall of endothelial cells in blood capillaries in adipose tissue . The lipoprotein lipase will break lipids that are attached to protein, so lipids can be stored in adipose tissue.

[5] In D.M especially type 1 there is no ketone uptake which will lead to ketoacidosis

[6] Hormone - sensitive lipase Break adipose tissue . Inhibition of it will increase Anabolism and inhibit Catabolism → ↓ lipolysis
Patients with diabetes will experience weight loss because they don't have insulin, which help in fat storage they also will have muscle wasting because the breakdown of fat. They will also have high plasma lipids because this enzyme is no longer inhibited (complication).

Glucagon

- A 29-amino-acid polypeptide hormone that is a potent hyperglycemic agent.
- Produced by **α** cells in the pancreas.
- Opposite action to insulin.
- It's a very big molecule that can't be in the bloodstream, this is why it's broken down and rebuilt many times.

Glucagon Synthesis:

DNA in α cells (chromosome 2) → **mRNA** → **Preproglucagon** → **Proglucagon** → **Glucagon**

Factors Affecting Glucagon Secretion:

Stimuli	Inhibitors
- ↓ Blood glucose, starvation	- ↑ Blood glucose
- Sympathetic Nervous System (SNS) stimulation - ↑ Serum amino acids (arginine, alanine)[1] The only one that is same to insulin - Stress. - Exercise to maintain blood glucose during exercise	- Somatostatin - Insulin

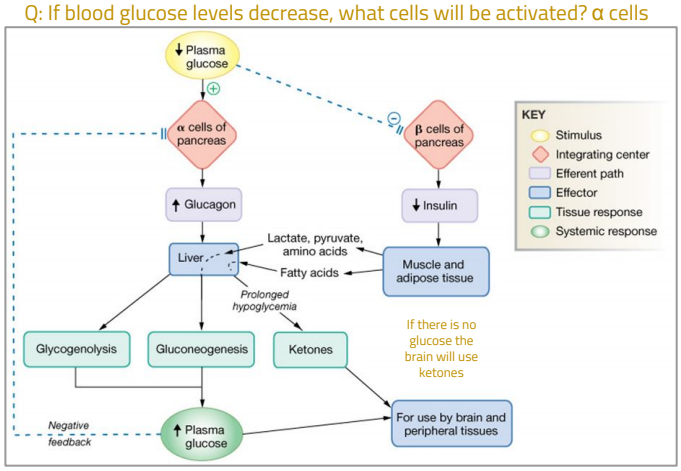
[1] Why A. A stimulate glucagon secretion? Because some A.A used in glucose synthesis and if you eat only protein this can lead to hypoglycemia because you haven't eaten any glucose so here the glucose obtained from A.A tries to maintain blood glucose level. (To antagonize the effect of insulin).

Glucagon Actions

Its major target is liver:

- **Glycogenolysis** The most important function
- **Gluconeogenesis**
- **Lipid oxidation** (fully to CO_2 or partially to produce keto acids ketone bodies"). (ketogenesis)
- **Release of glucose to the blood from liver cells**

Q: If blood glucose levels decrease, what cells will be activated? α cells



Diabetes

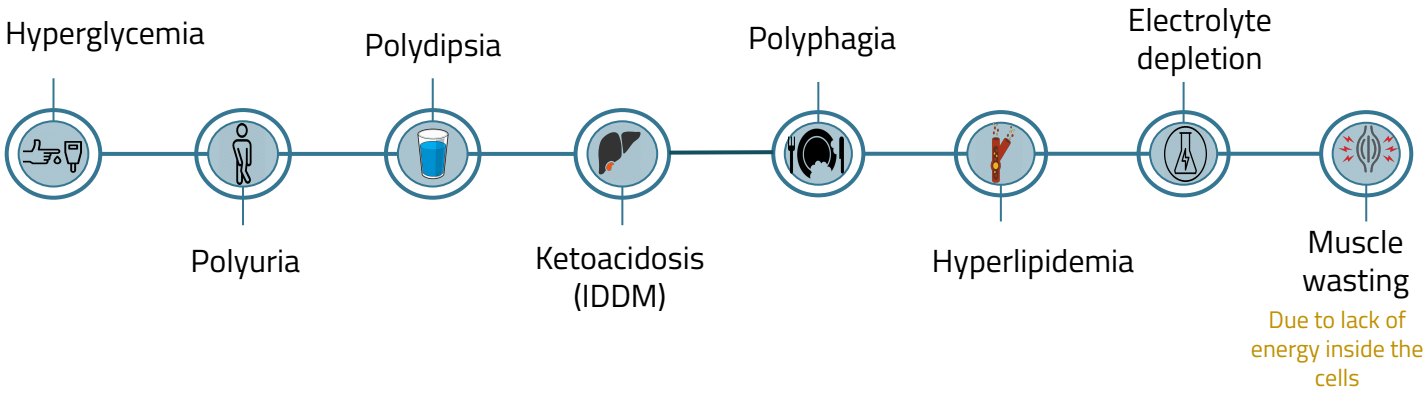
- Diabetes is probably the most important metabolic disease
- It affects every cell in the body and affects carbohydrate, lipid, and protein metabolism.
- Characterized by the polytriad seen on the right:

