AL-Mustaqbal university
College of Nursing

Pharmacology II

Dr. Ghada Ali
ghada.ali@uomus.edu.iq

lec5

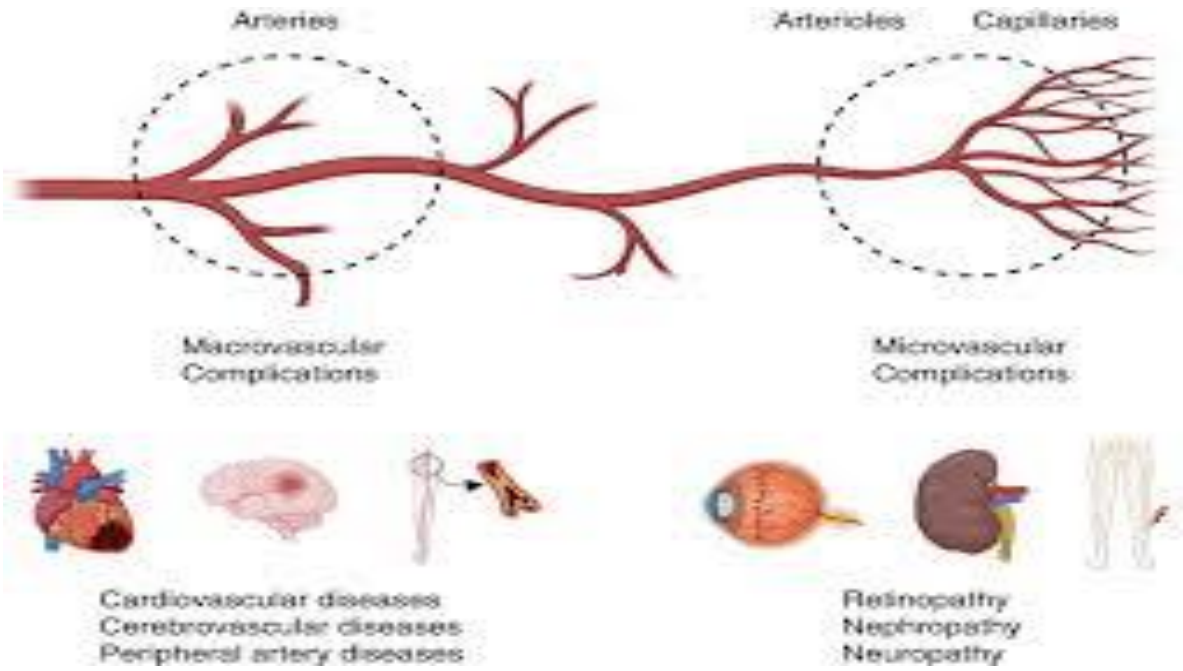
Drugs used for the treatment of Diabetes mellitus.

Metabolic problems occur early in people with diabetes mellitus and are related to ;

- **changes in the metabolism** of carbohydrate, fat, and protein. A major clinical manifestation of disordered metabolism is hyperglycemia, or fasting blood glucose levels exceeding 126 mg/dL. A person with a fasting blood glucose level between 100 and 125 mg/dL is said to have **impaired fasting glucose** (IFG), or prediabetes. Fasting plasma glucose, a 75g glucose tolerance test, and hemoglobin A1C are used to test for prediabetes and type 2 diabetes. Plasma blood glucose is used to diagnose the acute onset of type 1 diabetes in individuals with symptoms of hyperglycemia.

❖ **Vascular problems** include atherosclerosis throughout the body.

- **Macrovascular** (moderate and large vessels) clinical manifestations include hypertension, myocardial infarction, stroke, and peripheral vascular disease.
- **Microvasculature** changes in small blood vessels especially affect the retina and kidney, resulting in retinopathy and chronic kidney disease.



The classifications of diabetes mellitus

type 1 and type 2.

Although both are characterized by hyperglycemia, they differ in

- **onset**,
- **course**,
- **pathology**, and
- **treatment**.

