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New Trends in Diabetic Treatment: Advances in Insulin Therapy A Comprehensive Review.

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ABSTRACT

Diabetes mellitus, derived from Greek and Latin roots meaning "sweet urine," is a chronic metabolic condition characterized by elevated blood sugar levels caused by problems with insulin secretion, action, or both.New diabetes treatment trends include drug improvements, continuous glucose monitoring, and individualized methods, all with the goal of increasing glycemic control, lowering complications, and improving patient well-being. Anti-diabetic medications are also known as antihyperglycemic agents. They treat diabetes by reducing blood glucose levels. Type 1 diabetes, type 2 diabetes, gestational diabetes.Type 4 diabetes and type 5 diabetes are among the latest diabetes trends. Insulin therapy has advanced to include ultra-long-acting insulins, smart insulin pens and pumps, closed-loop insulin administration (artificial pancreas), and inhalable insulin updates.

DIABETES MELLITUS

New diabetes treatment trends include drug improvements, continuous glucose monitoring, and individualized methods, all with the goal of increasing glycemic control, lowering complications, and improving patient well-being.

Diabetes mellitus, derived from Greek and Latin roots meaning "sweet urine," is a chronic metabolic condition characterized by elevated blood sugar levels caused by problems with insulin secretion, action, or both.

Diabetes is a disease that requires lifelong treatment. It is one of the world's most serious diseases and the third largest cause of mortality in the United States, following heart disease and cancer.'Diabetes mellitus' implies 'excessive discharge of sweet urine'. Hyperglycemia occurs when insulin is either insufficiently produced or fails to stimulate its target cells.

Anti-diabetic medications are also known as antihyperglycemic agents. They treat diabetes by reducing blood glucose levels. Except for insulin, the majority of anti-diabetic medications are delivered orally. There are various types of anti-diabetic medicines, and their selection is determined by the type of diabetes, the patient's age and circumstances, and a variety of other criteria. Treatments include medications that enhance the quantity of insulin secreted by the pancreas or the sensitivity of target organs to insulin, as well as agents that reduce the rate at which glucose is absorbed from the gastrointestinal tract. Diabetes affects people of all ages. Most forms of diabetes are chronic (lifelong), and all forms are manageable with medications and/or lifestyle changes. Glucose (sugar) mainly comes from carbohydrates in your food and drinks, causing hyperglycemia.

TYPES OF DIABETES:

Two major types of diabetes mellitus are:

- Type 1 diabetes
- Type 2 diabetes
- Gestational diabetes
- New trends in diabetes
  - Type 4 diabetes
  - Type 5 diabetes

TYPE 4 DIABETES

• The phrase "Type 4 diabetes" refers to insulin resistance in older persons who are not obese or overweight.

• While not officially recognized as a kind of diabetes, there is considerable research in this area.

• Type 4 diabetes is not an autoimmune condition like type 1 or linked to weight like type 2 diabetes.

• However, it is linked to the aging process.

Causes:

Researchers are still learning about the causes of type 4 diabetes, so there is limited information available.

Symptoms:

Type 4 diabetes exhibits many of the same symptoms as other kinds of diabetes. Doctors may not suspect diabetes because it typically affects people of moderate weight. Common symptoms include:

• Fatigue • Increased thirst • Increased appetite.

Symptoms may include blurred vision, persistent sores, frequent urination, and unexpected weight loss.

Treatment:

Type 4 diabetes isn't officially a diagnosis yet. Many things about this condition, including treatment, are still being studied

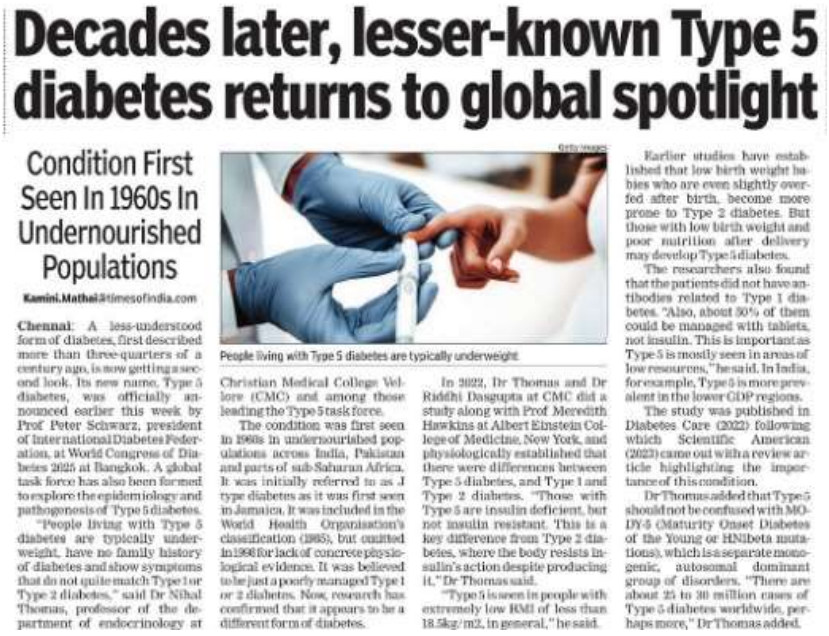
TYPE 5 DIABETES (malnutrition-related diabetes)

