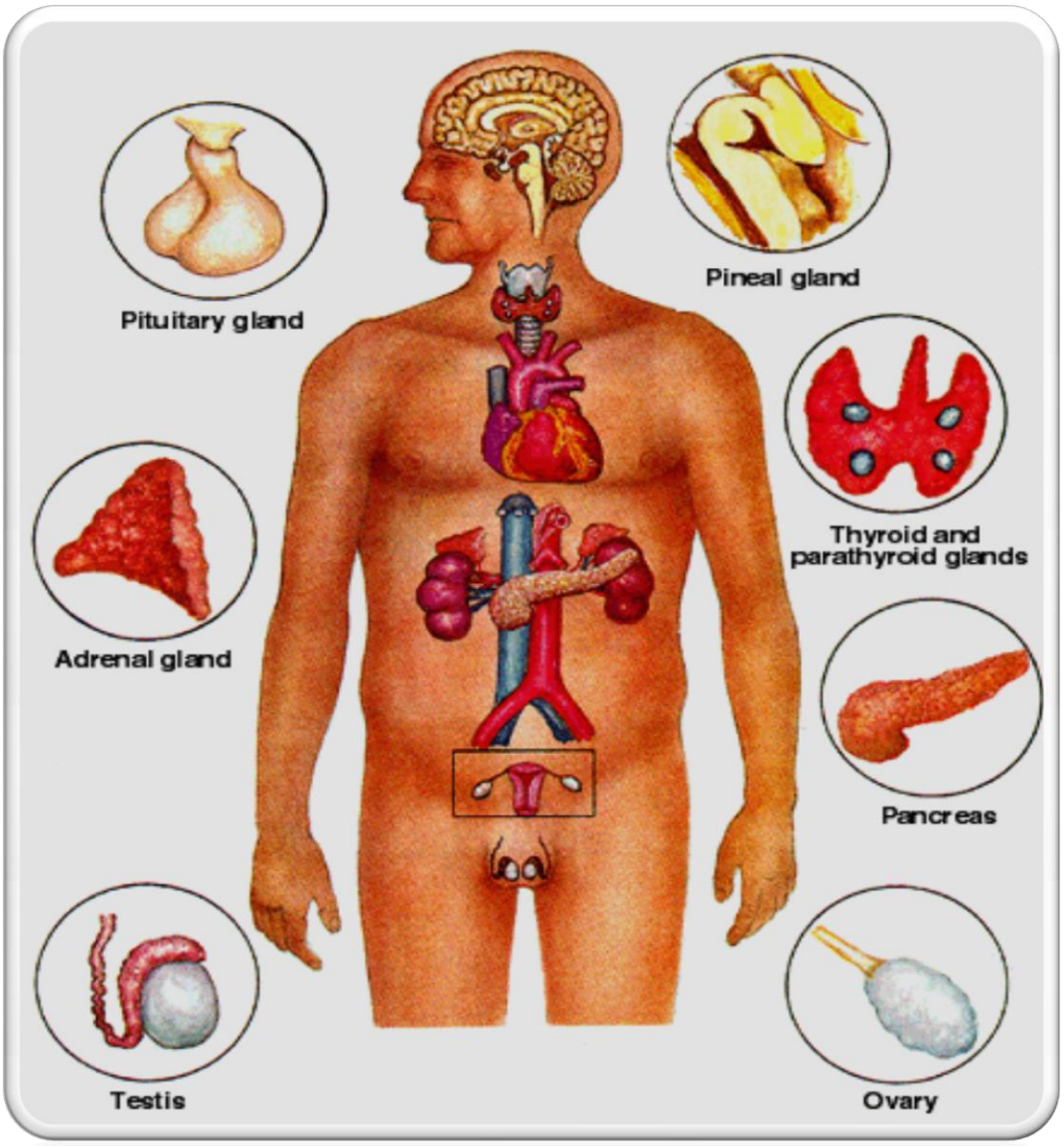
ENDOCRINE BLOCK

PHYSIOLOGY TEAM 431



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Blue : Team notes
Red : Important