Other types of diabetes may be induced by disease processes such as slowly progressing autoimmune disorders, certain drugs, and pregnancy

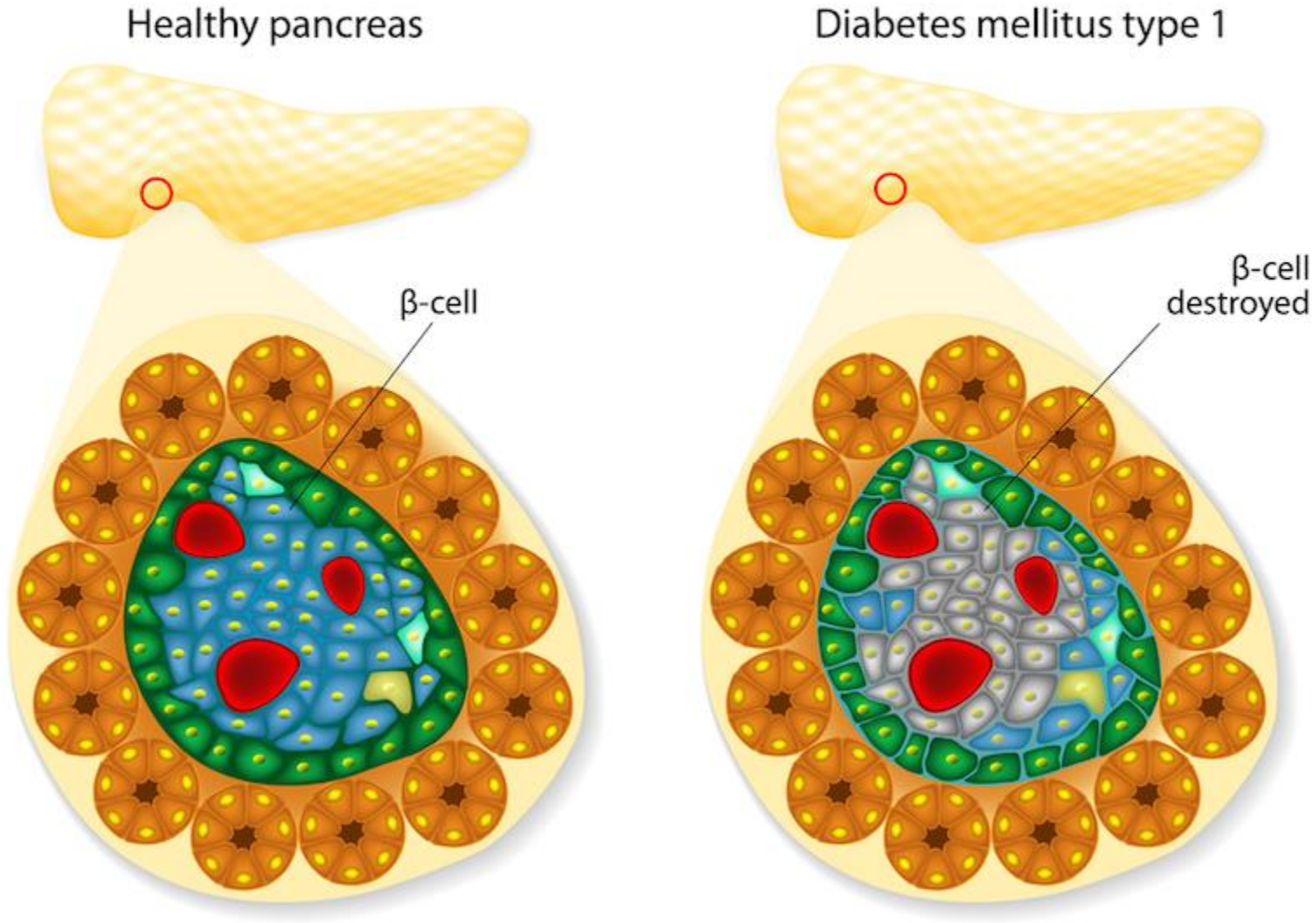
Pathophysiology

Beta cells in the pancreas secrete **insulin**. The average adult pancreas secretes 40 to 60 units of insulin daily. This includes a basal amount of 1 to 2 units/hour and additional amounts (4–6 units/hour) after meals or when the blood glucose level exceeds 100 mg/dL. After a meal, serum insulin levels increase and peak in a few minutes and then decrease to baseline levels in 2 to 3 hours.

Insulin is secreted into the portal circulation and transported to the liver, where about half is used or degraded. The other half reaches the systemic circulation, where it circulates mainly in an unbound form and is transported to body cells (Liver, muscle, and fat cells).

Insulin is cleared from circulating blood in 10 to 15 minutes because of rapid binding to peripheral tissues or metabolic breakdown

ISLETS OF LANGERHANS



Drug Therapy

Medications used in the treatment of diabetes mellitus depend on the type of diabetes and degree of glycemic control. Health care providers use many medications to control diabetes .**Insulin is the prototype** drug for treatment of type 1 diabetes. Several different classes of other drugs are also available for the treatment of type 2 diabetes .