• It is a distinct form of diabetes primarily caused by chronic undernutrition, especially during childhood or adolescence.

• Formal classification and global recognition as Type 5 diabetes occurred in January 2025, during an international meeting in India. This classification was subsequently endorsed at the International Diabetes Federation (IDF) World Diabetes Congress 2025, held in Bangkok, Thailand, from April 7-10.

• It affects lean, malnourished teenagers and young adults, particularly in low- and middle-income countries.

• Type 5 is characterized by a severely low insulin secretion due to malnutrition-induced damage to pancreatic beta cells.



Decades later, lesser-known Type 5 diabetes returns to global spotlight

Condition First Seen In 1960s In Undernourished Populations

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Chennai: A less-understood form of diabetes, first described more than three-quarters of a century ago, is now getting a second look. Its new name, Type 5 diabetes, was officially announced earlier this week by Prof Peter Schwarz, president of International Diabetes Federation, at World Congress of Diabetes 2025 at Bangkok. A global task force has also been formed to explore the epidemiology and pathogenesis of Type 5 diabetes.

"People living with Type 5 diabetes are typically underweight, have no family history of diabetes and show symptoms that do not quite match Type 1 or Type 2 diabetes," said Dr Nihal Thomas, professor of the department of endocrinology at Christian Medical College Vellore (CMC) and among those leading the Type 5 task force.

People living with Type 5 diabetes are typically underweight

The condition was first seen in 1960s in undernourished populations across India, Pakistan and parts of sub-Saharan Africa. It was initially referred to as J type diabetes as it was first seen in Jamaica. It was included in the World Health Organisation's classification (1985), but omitted in 1998 for lack of concrete physiological evidence. It was believed to be just a poorly managed Type 1 or 2 diabetes. Now, research has confirmed that it appears to be a different form of diabetes.

In 2022, Dr Thomas and Dr Riddhi Dasgupta at CMC did a study along with Prof Meredith Hawkins at Albert Einstein College of Medicine, New York, and physiologically established that there were differences between Type 5 diabetes, and Type 1 and Type 2 diabetes. "Those with Type 5 are insulin deficient, but not insulin resistant. This is a key difference from Type 2 diabetes, where the body resists insulin's action despite producing it," Dr Thomas said.

"Type 5 is seen in people with extremely low BMI of less than 18.5kg/m2, in general," he said.

Earlier studies have established that low birth weight babies who are even slightly overfed after birth, become more prone to Type 2 diabetes. But those with low birth weight and poor nutrition after delivery may develop Type 5 diabetes.

The researchers also found that the patients did not have antibodies related to Type 1 diabetes. "Also, about 50% of them could be managed with tablets, not insulin. This is important as Type 5 is mostly seen in areas of low resources," he said. In India, for example, Type 5 is more prevalent in the lower GDP regions.

The study was published in Diabetes Care (2022) following which Scientific American (2023) came out with a review article highlighting the importance of this condition.

Dr Thomas added that Type 5 should not be confused with MODY-5 (Maturity Onset Diabetes of the Young or HNFbeta mutations), which is a separate monogenic, autosomal dominant group of disorders. "There are about 25 to 30 million cases of Type 5 diabetes worldwide, perhaps more," Dr Thomas added.

CREDIT: Times Of India

Poorer countries have a higher prevalence of type 5 diabetes, which has been linked to malnutrition throughout childhood. It affects between 20 and 25 million people worldwide.

Cause:

Chronic undernutrition, especially during early development.

Symptoms

Include extreme weariness, weight loss, and frequent infections.

Treatment

Focuses on nutritional deficits, which may include oral medicines or insulin injections.