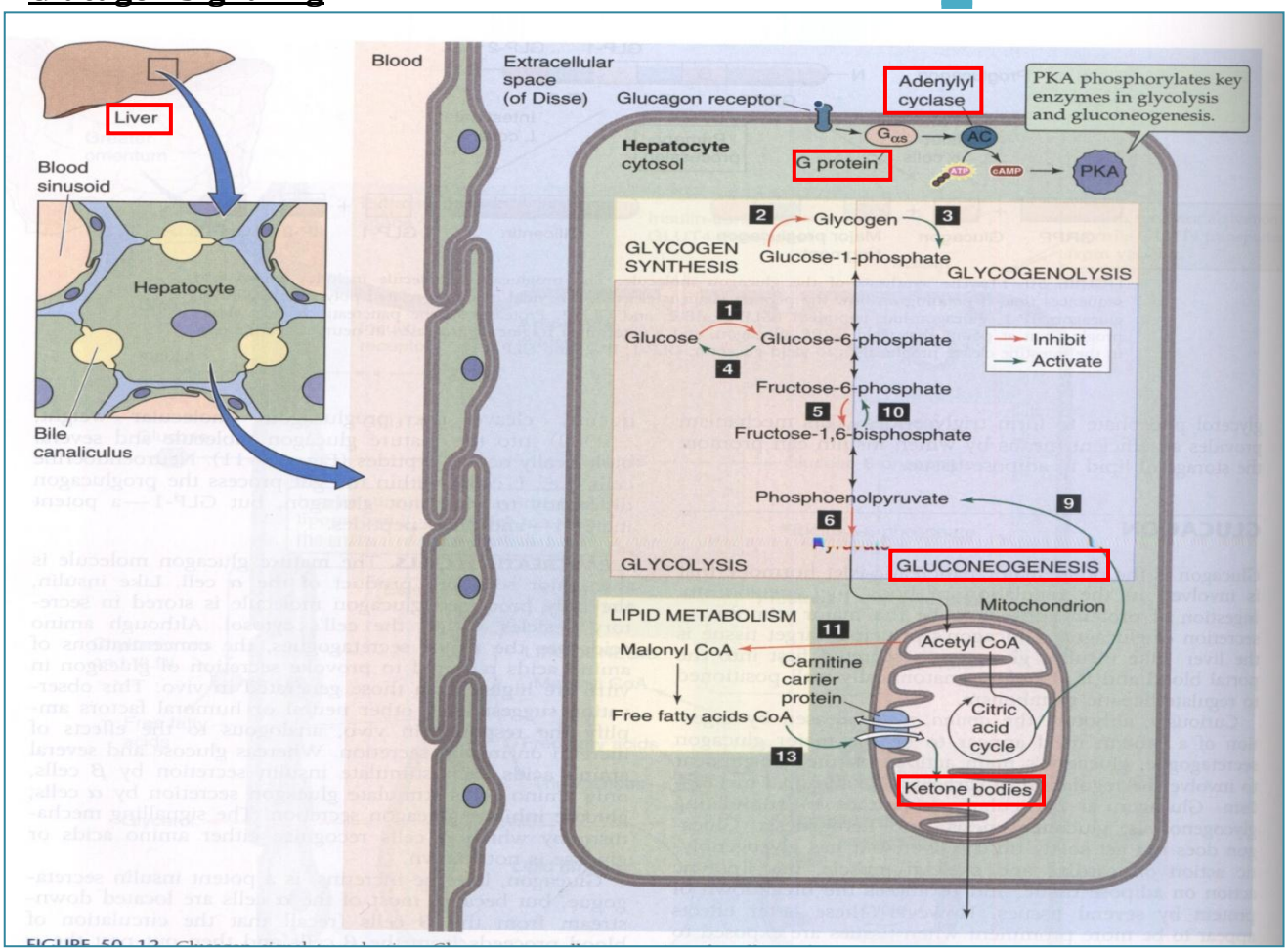
Physiology of Pancreas and Insulin – part II

A. Glucagon

- A 29-amino-acid polypeptide hormone that is a potent hyperglycemic agent
- Produced by α cells in the pancreas

Hypoglycemia → Glucagon→ **liver** (has no action on the muscles) → **G-protein**→Glycogenolysis + Gluconeogenesis + Lipid oxidation (to produce keto acids)+Release of glucose to the blood from liver cells

- **Glucagon Signaling**



- **Synthesis**

- DNA in α cells (chromosome 2) → mRNA → Preproglucagon → proglucagon → glucagon

- **Factors Affecting Glucagon Secretion:**

- **Stimulators:**

✓ ↓ Blood glucose
✓ ↕ Serum amino acids (arginine, alanine) (Amino acids increase **both** insulin and glucagon).
✓ Sympathetic stimulation (Because you need energy).
✓ Stress (Because you need energy).
✓ Exercise (**Exercise** helps in making the insulin-dependent GLUT-4 to be expressed on the cell membranes without the need for the insulin!!).