لأن الجلوكوز يسحب الماء معه (diuresis)

بسبب نقص الماء ولأن الخلايا برا ECF مرة عالي السكر > فالخلايا بتطلع الماء اللي فيها لبرا.

1. لأن الخلايا ما تأخذ طاقة كافية.
2. لما يطلع الجسم السكر، راح يحتاج يعوضها بالأكل.
3. الخلايا الوحيدة بال Brain اللي تعتمد على الأنسولين موجودة في satiety center مركز الشبع، وهو في hypothalamus ، واذا فيه انسولين فهو يدخل الجلوكوز داخل ال Brain، اما اذا ما فيه فما يدخل لها جلوكوز وتحس انها جوعانه.

Symptoms of Diabetes:

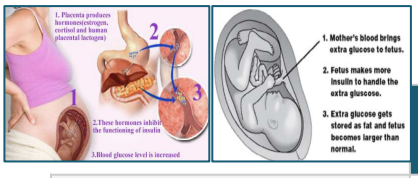


Types of Diabetes:

	Diabetes Mellitus Type I (Autoimmune attack, 10%)
Epidemiology	- Mainly affects children - Juvenile onset
Cause	- Immune-mediated selective destruction of β cells, leading to: - Hyposecretion of insulin
Pathogenesis	- **No insulin,↑ glucagon >** High production of glucose and ketones by liver - ↑ **Glucose & ketones >** Osmotic diuresis - ↑ **Keto acids >** Diabetic ketoacidosis
Management and Treatment	- Insulin dependent, so the treatment is: - Insulin Injection

Types of Diabetes Cont. :

	Diabetes Mellitus Type II (85%-90%)
Epidemiology	- More common in some ethnic groups - Late onset, genetic and family related risk factors.
Cause	- Unhealthy foods and inactive lifestyles with sedentary behaviour - Resistance of body cells to insulin keeps blood glucose too high - الأسباب: قلة الحركة + fast food + ونظام الأكل. - ربع المجتمع (كل أربعة أشخاص شخص مصاب) في السعودية فيهم سكر.
Management and Treatment	- Lifestyle modification with physical activity and/or healthy diet - Diet and oral hypoglycemic agents> يحفز إفراز الإنسولين
Complications	- Atherosclerosis - Renal failure - Blindness.



Gestational Diabetes (during pregnancy)	
Epidemiology	Occurs in 2-5% of pregnancies
Cause	Associated with decreased insulin levels and/or insulin resistance
Pathogenesis	Resembles Type 2 Diabetes
Management and Treatment	Usually transient: symptoms improve following delivery
Complications	If untreated ⟶ macrosomia (high birth weight)

Long Term Complications of Uncontrolled Diabetes (microvascular disease):

Hyperglycemia damages small blood vessels:

Diabetic retinopathy	Vision loss
Diabetic neuropathy	-Damage to the nerve -Most common cause of amputation in western world
Diabetic nephropathy	Kidney damage —> chronic renal failure

- أحد الأشياء المهمة في مرضى السكر ، ارتفاع مستوى الدهون (الكوليسترول) في الدم> تسبب لزوجة عالية> جلطات.
- السكر يجرح الشعيرات الدموية الصغيرة microvessels ويسبب: (واللي ممكن تؤدي للوفاة)
- مشاكل بالنظر : retinal.
- ما يحسون باعصابهم، مشاكل ب proprioception : neuropathy.
- بالكلى : renal problem or failure.
- غالبًا مرضى السكر يموتون بجلطات بالقلب، وأول ما يجي مريض سكر نعطيه ادوية كوليسترول حتى لو ما عنده.

