The pancreas

Prof. Dr.AZZA SAJID

2nd STAGE

Physiology#II

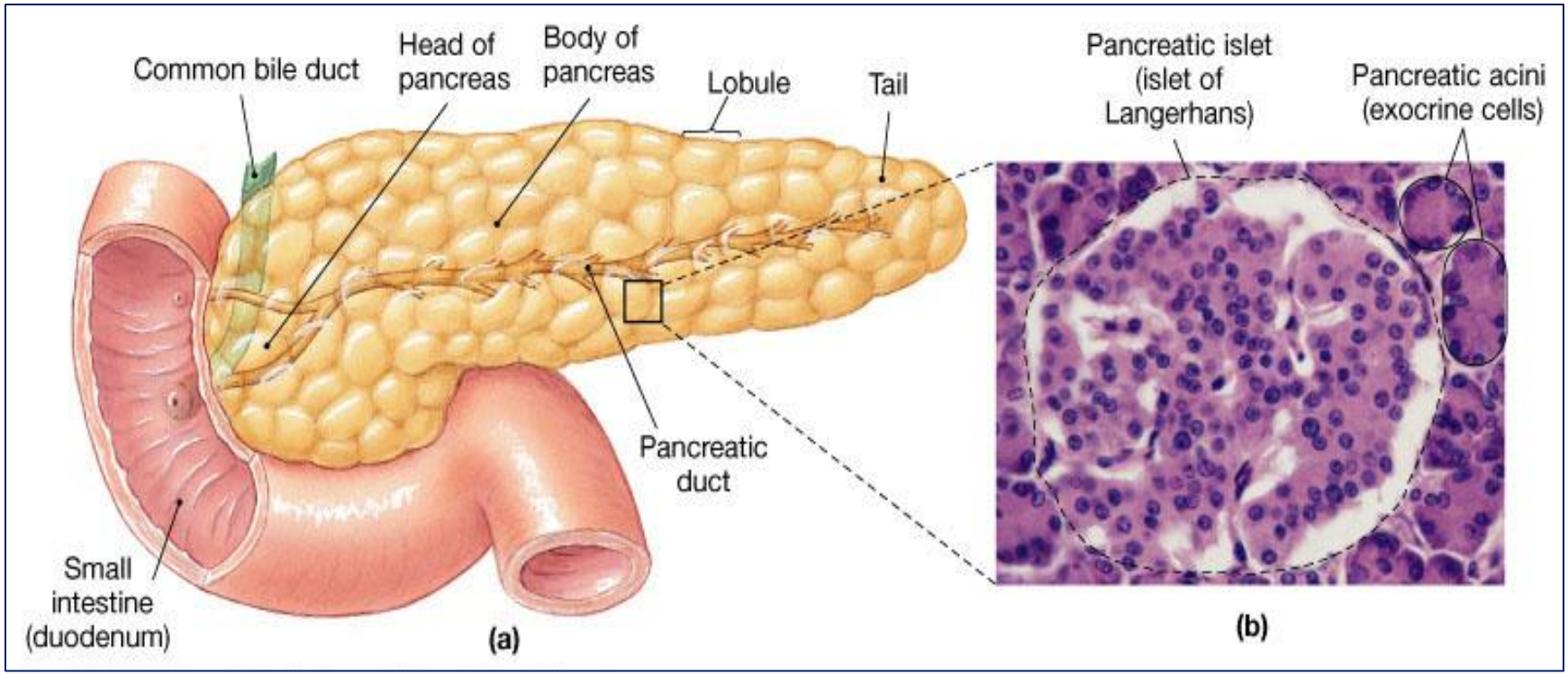
Prof.Dr.Azza Sajid

Pancreas

Overview

- Pancreas is an exocrine and endocrine organ.
- Its function as **exocrine** is the secretion of digestive enzymes and bicarbonates, into the duodenum ,while its function as **endocrine** is to synthesize and release hormones by the cells of the **Islet of Langerhans** into the circulation
- It is located horizontally behind the stomach, upper left abdominal quadrant.
- Humans have roughly **one million islets.**
- The **islets of Langerhans** are clusters of **4 types endocrine cells** these are:
- **β cells**-secrete ***insulin*** and amylin;
- **α cells**- secrete ***glucagon;***
- **δ cells**-secrete ***somatostatin***
- **γ cells**-secrete a ***polypeptide*** of unknown function.
- Nerves from both divisions of autonomic nervous system innervate the pancreatic islets.
- There is well developed capillary network surround each islet.
- Pancreatic hormones play an important role in regulating the concentrations of nutrients in the circulating especially glucose and amino acids.
- Insulin and glucagon maintain blood sugar at level of **100mg/100ml** of blood.

Prof.Dr.Azza Sajid



The pancreas.

