**Insulin** is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle,, Therefore, deficiency of insulin or the insensitivity of its receptors play a central role in all forms of diabetes mellitus.

The body obtains glucose from three main sources:

1-the intestinal absorption of food from the breakdown of glycogen (glycogenolysis),

2-the storage form of glucose found in the liver;

3- gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body.

Insulin plays a critical role in regulating glucose levels in the body. Insulin can inhibit the breakdown of glycogen or the process of gluconeogenesis, it can stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen.

Insulin is released into the blood by beta cells (β-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body's cells to absorb glucose from the blood for use as **fuel**, for conversion to other needed molecules, or for storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. This process is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin.

**If** the amount of insulin available is insufficient, or if cells respond poorly to the effects of insulin (**insulin resistance**), then glucose is not absorbed properly by the body cells that require it, and is not stored appropriately in the liver and muscles. **The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as metabolic acidosis in cases of complete insulin deficiency.**

When glucose concentration in the blood remains high over time, the kidneys reach a threshold of reabsorption, and the body excretes glucose in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume is replaced osmotically from water in body cells and other body compartments, causing dehydration and increased thirst (polydipsia). In addition, intracellular glucose deficiency stimulates appetite leading to excessive food intake (polyphagia).

**Diabetes mellitus,**commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time.

**Type 1 diabetes** is characterized by loss of the insulin-producing beta cells of the pancreatic islets, leading to insulin deficiency. This type can be further classified as immune-mediated or idiopathic. The majority of type 1 diabetes is of an immune-mediated nature, in which a T cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin. It causes approximately 10% of diabetes mellitus cases. Most affected people are otherwise healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early stages.

Type 1 diabetes is partly inherited, with multiple genes, including certain HLA genotypes.

Type 1 diabetes can occur at any age, and a significant proportion is diagnosed during adulthood.

**Type 2 diabetes** is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. Type 2 diabetes is the most common type of diabetes mellitus. **Many people with type 2 diabetes have evidence of prediabetes (impaired fasting glucose and/or impaired glucose tolerance) before meeting the criteria for type 2 diabetes. The progression of prediabetes to overt type 2 diabetes can be slowed or reversed by lifestyle changes or medications that improve insulin sensitivity or reduce the liver's glucose production.**

Type 2 diabetes is primarily due to lifestyle factors and genetics. A number of lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet, stress, and urbanization.

Dietary factors such as sugar-sweetened drinks are associated with an increased risk. The type of fats in the diet is also important, with saturated fat and trans fats increasing the risk and polyunsaturated and monounsaturated fat decreasing the risk. Eating white rice excessively may increase the risk of diabetes. Lack of physical activity may increase the risk of diabetes in some people.

**Gestational diabetes** resembles type 2 diabetes in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. It occurs in about 2–10% of all pregnancies and may improve or disappear after delivery. It is recommended that all pregnant women get tested starting around 24–28 weeks gestation. It is most often diagnosed in the second or third trimester because of the increase in insulin-antagonist hormone levels that occurs at this time. However, after pregnancy approximately 5–10% of women with gestational diabetes are found to have another form of diabetes, most commonly type 2. Gestational diabetes is fully treatable, but requires careful medical supervision throughout the pregnancy. Management may include dietary changes, blood glucose monitoring, and in some cases, insulin may be required.

Though it may be transient, untreated gestational diabetes can damage the health of the fetus or mother. Risks to the baby include macrosomia (high birth weight), congenital heart and central nervous system abnormalities, and skeletal muscle malformations.

**Diagnosis OF DM**

1. Fasting plasma glucose level ≥ 7.0 mmol/L (126 mg/dL). For this test, blood is taken after a period of fasting, i.e. in the morning before breakfast, after the patient had sufficient time to fast overnight.
2. Random Plasma glucose ≥ 11.1 mmol/L (200 mg/dL) two hours after a 75 gram oral glucose load as in a glucose tolerance test (OGTT)
3. Glycated hemoglobin (HbA1C) ≥ (≥ 6.5 %).

**Impaired Fasting Glucose**

**When FBS= >110 mg/dl – 125 mg/dl, impaired glucose tolerance RBS= 140-180 mg/dl**

**Sign and symptomes**

The classic symptoms of untreated diabetes are unintended weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes.

**Prevention**

There is no known preventive measure for type 1 diabetes.
 Type 2 diabetes—which accounts for 85–90% of all cases worldwide—can often be prevented or delayed by

1. maintaining a normal body weight,
2. engaging in physical activity,
3. eating a healthy diet. include maintaining a diet rich in whole grains and fiber, Limiting sugary beverages and eating less red meat and other sources of saturated fat can also help prevent diabetes.
4. Higher levels of physical activity (more than 90 minutes per day) reduce the risk of diabetes by 28%.
5. Tobacco smoking is also associated with an increased risk of diabetes and its complications, so smoking cessation can be an important preventive measure as well.

**Management**

1. **Lifestyle**

People with diabetes can benefit from education about the disease and treatment, dietary changes, and exercise, .Weight loss can prevent progression from prediabetes to diabetes type 2, decrease the risk of cardiovascular disease, or result in a partial remission in people with diabetes.

1. **Medications**

**Glucose control**

Most medications used to treat diabetes act by lowering blood sugar levels through different mechanisms. keeping the glucose levels within normal ranges decrease complications, such as kidney problems or eye problems.

Type 1 diabetes requires treatment with insulin, long-acting insulin for the basal rate and short-acting insulin with meals.

 Type 2 diabetes is generally treated with medication that is taken by mouth (e.g. metformin) although some eventually require injectable treatment with insulin or GLP-1 agonists.

Metformin is generally recommended as a first-line treatment for type 2 diabetes, as there is good evidence that it decreases mortality. It works by decreasing the liver's production of glucose. Several other groups of drugs, mostly given by mouth, may also decrease blood sugar in type 2 diabetes. These include agents that

1. increase insulin release (sulfonylureas) daonil ,
2. agents that inhibit the enzyme dipeptidyl peptidase-4 (DPP-4) that inactivates incretins such as GLP-1 and GIP (sitagliptin),
3. agents that make the body more sensitive to insulin (thiazolidinedione)
4. agents that increase the excretion of glucose in the urine (SGLT2 inhibitors).

When insulin is used in type 2 diabetes, a long-acting formulation is usually added initially, while continuing oral medications. Doses of insulin are then increased until glucose targets are reached

**Complication**

The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves.

1. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and eventual blindness. Diabetes also increases the risk of having glaucoma, cataracts, and other eye problems. It is recommended that people with diabetes visit an eye doctor once a year.
2. Damage to the kidneys, known as diabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplantation.
3. Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes. The symptoms can include numbness, tingling, altered pain sensation, which can lead to damage to the skin.
4. Diabetes-related foot problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation.
5. proximal diabetic neuropathy causes painful muscle atrophy and weakness.

**Diabetic Emergencies**

1. Diabetic Ketoacidosis (DKA),(usually in type I DM) a metabolic disturbance characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness. DKA requires emergency treatment in hospital.
2. hyperosmolar hyperglycemic state (HHS), ( in type 2 diabetes ) is mainly the result of dehydration caused by high blood sugars.
3. Hypoglycemia is common in people with type 1 and also type 2 diabetes depending on the medication being used. Effects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious effects such as confusion, changes in behavior such as aggressiveness, seizures, unconsciousness, and rarely permanent brain damage or death in severe cases. Mild to moderate cases are self-treated by eating or drinking something high in rapidly absorbed carbohydrates. Severe cases can lead to unconsciousness and must be treated with intravenous glucose or injections with glucagon.