Glucose Tolerance Test

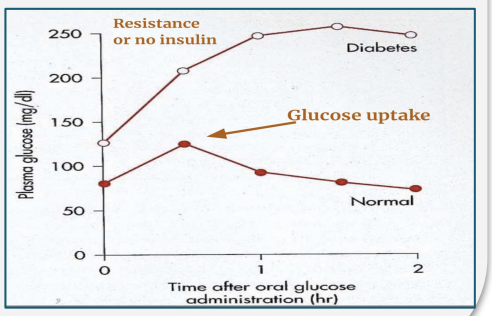
- أفضل diagnostic test ، ويساعدني بمعرفة الأشخاص اللي عندهم قابلية للسكر.
- Both the Fasting Plasma Glucose (FPG) test and Oral Glucose Tolerance Test (OGTT) require that the patient fast for at least 8 hours (ideally 12 hr) prior to the test.

The oral glucose tolerance test (OGTT):

Fasting plasma glucose (FPG) test

Blood is then taken 2 hours after drinking a special glucose solution

- Following the oral administration of a standard dose of glucose(محلول جاهز حسب الوزن), the plasma glucose concentration normally rises but returns to the fasting level within 2 hours.
- If insulin activity is reduced, the plasma glucose concentration takes longer than 2 hours to return to normal and often rises above 200 mg/dl.
- Measurement of urine glucose allows determination of the renal threshold for glucose
- **About the graph:**
  - **Normal:** 30 minutes after a meal you will see that glucose levels will stop rising and start decreasing. This is because of the release of insulin.
  - **Diabetes:** We see that glucose levels don't stop rising due to lack of insulin activity (either its absent or there is resistance). And if the decrease happens, it's much later and the decrease is a lot smaller than the normal.



The Following Results Suggests Different Conditions (Very Important):

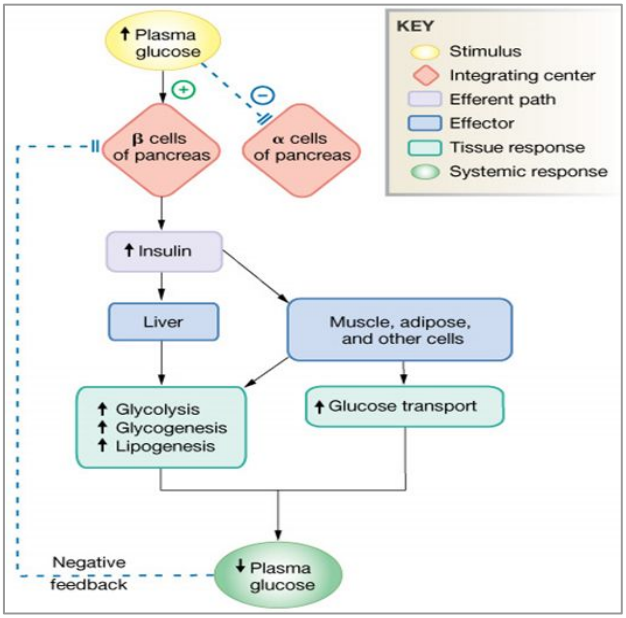
مهمة القيم + حفظ صم	FPG	2h PPG Postprandial Glucose, after a meal
Normal value	**<100 mg/dL**	**< 140 mg/dL** يرجع لل fasting level بعد ساعتين
Impaird glucose tolerance prediabeteic قابل للإصابة، ولازم يسوي رياضة وحمية	-	**= 140 - 199 mg/dL**
Diabetes	**≥ 126 mg/dL**	**≥ 200 mg/dL** يأخذ وقت طويل يمكن ٥ ساعات حتى يرجع لل fasting level

