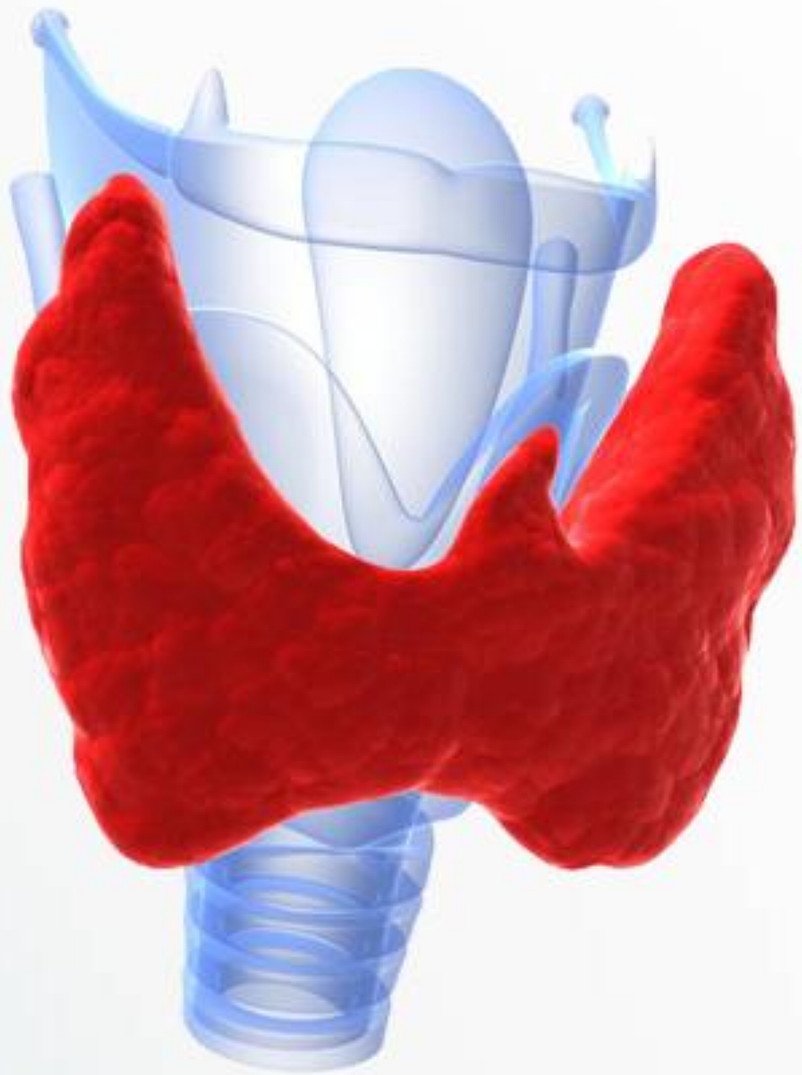
Physiology team



15 Cont.physiology of pancreas

Sources:
FEMALE SLIDES

MED 433 Teams

Glucagon:

A 29-amino-acid polypeptide hormone that is a potent hyperglycemic agent.

- Produced by α cells in the pancreas.
- Use cAMP \ Adenylyl cyclase system (second messenger).

Glucagon Action :

Its major target is liver: ❖

- Increase Glycogenolysis.
- Increase Gluconeogenesis*.
- Increase Lipid oxidation (fully to CO2 or partially to produce keto acids “ketone bodies”). For use it by brain and peripheral tissue
- Inhibits glycolysis.
- Release of glucose to the blood from liver cells.

*There is no receptor for glucagon in the muscle and a little of receptor in adipose tissue.

Glucagon synthesis :

DNA in α cells (chromosome 2)

↓

mRNA

↓

Preproglucagon

↓

proglucagon

↓

glucagon

Factors Affecting the Metabolism :

Effects on Glucagon Secretion

Stimuli for Glucagon Secretion

↓ Blood glucose
↑ Serum amino acids (arginine, alanine)
Sympathetic nervous system stimulation
Stress
Exercise

Inhibitors of Glucagon Secretion

Somatostatin
Insulin
↑ Blood glucose

* Glucagon stimulate insulin secretion while insulin inhibit glucagon secretion .