Prof.Dr.Azza Sajid

1-Insulin

- Insulin is a rather small protein, with a molecular weight of about 6000 Daltons. It composed of 2 chains held together by disulfide bonds.
- It is continuously produced but production increases when there is **a high blood glucose** ,it thus to decrease blood glucose by :
- Encouraging all cells to take up more glucose out of the blood.
- Insulin molecules binds to **membrane bound receptors** on the target cells (the **GLUT-4** is the major transporter used for uptake of glucose which is made available in the plasma membrane through the action of insulin).Then the receptors cause specific protein in the membrane to become phospherylated, part of the cells response to insulin is to increase number of transport proteins in the membrane of cells for glucose and amino acids .
- Finally insulin and its receptors are taken by **endocytosis.**
- Insulin molecules are released from receptors and broken down within the cell. The receptors can again become associated with plasma membrane.

- Stimulate the **liver** to convert glucose to glycogen.
- Stimulate the **adipose tissues** to convert glucose to fat.
- Acts on **satiety center** of the hypothalamus so that no longer feel hungry to stop eating more sugar

Physiological effects of insulin

Action of insulin on the liver

- ↑ Glucose uptake when glucose level is high
- ↑ Glucose use to:
- ↑ **glycogenesis** and ↓**glycogenolysis**
- ↑ **glycolysis** , ↓**gluconeogenesis**
- ↑ Fatty acid synthesis and very **low density lipoprotein** formation,
- ↓ **ketogenesis**
- ↓ Urea cycle activity.

Action of insulin on the adipose tissues

- ↑ Glucose uptake by ↑**GLUT-4** availability.
- ↑ Glucose use to:
- ↑ Glycolysis.
- ↑ production **of α-glycerol phosphate**
- ↑ Esterification of fats.
- ↓ Lypolysis

Action of insulin on the muscle

- ↑ Glucose uptake by ↑ GLUT-4 availability.
- ↑ Glucose use to:
- ↑ Glycogenesis and ↓ glycogenolysis
- ↑ Glycolysis.
- ↑ amino acid uptake
- ↑ Protein synthesis, ↓ proteolysis.