- **Inhibitors:**

✓ Somatostatin (inhibit **both** insulin and glucagon)
✓ Insulin (glucagon **stimulates** insulin secretion BUT insulin **inhibits** glucagon secretion)
✓ ↑ Blood glucose

- **Glucagon Actions**

- Its major target is liver :

- ✓ Glycogenolysis
- ✓ Gluconeogenesis
- ✓ Lipid oxidation (fully to CO2 or partially to produce keto acids "ketone bodies").
- ✓ Release of glucose to the blood from liver cells

- **Glucagon Action on Cells:**

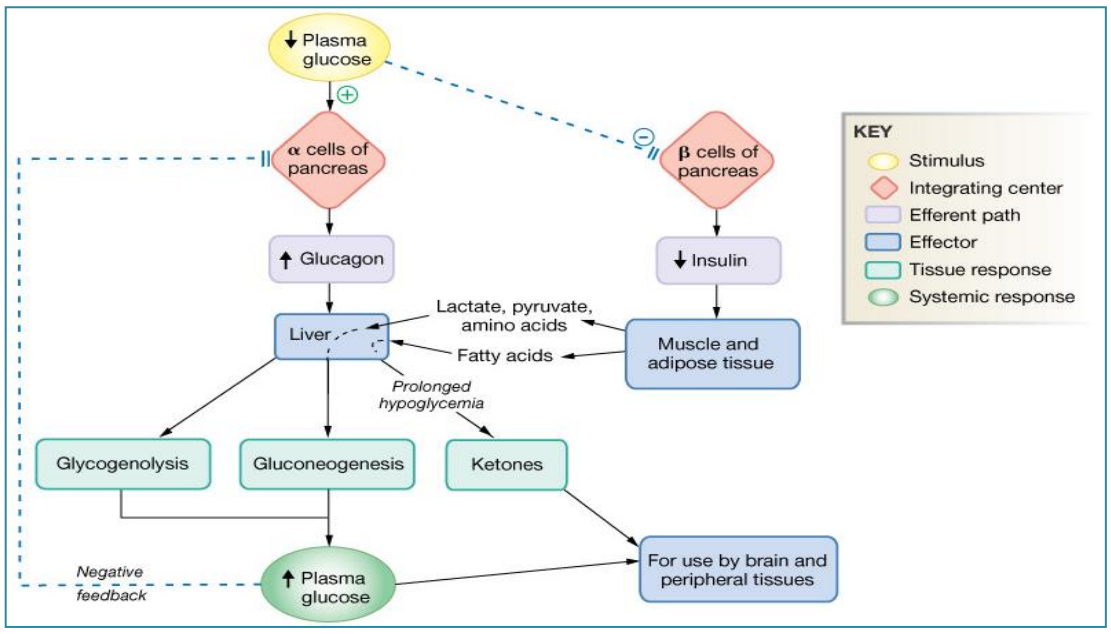
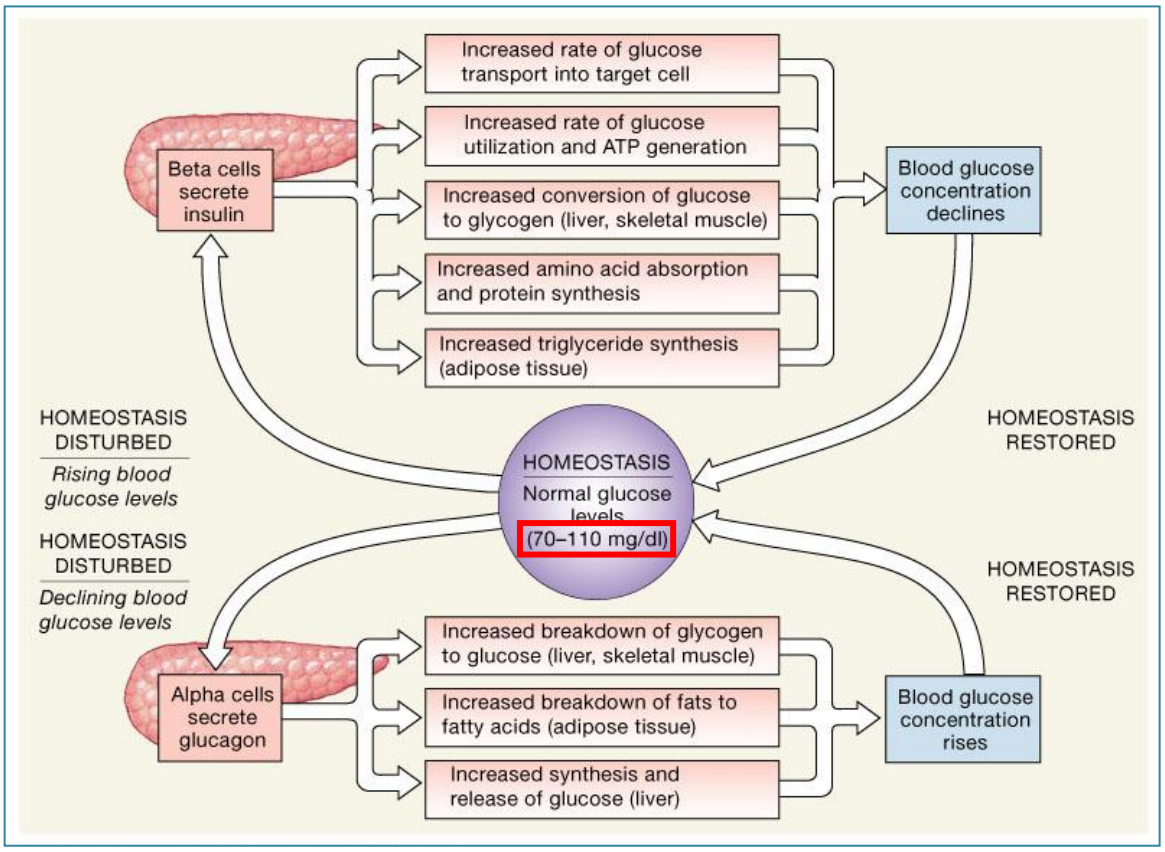