Diabetes

What is Diabetes :

Diabetes is probably the most important **metabolic disease**.
It affects every cell in the body and affects carbohydrate, lipid, and protein metabolism.

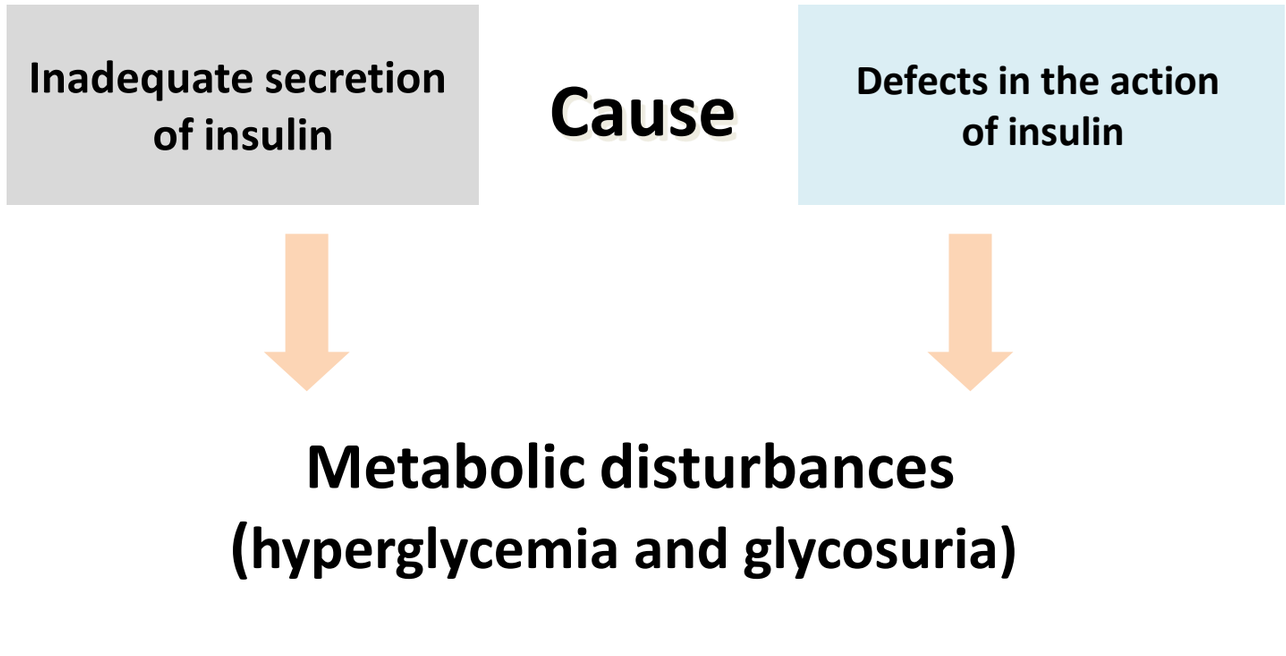
characterized by the polytriad:

Polyuria (excessive urination)
Polydypsia (excessive thirst)
Polyphagia (excessive hunger).

Types of Diabetes :

Type 1 Diabetes
Affects **children**
Cause: inadequate insulin secretion
Treatment : insulin injection

Type 2 Diabetes
Affects **adults**
Cause defect in insulin action
Treatment : diet or OHA