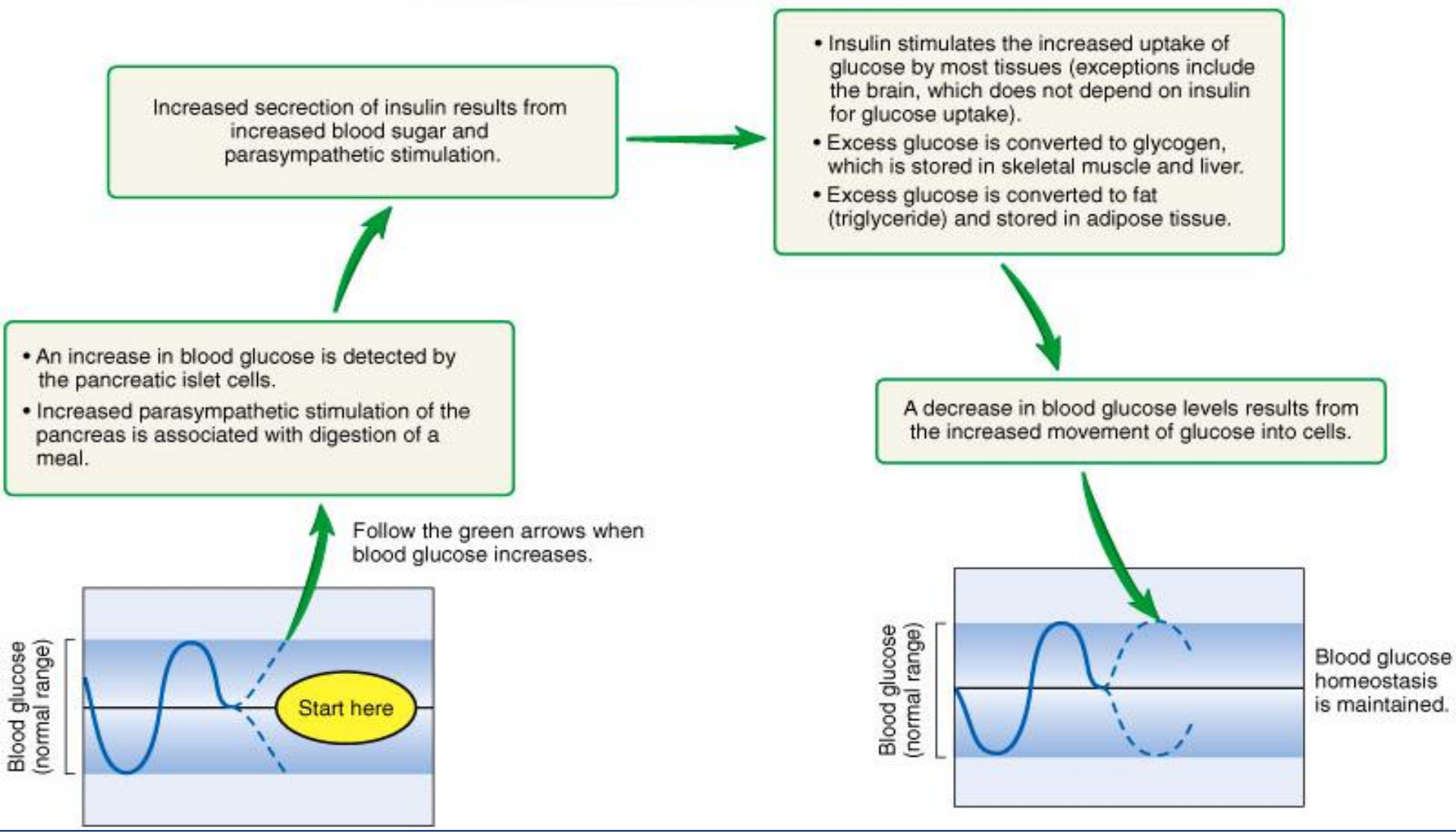
- **Regulation of insulin secretion**

- **The factors that increase insulin secretion are:**
- ↑ Blood glucose
- ↑ Amino acids
- ↑Fatty acids
- Glucagon
- Ach

The factor that decrease insulin secretion are:
- ↓ Blood glucose
- Somatostatin
- Epinephrine and norepinephrine

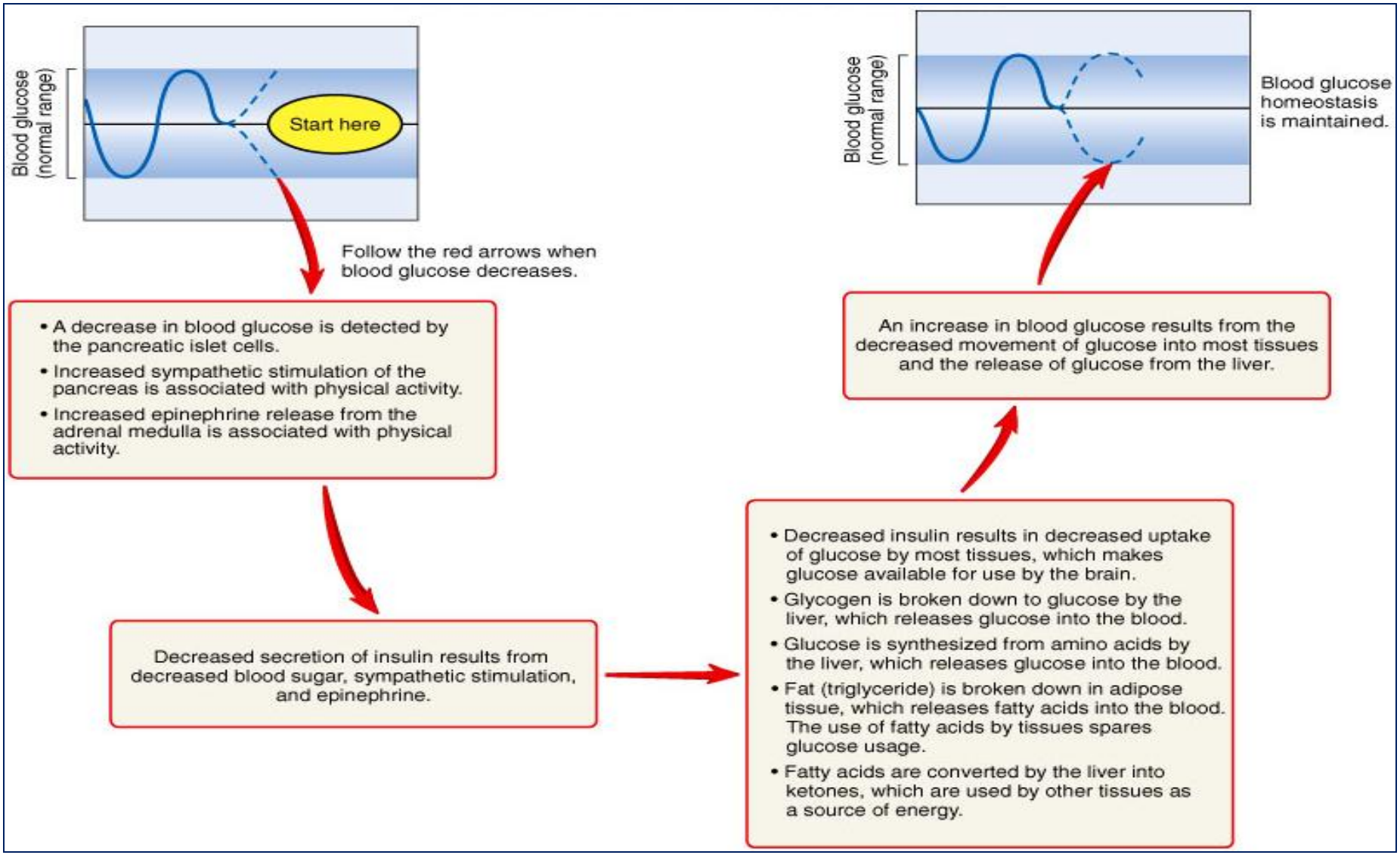
- **Pathophysiology of insulin**
- **In the absence of insulin the following events occur:**
- Movement of glucose and amino acids into the cells decline.
- Satiety center cannot detect the presence of glucose in the extracellular fluid result in intense sensation of hunger inspite of high blood glucose **(polyphagia)**
- These events lead to increase blood glucose level.
- Increase urine volume (**Polyuria)**: [↑ concentrations of glucose enter kidney tubules result in water osmosis and increase amount of water in the urine].
- Increase sensation of thirst **(polydipsia**).
- The patients present initially in **diabetic ketoacidosis (DKA)** (the acidity of some **ketone bodies (aceton)** which formed during the **lipolysis** in adipose tissue which metabolize the fatty acids to **ketone bodies).**