Summary of Insulin

Slides

Table 22-3: Insulin

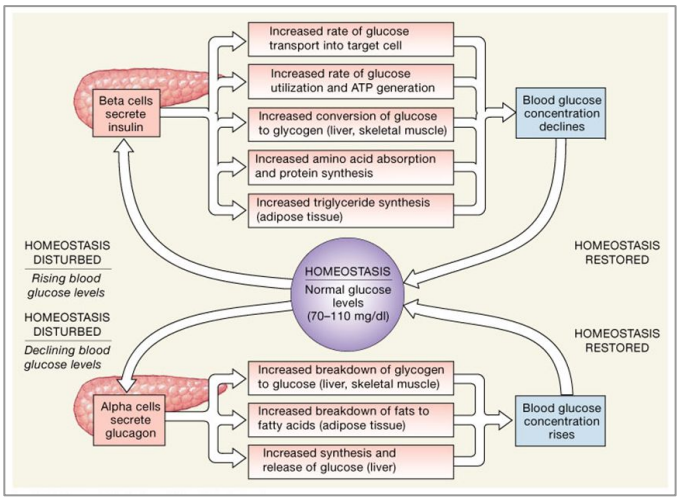
Cell of origin	Beta cells of pancreas
Chemical nature	51-amino acid peptide
Biosynthesis	Typical peptide
Transport in the circulation	Dissolved in plasma
Half-life	5 minutes
Factors affecting release	Plasma [glucose] > 100 mg/dL; ↑ blood amino acids; GI hormones (feedforward reflex) and parasympathetic amplify. Sympathetic inhibits.
Target cells or tissues	Liver, muscle, and adipose tissue primarily; brain, kidney, and intestine not insulin-dependent
Target receptor	Membrane receptor with tyrosine kinase activity; pathway with insulin-receptor substrates
Whole body or tissue action	↓ Plasma [glucose] by ↑ transport into cells or ↑ metabolic use of glucose
Action at cellular level	↑ Glycogen synthesis; ↑ aerobic metabolism of glucose; ↑ protein and triglyceride synthesis



Summary of Glucagon

Table 22-5: Glucagon

Cell of origin	Alpha cells of pancreas
Chemical nature	29-amino acid peptide
Biosynthesis	Typical peptide
Transport in the circulation	Dissolved in plasma
Half-life	4–6 minutes
Factors affecting release	Stimulated by plasma [glucose] < 200 mg/dL, with maximum secretion below 50 mg/dL; ↑ blood amino acids.
Target cells or tissues	Liver primarily
Target receptor/second messenger	G protein-coupled receptor linked to cAMP
Whole body or tissue action	↑ Plasma [glucose] by glycogenolysis and gluconeogenesis; ↑ lipolysis leads to ketogenesis in liver
Action at molecular level	Alters existing enzymes and stimulates synthesis of new enzymes
Feedback regulation	↑ Plasma [glucose] shuts off glucagon secretion
Other information	Member of secretin family along with VIP, GIP, and GLP-1