Diabetes Mellitus Type I

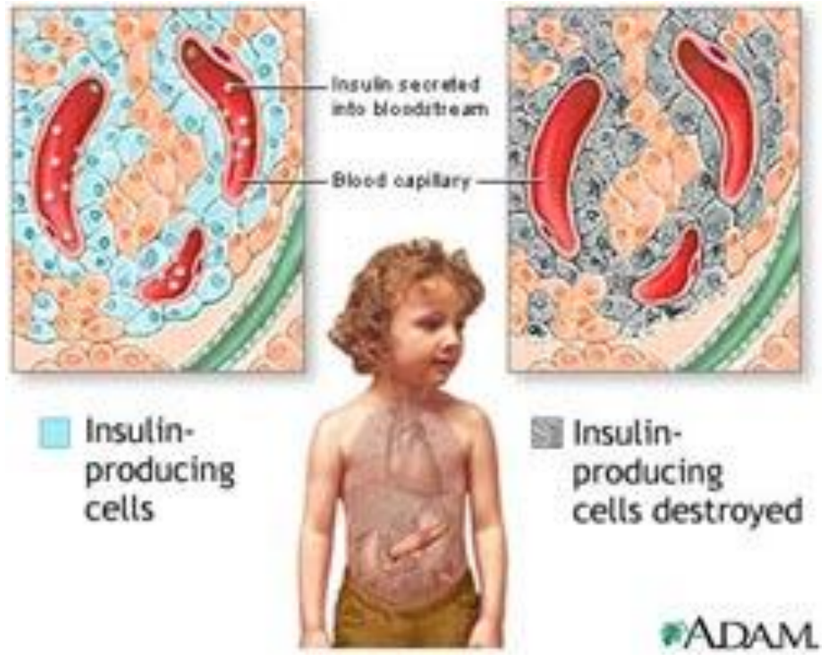
Caused by an **immune-mediated** selective destruction of β cells.

β cells are destroyed while α cells are preserved:

- **No insulin :::: high glucagon <** high production of glucose and ketones by liver.

⬆ Glucose & ketones< osmotic diuresis

⬆ Keto acids < diabetic ketoacidosis



Type 1 Diabetes

Diabetes Mellitus: Type II

relating to a population)) More common in some ethnic groups

Insulin resistance keeps blood glucose too high

.Chronic complications :

1- atherosclerosis (Because of Lipid accumulation)

2- renal failure &

3- blindness Retinopathy is a complication of diabetes that can lead to blindness. It results from damage to the blood vessels in the back of the eye due to prolonged hyperglycemia

4- coma

Glucose Tolerance Test GTT and Fasting plasma glucose (FPG)

Test 1: Fasting plasma glucose (FPG)

The fasting plasma glucose test is the preferred method for diagnosing diabetes in children, men, and nonpregnant women.
The test measures blood glucose levels after an overnight fast (no food intake for at least **eight hours**).

Normal fasting blood glucose level is **less than 100 mg/dL.**
A diagnosis of **diabetes** is made when the fasting blood glucose level **is 126 mg/dL or higher** on at least two tests.
Values of 100–125 mg/dL indicate prediabetes.

For your information
If you have a diabetic patient ask him to do an exercise because the active muscle does not need GLUT4. .

Test 2 : Oral Glucose Tolerance Test OGTT (**IMPORTANT TO UNDERSRAND**)

This test is done when diabetes is suspected, but you have normal results on a fasting plasma glucose test. For the test, you'll have to : 1- fast overnight.(FPG) 2- Then drink a very sweet solution containing 75 g of glucose. 3- A sample of your blood will be drawn **two hours later**.

Normal glucose levels are **less than 140 mg/dL** at two hours.
The criterion for **a diagnosis of diabetes** with this test is a two-hour blood glucose level **of 200 mg/dL or higher.** Prediabetes is diagnosed if the two-hour blood glucose level is 140–199 mg/dL.

For your information
BUT :
During the test you should ask the patient to stay calm and do no exercise to avoid the cells from using the glucose .

