

Insulin: Comprehensive Review on its Crucial Role in Metabolism and Disease Management

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Abstract

Insulin's pivotal function lies in meticulously regulating blood sugar levels, thus guaranteeing cells access to the necessary energy for optimal functionality. When there is a rise in blood sugar, after a meal, the released insulin gets released from the pancreas to facilitate the uptake of glucose by cells. Insulin primarily acts on muscle, fat, and liver cells, promoting the uptake of glucose from the blood. Another way to store glucose for later use is as glycogen, which produces energy. Additionally, insulin also a vital role in suppressing the breakdown of stored glycogen and promoting the synthesis of proteins and fats. Glucagon, another hormone produced by the pancreas, works in opposition to insulin. Between the meals or when fasting the blood sugar levels are low. Hence the glucagon signals the liver to release stored glucose, to help maintain the normal blood glucose level. In diabetes mellitus, the body's ability to produce or respond to insulin is impaired, leading to chronically elevated blood sugar levels. This may be harmful to the blood vessels, nerves, and organs, among other things. Insulin therapy is a mainstay of diabetes management, mainly in type 1 diabetes. It may also be used in type 2 diabetes when other treatments are not sufficient to control blood sugar levels. Based on their start, peak, and duration of action, many insulins are available for therapeutic use. These consist of insulins that act quickly, briefly, moderately, and slowly. Some newer formulations, such as insulin analogs, offer more predictable blood sugar control and fewer side effects compared to traditional insulin. In recent years, advancements in insulin delivery systems, such as insulin pumps and continuous glucose monitors, have also improved the management of diabetes by providing more precise dosing and real-time monitoring of blood sugar levels.

Keywords: Type 1 DM, Type 2 DM, Insulin, Blood glucose or sugar, Pancreas, Beta cells

INTRODUCTION

Because it facilitates the uptake of glucose into cells, insulin is an essential hormone for controlling blood sugar levels. The pancreatic islets of Langerhans' beta cells are responsible for producing it.

A disulfide link connects two polypeptide chains that make up the structure of the insulin protein. These chains consist of 51 amino acids in total, forming a specific sequence that determines its biological activity and function. With a molecular weight of approximately 5808 Daltons (Da), insulin's relatively small size allows it to circulate in the bloodstream efficiently and interact with its receptors on target cells [1].

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Dysfunction or imbalance in insulin production can lead to metabolic disorders such as diabetes mellitus, underscoring the significance of this hormone in overall health and wellness.

Insulin Secretion

Understanding the physiology of insulin-producing cells is crucial for comprehending how

insulin secretion is regulated. Insulin, a peptide hormone, is primarily secreted by beta (β) cells located within the pancreatic islets. These islets, numbering around one to two million in the human pancreas, house various endocrine cells responsible for producing hormones essential for regulating blood sugar levels. In addition to insulin-secreting beta cells, pancreatic islets also contain alpha (α) cells, which produce glucagon, and delta (δ) cells, which secrete somatostatin. These hormones collectively play key roles in maintaining glucose homeostasis in the body.

Insulin secretion is regulated, primarily due to changes in blood glucose levels. After ingesting glucose, a process known as glucose-induced insulin stimulation occurs. This process involves the uptake of glucose into beta cells, where it undergoes intracellular metabolic processes, ultimately leading to the secretion of insulin into the bloodstream. The digestive tract releases incretin hormones when food is eaten, including glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). These hormones are important in stimulating the release of insulin that is triggered by nutrients. GLP-1 and GIP enhance insulin secretion from beta cells, contributing to the overall regulation of blood sugar levels [1–2]. Overall, the complex interplay between pancreatic beta cells, incretin hormones, and glucose metabolism is essential for maintaining glucose homeostasis. Understanding these physiological mechanisms provides insights into the regulation of insulin secretion shown in Figure 1 the development of therapeutic strategies for managing conditions such as diabetes mellitus.