Summary of diabetes mellitus effect

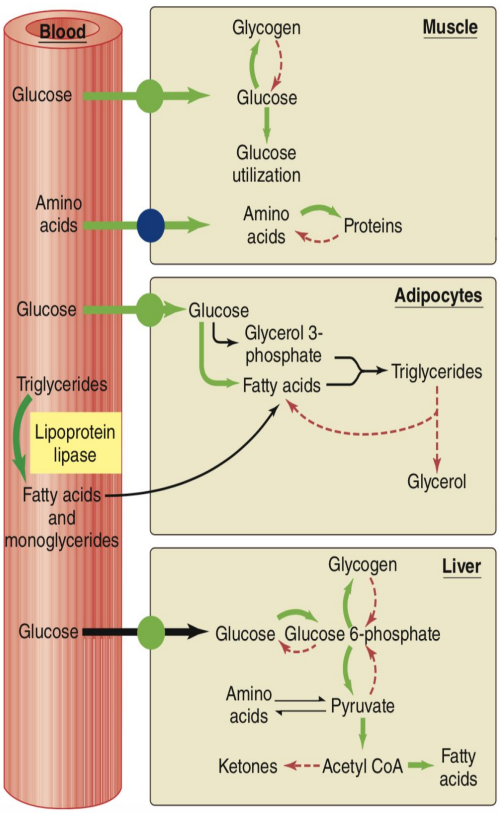
Slides

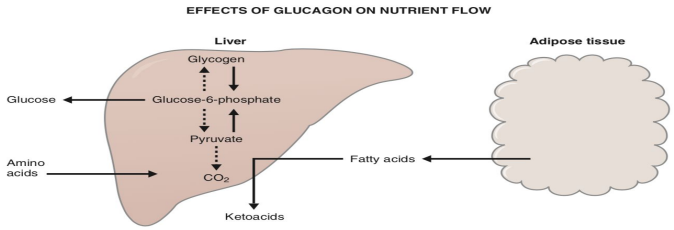
Organs/tissue involved	Organ/tissue responses to insulin deficiency	Resulting condition of:		Signs and symptoms
		Blood	Urine	
	Decreased glucose uptake and utilization	Hyperglycemia	Glycosuria	**Polyuria** - dehydration - soft eyeballs
	Glycogenolysis		Osmotic diuresis	**Polydipsia** Fatigue Weight loss
	Protein catabolism and gluconeogenesis			**Polyphagia**
	Lipolysis and ketogenesis	Lipidemia and ketoacidosis	Ketonuria Loss of Na^+, K^+; electrolyte and acid-base imbalances	Acetone breath Hyperpnea Nausea/vomiting/ abdominal pain Cardiac irregularities Central nervous system depression; coma

= Muscle = Adipose tissue = Liver

Extra

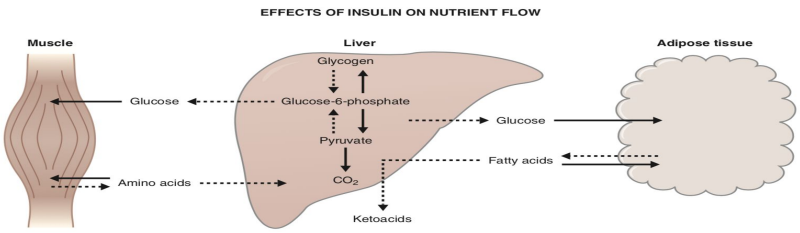
Insulin:





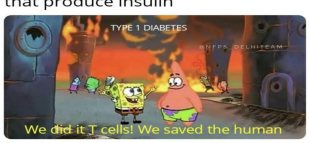
Nutrient	Effect of Glucagon on Blood Level
Glucose	Increased
Fatty acids	Increased
Ketoacids	Increased

Solid arrows indicate that the step is stimulated; dashed arrows indicate that the step is inhibited.



Nutrient	Effect of Insulin on Blood Level
Glucose	Decreased
Fatty acids	Decreased
Ketoacids	Decreased
Amino acids	Decreased

The immune system after killing the beta cells in the pancreas that produce insulin



My blood sugar: *gets slightly high*
All the pee in my body:

Extra: تعرفون ليش؟
Normally your body reabsorbs glucose as it passes through your kidneys, but when diabetes raises your blood sugar, your kidneys may not be able to bring it all back in. This causes the body to make more urine. Because you're urinating so much, you can get thirsty. When you drink more, you'll also urinate more.

MCQ & SAQ:

Q1: Insulin secretion is increased by which of the following?

A. Beta adrenergic stimulation
B. Somatostatin
C. Low blood Glucose
D. Alpha adrenergic stimulation

Q2: Which of the following structures does not contain C chain?

A. Preproinsulin
B. Proinsulin
C. Preinsulin
D. Insulin

Q3: Which of the following is a complications of untreated gestational diabetes

A. Chronic liver failure
B. High birth weight
C. Macromania
D. Microsomia

Q4: Which of the following increases insulin and glucagon secretion?

A. Sympathetic stimulation
B. High serum amino acids
C. Low glucose levels
D. Parasympathetic stimulation

Q5: Which of the following is a function of insulin?

A. Decrease gluconeogenesis
B. Inhibit glucose uptake by muscle cells
C. Increase activity of human sensitive lipase
D. A+C

Q6: A patient came complaining polyuria, polyphagia, and polydipsia. Which of the following results is a diagnosis of DM?

A. FPG = 80 mg/dl
B. PPG = 120 mg/dl
C. FPG= 150 mg/dl
D. PPG=160 mg/dl

answer key:
1: A
2:D
3: B
4: B
5: A
6: C

1- list 3 long term complications of uncontrolled diabetes?

2- List the steps for insulin secretion.

3- List 6 factors that stimulate Insulin secretion.

A1: -1-diabetic nephropathy (kidney damage->chronic renal failure) 2-diabetic retinopathy (vision loss) 3-diabetic neuropathy (damage to the nerve)

A2: Slide 5

A3: Slide 6

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