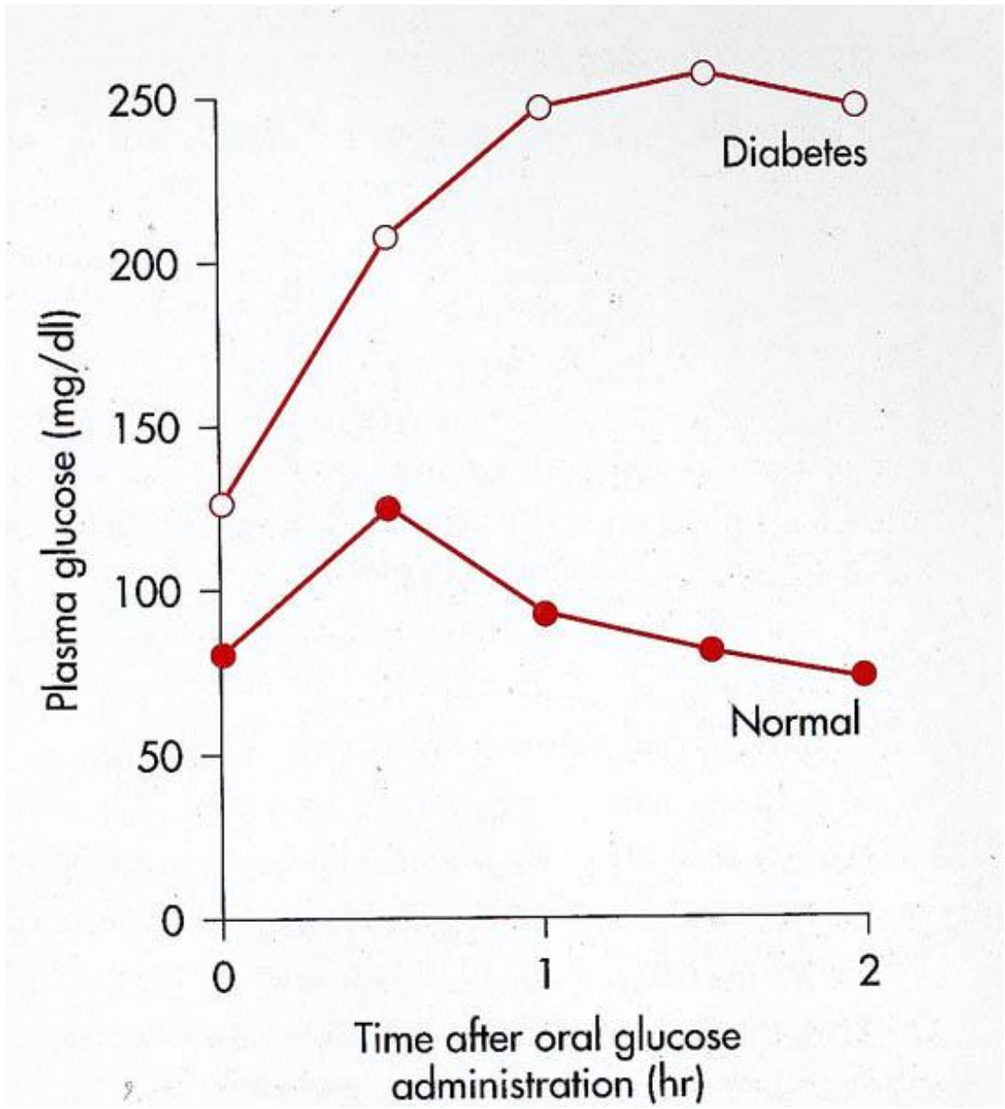
Glucose Tolerance Test GTT and Fasting plasma glucose (FPG)

Glucose Tolerance Test GTT :

Following the oral administration of a standard dose of glucose, the plasma glucose concentration **normally** rises but returns to the fasting level within 2 hours. (in normal people).

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. (the diabetics)

Measurement of urine glucose allows determination of the renal threshold for glucose.



The following results suggest different conditions:

Normal values:

test1 : FPG <100 mg/dl

test2 : 2hr PPG < 140 mg/dL

Impaired glucose tolerance

test 2 : 2hr PPG = 140 - 199 mg/dL

Diabetes

Test 1: FPG ≥ 126 mg/dl

Test2 : 2hr PPG levels ≥ 200 mg/dL

Symptoms of Diabetes Mellitus

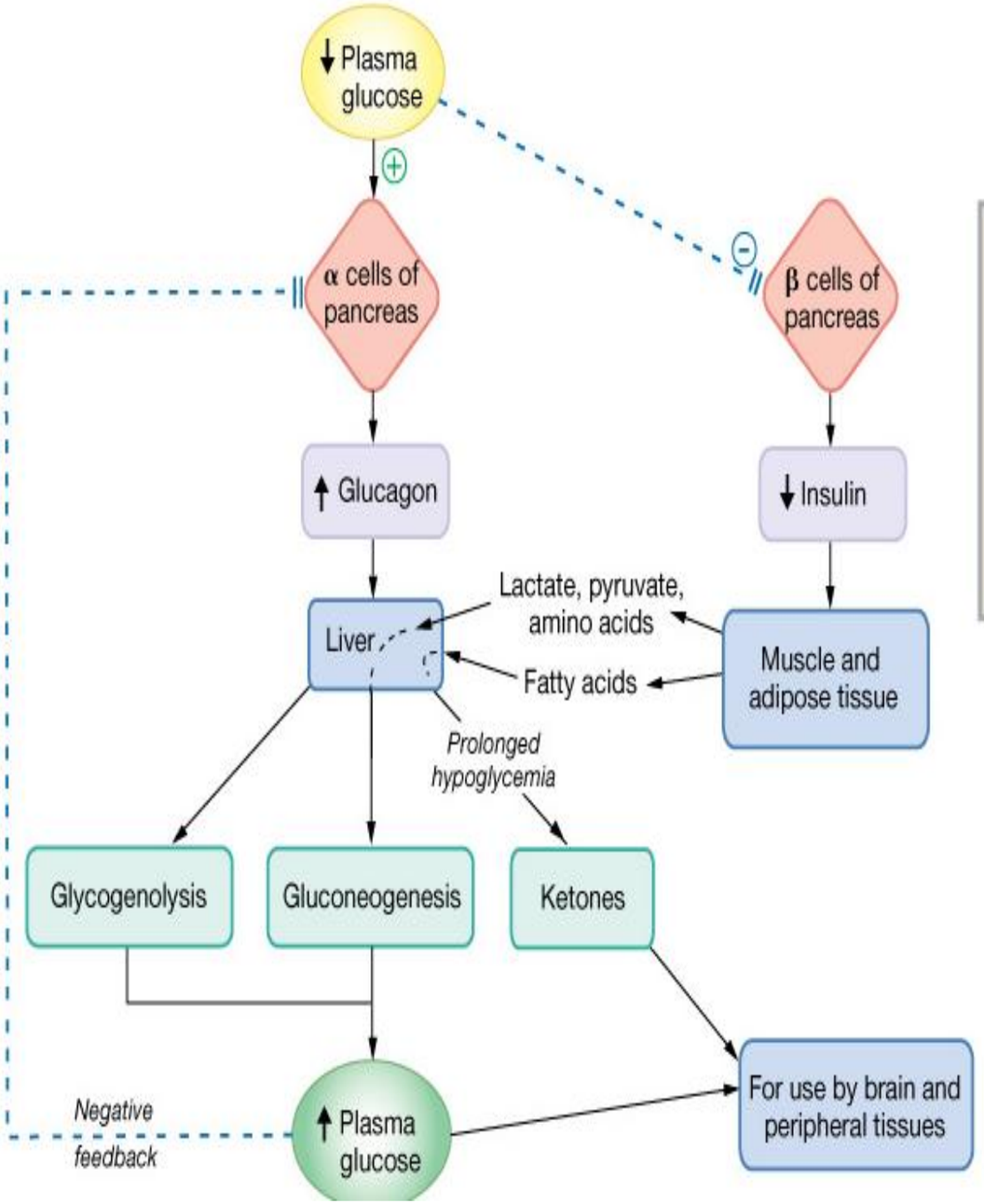
Hyperglycemia
Polyuria
Polydipsia
Polyphagia
Ketoacidosis (IDDM)
Hyperlipidemia
Muscle wasting
Electrolyte depletion

The activity of the satiety مركز الشبع center in the ventromedial nuclei (in hypothalamus) is probably governed by the glucose utilization in the neurons. The entry of glucose is controlled by the **insulin** , when the insulin is low there will be no enough gloucoe and the individual .feels hungry