Table 22-5: Glucagon

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

- **<u>The Regulation of Blood Glucose Concentrations</u>:**



B. 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:

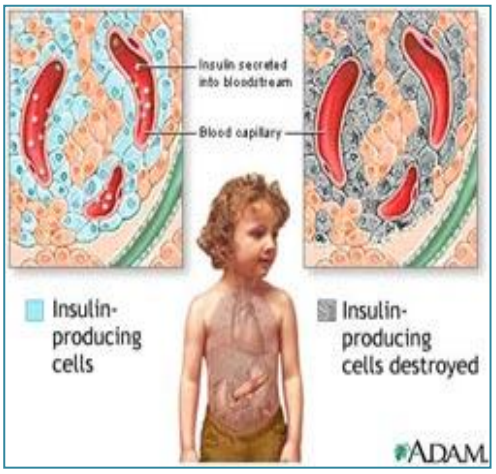
✓ **Polyuria** (excessive urination) (high glucose filtrated →osmotic effect → drag water → osmotic diuresis)

✓ **Polydipsia** (excessive thirst) (1. due to polyuria 2. Cells of the body are dehydrated because; the intracellular water has been dragged extracellularly by osmosis).

✓ **Polyphagia** (excessive hunger) (1. ↓ insulin → activate the **satiety center** <the only center in the brain that is insulin-dependent> , 2.due to glucose loss in the urine → loss of calories).

✓ **Weight loss in type 1** **(due t**o fat li**p**olys**i**s by hormone sensitive lipase).

	Type 1 Diabetes	Type 2 Diabetes
Affects	Children, Usually before 20	Adults, Usually after 30
Cause	inadequate insulin secretion by immune-mediated selective destruction of β cells	defect in insulin action by impaired insulin receptors or second messenger system
Treatment	insulin injection	diet, lifestyle, OHA, or insulin injections
Symptoms	Polyuria - Polydipsia – Polyphagia – Hyperglycemia - Ketoacidosis (IDDM) – Hyperlipidemia - Muscle wasting - Electrolyte depletion - glycosuria	



- **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 (coma)

- **Diabetes Mellitus: Type II :**

- More common in some ethnic groups

- Insulin resistance keeps blood glucose too high

- Chronic complications: atherosclerosis, renal failure & blindness

- (the doctor said "I don't think I will ask about this")

Glucose Tolerance Test: - Fasting blood glucose "or sugar" (FBG)

- Oral glucose tolerance test (OGTT)

- Both are require that the patient fast for at least 8 hours (ideally 12 hr) prior to the test.