❑ Insulin

Insulin in its various forms is the only effective drug treatment for type 1 diabetes, where pancreatic beta cells are unable to secrete endogenous insulin and metabolism is severely impaired.

❖ Regular insulin

is the prototype(OTC) preparations . Insulin is also necessary in patients with type 2 diabetes who cannot control their disease with diet, weight control, and oral agents.

❖ **Rapid-acting insulins** have a rapid onset (15 minutes or less) and a short duration of action (4–8 hours). Rapid-acting products include

- **insulin lispro**
- **insulin aspart**
- **insulin glulisine**

❖ **Intermediate-acting insulin** preparations such as isophane (NPH) suspension possess zinc insulin crystals that have been modified by protamine in a neural buffer. The addition of zinc assists in slowing the absorption and thus prolongs the duration of action

❖ **Long-acting insulin preparations** include insulin glargine and insulin detemir. Health care providers use them to provide a basal amount of insulin through 24 hours, similar to normal, endogenous insulin secretion.

❑ Sulfonylureas

The sulfonylureas are the oldest and largest group of oral agents used in patients living with type 2 diabetes. The sulfonylureas stimulate insulin secretion in patients who still have some beta cell production in the pancreas. Second generation sulfonylureas have largely replaced first-generation sulfonylureas

Glyburide (Glynase) is the prototype sulfonylurea.

Other drugs include **glimepiride**(Amaryl) and **glipizide**, which resemble glyburide in terms of therapeutic and adverse effects.

Tolazamide and **tolbutamide** are older oral hypoglycemic medications that have been replaced by glyburide, glimepiride, and glipizide.

❑ Biguanide

The prototype **metformin** (Glucophage, Glucophage XR). Experts prefer to call it an antihyperglycemic rather than a hypoglycemic because it does not cause hypoglycemia, even in large doses, when used alone.

Alpha-glucosidase inhibitors

inhibit alpha-glucosidase enzymes (e.g., sucrase, maltase, amylase) in the GI tract, thereby delaying digestion of complex carbohydrates into glucose and other simple sugars.

Acarbose

prototype alpha-glucosidase inhibitor, is known best for improving glycosylated hemoglobin levels. The drug is obtained through the fermentation process of microorganisms. Because acarbose does not enhance insulin, it works best when given with a sulfonylurea to control blood glucose levels

❑ Thiazolidinediones

are sometimes called "**glitazones**" and are also referred to as insulin sensitizers. These drugs decrease insulin resistance, a major factor in the pathophysiology of type 2 diabetes.

Rosiglitazone maleate is the prototype for the thiazolidinediones.

Pioglitazone acts by resensitizing the tissues to insulin. This drug stimulates the insulin receptor sites, lowering blood glucose levels to improve the action of insulin

❑ Meglitinides

are nonsulfonylureas that lower blood sugar by stimulating pancreatic secretion of insulin.

Repaglinide is the prototype meglitinide drug. The ability of repaglinide to work effectively depends on the existence of functioning beta cells left in the pancreas. Administration in combination with metformin or insulin results in a greater reduction in a patient's hemoglobin A1C than when either medication is administered alone

❑ Dipeptidyl peptidase 4 inhibitors

GLP-1 (incretin hormone) has been known for some time to have a hypoglycemic action via its ability to stimulate insulin secretion.

The DPP-4 enzyme inhibitor **sitagliptin** is minimizes the rate of inactivation of the incretin hormones to increase hormone levels and Incretin hormones stimulate insulin release in response to a meal to normalize glucose levels prolong their activity.

❑ Amylin analogs

Some people with type 1 or type 2 diabetes cannot achieve optimal glucose control with insulin therapy alone. **Pramlintide acetate** is a newer drug used as an adjunctive treatment with mealtime insulin that is important in the regulation of glucose control during the postprandial period. A synthetic analog of amylin, pramlintide is a peptide hormone secreted with insulin by the beta cells of the pancreas

❑ Glucagon-like peptide-1receptor agonists (incretin Mimetics)

The glucagon-like peptide-1 receptor agonist is also known as the incretin mimetic **exenatide** a synthetic GLP-1 analog; it is possible to improve glycemic control in patients with type 2 diabetes who are already taking an oral hypoglycemic medication but having difficulty in achieving glycemic control.

❑ Sodium glucose cotransporter 2 (Sglt2) inhibitors

The prototype of this class is **canagliflozin** (Invokana). The drug inhibits renal SGLT2, thus blocking reabsorption of glucose in the kidney. In addition, it promotes the excretion of excess glucose in the urine. All the SGLT2 inhibitors provide renal protection by decreasing the protein loss and reducing the damage caused by hyperfiltration


Thank
you