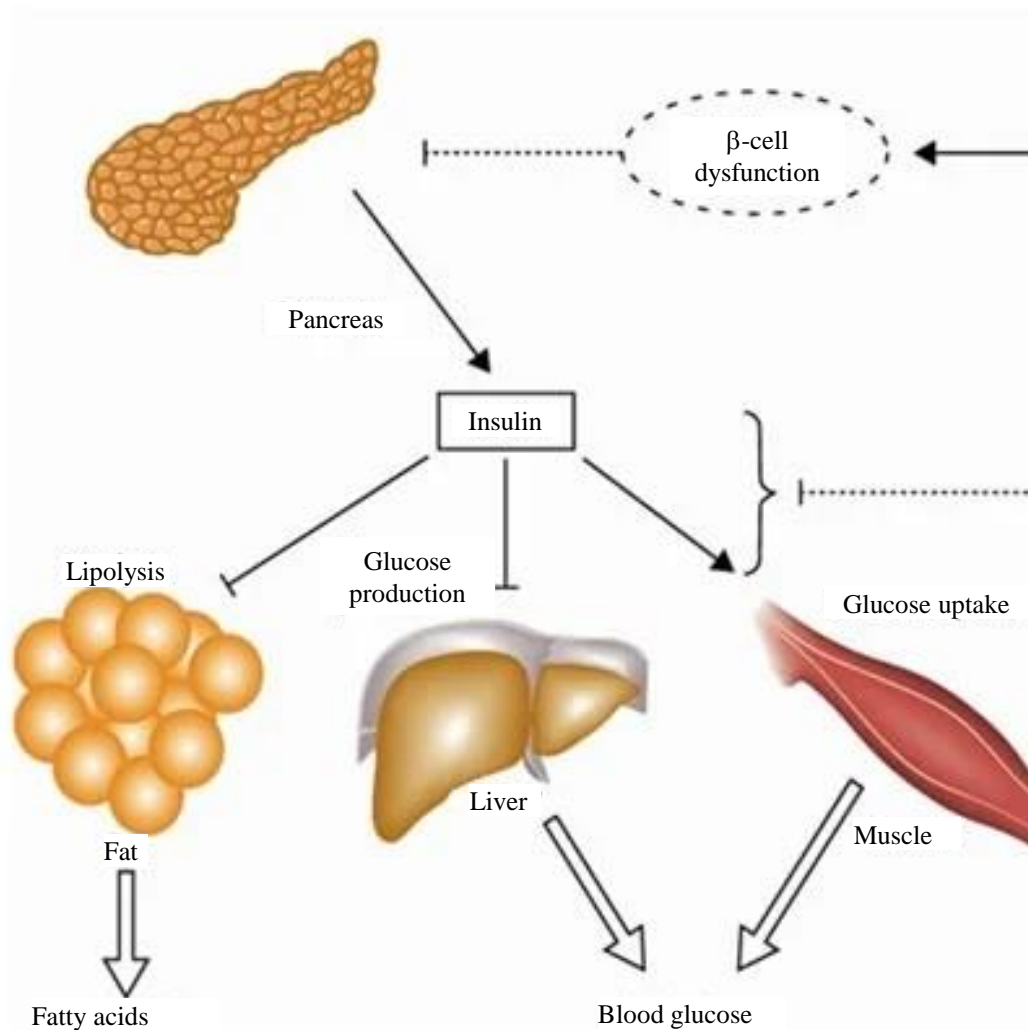


Figure 1. Secretion of Insulin.

Insulin Resistance

Cells within the body lose their sensitivity to the effects of insulin, a condition known as insulin resistance. Several factors, such as an individual's genetic makeup and lifestyle, may contribute to this. Insulin resistance has a high correlation with obesity, especially extra abdominal fat. Adipose tissue, especially the belly fat around the abdomen, interferes with insulin action, contributing to insulin resistance. A sedentary lifestyle exacerbates insulin resistance, whereas physical activities help cells become more sensitive to insulin's effects, and improve glucose uptake.

Dietary habits, especially consuming a diet high in carbohydrates and sugars, can also promote insulin resistance. Excessive intake of refined carbohydrates leads to rapid spikes in blood sugar levels, placing increased demand on the body's insulin production and contributing to insulin resistance over time. Rarely, when insulin resistance appears during pregnancy, gestational diabetes may result. Insulin resistance has been connected to several diseases and conditions. Heart disease, for example, is closely linked to insulin resistance due to its role in promoting inflammation and atherosclerosis. In liver disease such as nonalcoholic fatty liver disease (NAFLD) condition characterized by insulin resistance, which causes fats to accumulate in the liver. Polycystic ovary syndrome (PCOS), a hormonal disorder common in women of reproductive age, is also associated with insulin resistance, contributing to symptoms such as irregular menstruation and infertility.

A balanced diet low in refined carbs, frequent exercise, and weight loss are all part of managing insulin resistance. Medications may also be prescribed to improve insulin sensitivity and control blood sugar levels, particularly in individuals with diabetes or related conditions [3–4]

The Role of Insulin

The main role of insulin is to ensure that glucose from food is properly utilized or stored in the body.