- **The oral glucose tolerance test (OGTT):**

- FBG

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

- 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.

- 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.

- **The following results suggest different conditions:**

- **Normal values:**

✓ Fasting <100 mg/dl

✓ 2hr < 140 mg/dL

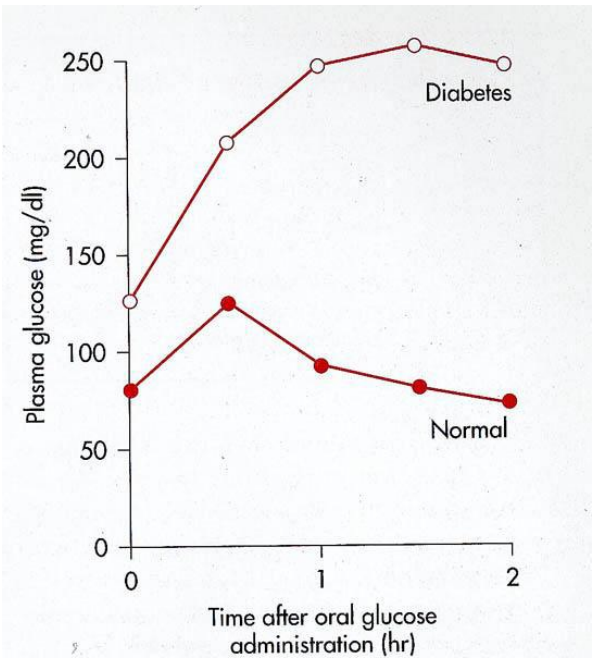
- **Impaired glucose tolerance**

✓ 2hr PPG = 140 - 199 mg/dL

- **Diabetes**

✓ FPG ≥ 126 mg/dl

✓ 2hr PPG levels ≥200 mg/dL



-Diabetes Mellitus (DM)

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 **Polyphagia**
	Protein catabolism and gluconeogenesis			
	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				

Summary

A- Glucagon:

- A 29 amino-acid polypeptide hormone, hyperglycemic agent, produced by α cells of pancreas.
- Synthesis: DNA on chromosome 2 of α cells → mRNA → preproglucagon → proglucagon → glucagon
- Stimuli for glucagon secretion: ↓ blood glucose, ↑ serum amino acid (arginine and alanine), sympathetic, stress, exercise.
- Inhibitors: somatostatin, insulin, ↑ blood glucose.
- Actions (primarily in liver): Glycogenolysis, Gluconeogenesis, Lipid oxidation, and release of glucose to the blood from liver
- Target receptor: G coupled-protein receptor linked to cAMP

B- Diabetes:

- Metabolic disease that affects every cell in the body, and carbohydrate, lipid, and protein metabolism.
- Characterized by: Polyuria, Polyphagia, Polydipsia.
- Types:

	Type 1	Type 2
Affects	Children, usually before 20	Adults, usually after 30
Cause	Inadequate insulin secretion by immune-mediated selective destruction of β cells	defect in insulin action by impaired insulin receptors or second messenger system
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- OGTT: 8hr fasting → FBG → drinking special glucose solution & measuring every 30 min for 2hr.

Questions

Q1- Which one of the following stimulates glucagon secretion:

A) Somatostatin

B) Insulin

C) LOW blood glucose

D) HIGH blood glucose

Q2- Which one of the following is the target receptor for glucagon:

A) G coupled-protein receptor linked to cGMP

B) Tyrosine kinase

C) Intracellular receptor

D) G coupled-protein receptor linked to cAMP

Q3- Which of the following does NOT belong to type 2 diabetes:

A) Caused by defect in insulin action

B) Affects adults

C) Causes diabetic ketoacidosis

D) Managed by changing diet & life style.

Q4- In which situation of OGTT the patient is considered diabetic:

A) FBG < 100 mg/dl

B) FBG 100 – 126 mg/dl

C) 2 hours PPG 140-199 mg/dl

D) 2 hours PPG ≥ 200 mg/dl

Answers; C,D,C,D