ADVANCES IN INSULIN THERAPY

- **Ultra-long-acting insulins:**

Ultra-long-acting insulins are intended to give diabetics with a continuous, low-level basal insulin infusion for 24 hours or more, with some extending to 42 hours. These insulins help to control blood sugar levels by mimicking the body's natural basal insulin release, minimizing the need for frequent injections. Ultra-long-acting insulins, such as insulin glargine U-300 and degludec, have long-lasting glucose-lowering effects, generally lasting more than 24 hours, making them suitable for basal insulin therapy in both Type 1 and Type 2 diabetes. These insulins can be given once a day and have a more constant basal insulin level than traditional long-acting insulins, potentially lowering the risk of hypoglycemia, particularly nocturnal hypoglycemia.

There are 3 different types of long-acting insulin: insulin detemir (Levemir) insulin glargine (Abasaglar, Lantus, Semglee and Toujeo) insulin degludec (Tresiba).

How it Works: Ultra-long-acting insulins are administered once a day (or weekly in newer varieties) and gradually release insulin into the bloodstream over 24 to 42 hours. They produce persistent insulin depots beneath the skin, which eventually dissolve, resulting in a consistent, peakless insulin level. This replicates the body's natural basal insulin and helps maintain constant blood glucose levels while lowering the risk of hypoglycemia.

- **Smart insulin pens and pumps**

With the introduction of the first commercially available smart insulin pens, the most common insulin administration device for millions of diabetics has entered the digital age. Smart insulin pens (SIPs) have the potential to transform a diabetic care ecosystem by connecting patients, clinicians, and health systems. Existing SIPs have been upgraded with real-time wireless communication, digital dose capture, and integration with tailored dosing decision support. SIPs play an important role in updating diabetes care for a large number of persons with diabetes.

Smart insulin pens and pumps are advanced diabetes care devices that use digital technology to improve insulin delivery and surveillance. Smart pens provide features such as dose tracking, dose recommendations, and missed dose alarms, whereas smart pumps dispense insulin continuously based on glucose levels, typically with automatic changes. Both types of devices connect to smartphone apps, which allow users to monitor data, change settings, and share information with healthcare providers.

Smart Insulin Pens – How it Works:

The user manually selects and injects the insulin dose with the smart pen. The pen records the dosing amount and timing before sending the information to a mobile app via Bluetooth. The app offers dosage reminders, insulin tracking, and occasionally bolus calculation assistance. Although dosing is not automated, it allows consumers to make more informed insulin decisions.

Insulin Pumps – How it Works:

The pump constantly provides basal insulin and lets the user to administer bolus doses before meals. In more modern systems, the pump may connect to a continuous glucose monitor (CGM) and utilize an algorithm to automatically alter insulin delivery based on actual glucose levels. This decreases the need for physical intervention while also improving glucose control.

- **Closed-loop insulin delivery (artificial pancreas):**

A closed-loop insulin delivery system, often known as an artificial pancreas, is a technological innovation in diabetes care that seeks to automate insulin delivery based on real-time glucose levels. It connects a continuous glucose monitor (CGM) and an insulin pump via a control algorithm to alter insulin delivery and maintain target glucose levels.

A closed-loop system consists of the following components:

• The Continuous Glucose Monitor (CGM) measures glucose levels in the interstitial fluid (fluid between cells) and transmits data to the control algorithm.
• The insulin pump follows an algorithm to deliver insulin into the body.

• Control Algorithm: A computer program analyzes glucose readings from the CGM and calculates insulin dosage for the pump.

How it Works:

The CGM continuously checks glucose levels and transmits this data to the control algorithm. The algorithm then determines the quantity of insulin required to maintain the specified glucose range and directs the insulin pump to deliver the correct dose. This process is automated, so the user does not need to enter any information manually.

❖ **Inhalable insulin updates:**

Afrezza, an inhalable insulin, recently got regulatory approval in India for exclusive distribution and marketing by Cipla. This is an important milestone because Afrezza is the first ultra-rapid-acting inhaled insulin available in India, providing a needle-free option for diabetes control. A phase 3 clinical research in India found that Afrezza, when used with oral antidiabetic medicines, significantly reduced HbA1c levels.

How it Works:

Inhalable insulin, such as Afrezza, provides rapid-acting insulin in the form of a fine powder that users inhale using a small handheld inhaler. When breathed, insulin particles quickly absorb across the lung's enormous surface area into the bloodstream, resulting in a faster onset—usually within 12-15 minutes—than administered rapid-acting insulin. This helps to prevent blood sugar rises during meals. The inhaler allows for accurate dosing and is often used in conjunction with basal insulin injections. Recent improvements have centered on enhancing device usability, dosage accuracy, and broadening treatment options for type 2 and type 1 diabetes.

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