1. *Control of Blood Glucose Levels:* Insulin permits glucose to enter cells, especially those in the liver, muscle, and adipose tissues, which in turn regulates blood glucose levels. Following a meal, the liver and muscles store the glucose as glycogen, which lowers blood glucose levels.
2. *Promotion of Cellular Glucose Uptake:* Insulin facilitates the transport of glucose across cell membranes, allowing cells to utilize glucose as a primary source of energy for various metabolic processes, including ATP production.
3. *Inhibition of Glucose Production:* Insulin suppresses glucose production in the liver by inhibiting gluconeogenesis and glycogenolysis, processes by which the liver produces glucose from non-carbohydrate sources and releases stored glucose into the bloodstream [5].

Overall, insulin acts as a master regulator of metabolism, orchestrating the utilization, storage, and production of glucose, lipids, and proteins to maintain energy balance and support cellular function. Dysregulation of insulin signaling can lead to metabolic disorders such as diabetes mellitus, highlighting the critical importance of insulin in maintaining overall health and well-being.

Diabetes Mellitus

A chronic metabolic disease called diabetes mellitus is typified by high blood glucose levels. This elevation in blood glucose, also known as hyperglycemia, can result from various factors, including insufficient insulin production, resistance to insulin action, or both. Insufficient insulin synthesis characterizes type 1 diabetes mellitus, but diminished insulin sensitivity in cells characterizes type 2 diabetes shown in Table 1. The chronic elevation of blood glucose in diabetes mellitus can largely affect various organs and systems in the body, leading to long-term complications such as cardiovascular disease, neuropathy, nephropathy, retinopathy, and impaired wound healing. Therefore, effective management of diabetes mellitus is crucial. Diabetes affects an estimated 422 million individuals globally, the majority of whom reside in low- and middle-income nations. Each year, the illness is directly to blame for 1.5 million deaths [6].

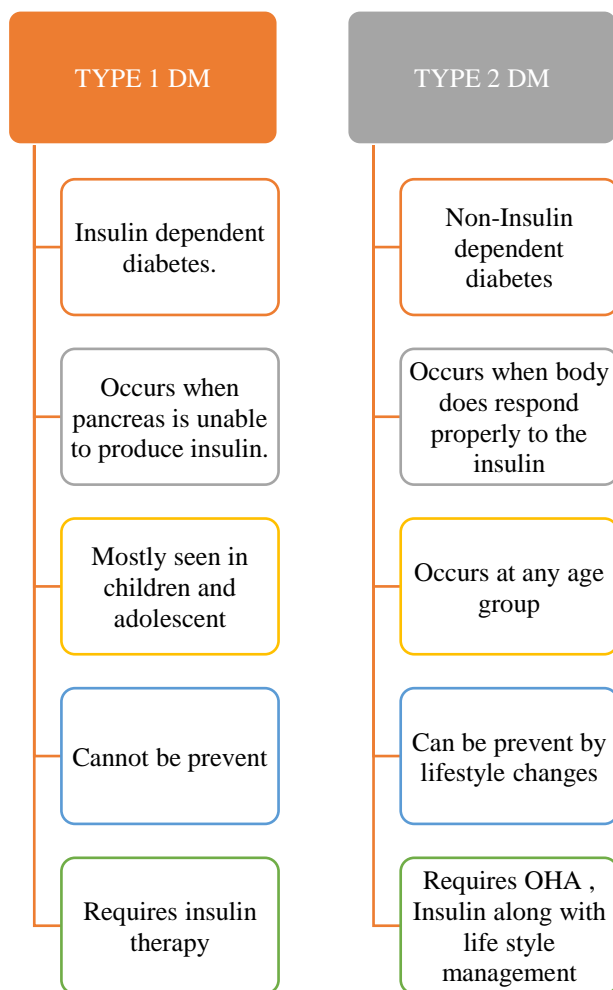


Table 1. Types of Diabetes mellitus:

TYPES OF INSULIN & HOW THEY WORK

A thorough summary of the several kinds of insulin that are available for controlling blood sugar levels is given in this breakdown. For each type, let’s review the salient features: 1,3)

Rapid-Acting Insulin

- Starts working between 2.5 to 20 minutes after injection, with effects lasting up to 5 hours.
- Best taken just before or after meals to manage postprandial glucose spikes.
- Examples include Fiasp, NovoRapid® (insulin aspart), Humalog® (insulin lispro), and Apidra® (insulin glulisine).