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

Summery



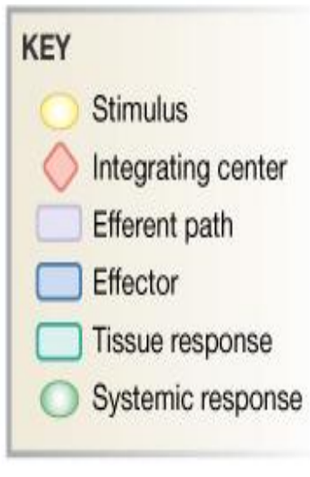


Table 22-5: Glucagon

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

table 7-8 Cell Types of the Islets of Langerhans

Type of Cell	Location	Function
Beta	Central islet	Secrete insulin
Alpha	Outer rim of islet	Secrete glucagon
Delta	Intermixed	Secrete somatostatin and gastrin

B. Glucagon

1. Regulation of glucagon secretion (Table 7-9)

- The major factor that regulates glucagon secretion is the blood glucose concentration. **Decreased blood glucose stimulates glucagon secretion.**

2. Actions of glucagon

- Glucagon acts on the liver and adipose tissue.
- The second messenger for glucagon is **cAMP**.

a. Glucagon increases the blood glucose concentration.

(1) It **increases glycogenolysis** and prevents the recycling of glucose into glycogen.

(2) It **increases gluconeogenesis.** Glucagon decreases the production of fructose 2,6-bisphosphate, decreasing phosphofructokinase activity; in effect, substrate is directed toward glucose formation rather than toward glucose breakdown.

b. Glucagon increases blood fatty acid and ketoacid concentration.

- Glucagon **increases lipolysis.** The inhibition of fatty acid synthesis in effect "shunts" substrates toward gluconeogenesis.
- Ketoacids (β-hydroxybutyrate and acetoacetate) are produced from acetyl coenzyme A (CoA), which results from fatty acid degradation.

c. Glucagon increases urea production.

- Amino acids are used for gluconeogenesis (stimulated by glucagon), and the resulting amino groups are incorporated into urea.

Summery

★ **Glucagon is a hyperglycemic polypeptide hormone**

★ **It Uses cAMP \ Adenylyl cyclase system (second messenger).**

★ **Its major target is the liver**

★ **Diabetes mellitus is a disease caused by deficiency or diminished effectiveness of endogenous insulin.**

- **Type 1 diabetes mellitus: results from the body's failure to produce sufficient insulin.**
- **Type 2 diabetes mellitus: results from resistance to the insulin, often initially with normal or increased levels of circulating insulin.**

★ **pregnant women who have never had diabetes before but who have high blood glucose levels during pregnancy are said to have gestational diabetes. It may precede development of type 2 (or rarely type 1) diabetes.**

★ **Patients with Type 1 DM always need insulin treatment and are prone to ketoacidosis**

MCQs

1) All of the following are true about glucagon action except ?

A) Increase Glycogenolysis

B) Increase Lipid oxidation

C) stimulate glycolysis

D) Increase Gluconeogenesis

2) Glucagon second messenger is ?

A) cGMP

B) Tyrosine kinase

C) cAMP

D) No second messenger

3) A fasting blood glucose test level of _____indicates diabetes.:

A) 50 mg/dl to 69 mg/dl

B) 70 mg/dl to 99 mg/dl

C) 100 mg/dl to 125 mg/dl

D) 126 mg/dl or higher on two separate tests

4)A fasting blood glucose test level of _____indicates prediabetes:

A) 50 mg/dl to 69 mg/dl

B) 70 mg/dl to 99 mg/dl

C) 100 mg/dl to 125 mg/dl

D) 126 mg/dl or higher on two separate tests

5) A fasting blood glucose test level of ____ is considered normal.:

A) 50 mg/dl to 69 mg/dl

B) 70 mg/dl to 99 mg/dl

C) 100 mg/dl to 125 mg/dl

D) 126 mg/dl or higher on

1-C 2-C 3- D 4- C 5- B

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Endocrine Block