Prof.Dr.Azza Sajid



Blood glucose homeostasis .Events occurring in case of increased blood glucose.

Prof.Dr.Azza Sajid



Blood glucose homeostasis .Events occurring in case of decreased blood glucose.

- **2-Glucagon**
- Glucagon is the primary hormone of the fasting state
- It is a primary regulator of plasma glucose homeostasis.
- Glucagon function is to increase plasma glucose levels, thereby opposing the action of insulin.
- **Regulation of glucagon**
- The primary stimulus for glucagon secretion is amino acids
- Glucagon secretion is also stimulated by low blood glucose levels and inhibited by high levels.

Physiologic effect of glucagon

- In the fasting state glucagon promotes **hepatic glycogenolysis** and **gluconeogenesis.**
- Glucagon stimulates β-oxidation of the fat by the liver which liberates energy that can be used to support **hepatic gluconeogenesis.**
- Glucagon has a minimal metabolic action on the adipose tissues and muscle. These actions include **stimulation of lipolysis** in adipose tissue and **inhibition of glucose utilization** by the peripheral tissues.
-

Prof.Dr.Azza Sajid

3.Somatostatin (SS)

- **SS** is secreted by a broad range of tissues, including pancreas, gastrointestinal tract (GIT) and regions of the central nervous system outside the hypothalamus.
- A majority of the circulating SS appears to come from the pancreas and GI tract.
- It inhibits the secretion of GH.

- **Physiologic Effects of SS**
- SS acts by both **endocrine and paracrine** pathways to affect its target cells.
- It affects the anterior pituitary to decrease GH.
- SS appears to act primarily in a paracrine manner to inhibit the secretion of both insulin and glucagon.
- It also has the effect in suppressing **pancreatic exocrine secretions**, by inhibiting CCK -stimulated enzyme secretion and Secretin stimulated bicarbonate secretion.
- It has an inhibitory effect on the secretion of some GIT hormones such as **gastrin, CCK** and **VIP**
- SS is often referred to as having neuromodulatory activity within the central nervous system, and appears to have a variety of complex effects on neural transmission.
-

- **Clinical note: Diabetes mellitus** is due to insulin problems. There are 2 types: **Type 1: insulin dependent**. This is a genetically controlled (inherited). Auto-immune disease in which the pancreas has insufficient b cells (due to destruction by antibodies) and so produces insufficient insulin. This means that:
- Blood glucose is excessively high and exceeds the kidney threshold resulting in excretion of glucose in the urine.
- Insulin is required for cells to take up glucose, so cell death occurs and the satiety center of the hypothalamus cannot record the blood glucose. The person thus keeps eating sugar, further boosting blood glucose and thus excretion. As cells switch to fat and protein metabolism as an alternative to glucose, the body wastes away. **Treatment** requires insulin injections throughout life.

- **Type 2 : Non-insulin dependent**. Lack of **insulin receptors** on target cells means that although insulin is normal, cells cannot take up glucose and die. This form of diabetes is associated with extreme overweight (and thus prolonged over-consumption of glucose and so prolonged excessive insulin production damaging receptors). In developed countries, it is one of the fastest expanding diseases. It is controlled by dieting.

THANKS