Short-acting Insulin

- Takes about 30 minutes to start working, with effects lasting 6 to 8 hours.
- Typically injected 30 minutes before meals.
- Examples include Actrapid® and Humulin® R.

Intermediate-acting Insulin

- Begins working about 60 to 90 minutes after injection, peaking between 4 to 12 hours, and lasting up to 24 hours.

- Cloudy in appearance and needs to be mixed well before administration.
- Examples include Humulin® NPH and Protaphane®.

Long-acting insulin

- - Provides a slow, steady release of insulin without a distinct peak action.
- - Lasts up to 24 hours, allowing for once-daily dosing.
- - Examples include Lantus® (glargine insulin), Toujeo (glargine insulin), and Levemir® (detemir insulin).

Mixed Insulin

- Contains a combination of either rapid-acting, short-acting, or long-acting insulin with intermediate-acting insulin.
- Provides both rapid-acting coverage for mealtime and longer-acting coverage between meals.
- Examples include NovoMix® 30, Humalog® Mix 25, Humalog® Mix 50, Ryzodeg 70:30, Mixtard® 30/70, Mixtard® 50/50, and Humulin® 30/70.

This classification allows healthcare providers to tailor insulin regimens to individual needs, considering factors such as mealtime flexibility, glycemic control, and lifestyle preferences.

WAYS TO TAKE INSULIN

The comparison between insulin delivery methods is quite comprehensive. Let's outline the advantages and disadvantages of each [5–10]:

Insulin Pens

Advantages

- Requires less training than an insulin pump.
- Often more cost-effective compared to pumps.
- Portable and easy to use.
- Needles are small, thin, and more comfortable.

Disadvantages

- Less discreet than syringes.
- Not all types of insulin are compatible with pens.
- May be more expensive than syringes, potentially not covered by insurance.

Tip: Rotate injection sites to avoid lumps or fatty deposits.

Insulin Pump

Advantages

- Shown to improve A1C levels.
- Offers precise insulin delivery.
- Facilitates bolus insulin administration.
- Eliminates unpredictability of intermediate- or long-acting insulin.
- Provides flexibility with meals, exercise, and daily schedule.
- Can improve overall well-being.

Disadvantages

- May lead to weight gain.
- Can be costly.
- Risk of infection.

- Risk of diabetic ketoacidosis if malfunction occurs.
- Constant reminder of diabetes.
- Requires training.

Inhaler

Advantages

- Non-invasive delivery method.
- Acts quickly and as effectively as injectable rapid-acting insulins.
- Can be taken at the start of meals.
- May reduce risk of hypoglycemia.
- Potential for less weight gain.
- Compact device.

Disadvantages:

- May cause coughing.
- Potentially more expensive.
- Requires injections or pump for basal insulin.
- Less precise dosing.

Artificial Pancreas

Advantages

- Mimics natural insulin regulation.
- Continuous glucose monitoring for real-time data.
- Precise insulin adjustment.
- Helps maintain target blood glucose levels.

Hence, insulin sensitivity and resistance help individuals make informed decisions about their insulin management therapy, considering factors such as effectiveness, and cost. Storage and safety practice of Insulin shown in Figure 2 [11].



Figure 2. Storage and safety practice.

CONCLUSION

In conclusion, insulin is a vital hormone for maintaining the blood glucose levels in individuals. Insulin therapy thus becomes a cornerstone in the treatment of people with metabolic disorders or severe diseases. One of the main characteristics of diabetes mellitus, a chronic metabolic disease, is elevated blood glucose levels. Whether in type 1 diabetes, where insulin production is deficient, or in type 2 diabetes, where there is insulin resistance, the administration of insulin plays a critical role in controlling blood sugar levels and preventing long-term complications. Advancements in insulin formulations and delivery methods, from rapid-acting to long-acting insulin analogs, along with innovations such as insulin pens and pumps, have enhanced the effectiveness and convenience of insulin therapy. These developments offer individuals with diabetes greater flexibility, precision, and ease of use in managing their condition. Insulin therapy represents remarkable effectiveness with low mortality rate and early disease management while increasing an individual's life span along with modern medicine. As research continues and technology advances, the future holds promise for further improvements in insulin therapy, ultimately contributing to better outcomes and quality of life for individuals affected by diabetes mellitus.

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