

Glossary of Terms

Alpha cell: Cells found in the pancreas that secrete glucagon. In patients with type 2 diabetes, alpha cells often secrete too much glucagon.

Amylin: A peptide hormone secreted by beta cells in the pancreas at the same time as insulin.

Antibodies: Proteins that the body produces to protect itself from foreign substances, such as bacteria or viruses.

Beta cell: The insulin and amylin producing cells in the pancreas. These cells fail as type 2 diabetes progresses.

Diabetes: A disease that occurs when the body cannot utilize the glucose (sugar) in the blood for energy because either the pancreas cannot make enough insulin or the insulin that is available is not effective. There are three primary types of diabetes: type 1 diabetes, type 2 diabetes, and gestational diabetes.

Dipeptidyl peptidase-IV (DPP-4): A naturally occurring enzyme that inactivates GLP-1 among many other peptides.

DPP-4 inhibitor: A medication that blocks the breakdown of GLP-1, thus increasing the concentration of native GLP-1 and lowering glucose.¹

Exendin-4: A hormone derived from the saliva of a Gila monster, a large lizard that lives in the desert areas of the southwestern United States and Mexico. Exendin-4, like human GLP-1, enhances the body's ability to secrete insulin only in response to elevated levels of glucose. However, unlike GLP-1, exendin-4 lasts much longer in the circulation because it is not metabolized as quickly; therefore, extending the glucose-regulating effects.

Fasting plasma glucose: A measurement of the concentration of glucose in the plasma after the patient has not eaten for at least eight hours.

First-phase insulin response: After eating, insulin is secreted by the beta cells in two phases, an early (first phase) and late phase. First phase occurs within minutes after eating, whereas late phase occurs hours after eating. Deterioration of the first phase is the earliest abnormality of insulin secretion in type 2 diabetes.

Glucagon: A hormone produced by the alpha cells in the pancreas that signals the liver to release stored sugar into the bloodstream. Glucagon is often overproduced in patients with type 2 diabetes, especially at mealtime.

Glucagon-like peptide-1 (GLP-1): A human incretin hormone that, in response to food intake, exerts multiple effects to mediate the body's ability to self-regulate blood glucose. The effects include enhancing glucose-dependent insulin secretion, suppressing glucagon secretion, reducing food intake, regulating gastric emptying and stimulating beta-cell proliferation and neogenesis (animal models).

Glucagon-like peptide-1 (GLP-1) receptor agonist: An agent that binds to and activates the human GLP-1 receptor, which leads to acutely enhanced beta cell function, improving glucose control and satiety.

Glucagon: A hormone produced in the pancreas that signals the liver to release stored sugar into the bloodstream. Glucagon is often overproduced in patients with type 2 diabetes, especially at mealtime.

Glucose: A simple sugar found in the blood that is the body's main source of energy.

Glucose-dependent insulin secretion: Insulin is secreted by the beta cell in response to many different stimuli, including glucose. The magnitude of the insulin response is therefore dependent on the circulating level of glucose (i.e., insulin secretion is greater with high blood glucose levels, whereas insulin secretion is very reduced with low blood glucose levels).

Glucose homeostasis: To balance the rate of glucose appearance in the circulation with the rate of glucose disappearance, thus maintaining a steady but not excessive supply of glucose in the blood stream.

Hemoglobin A_{1C} (HbA_{1C}; often referred to as A1C): A reflection of a person's average glucose level over approximately three months. It is often used by doctors as a measure of blood glucose management. The American Diabetes Association recommends a target A1C of less than 7 percent.²

Hypoglycemia: A condition of low blood sugar that usually occurs when there is too much insulin and not enough glucose in the body. It may cause dizziness, sweating, pale skin color, sudden moodiness, clumsy movements, seizure, difficulty paying attention or tingling sensations around the mouth. If left untreated, hypoglycemia can result in a coma and/or death.

Incretin: A hormone released by the gut in response to food that helps to regulate glucose levels in the body. GLP-1 is an example of an incretin hormone.

Incretin mimetic: A class of agents that mimics several of the actions of incretin hormones in the gut, such as glucagon-like peptide. GLP-1 receptor agonists are agents in this class.

Insulin: A hormone produced by beta cells in the pancreas that help regulate glucose levels in the body. Patients with diabetes can take various types of insulin to help regulate glucose levels.

L-cell: A type of cell found in the gut that is responsible for the secretion of GLP-1.

Metformin: An oral medication in the biguanide class of drugs, which lower blood glucose levels primarily by decreasing the amount of glucose produced by the liver. Metformin also

helps to lower blood glucose levels by making muscle tissue more sensitive to insulin so glucose can be absorbed.^{3,4}

Peptide hormones: A class of hormones that are secreted into the bloodstream and help regulate metabolism, amongst other functions.

Postprandial glucose: Measure of glucose after a meal.

Sulfonylurea (SFU): An oral medication that stimulates the beta cells of the pancreas to release more insulin in a non-glucose dependent manner.⁴

Self-regulating glycemc control: Improvement in glycemc control in patients with type 2 diabetes resulting from the combination of increased beta-cell response (enhanced glucose-dependent insulin secretion and restored first-phase insulin response) and decreased beta-cell workload (suppression of glucagon secretion, slowing of accelerated gastric emptying, and reduction of food intake).

Thiazolidineadione (TZD): An oral medication for type 2 diabetes that helps lower blood glucose by making cells more sensitive to insulin.⁵

Type 2 diabetes: Previously called non-insulin-dependent and/or adult-onset diabetes mellitus, type 2 diabetes is the most common form of diabetes and accounts for approximately 90 to 95 percent of all diabetes patients in the United States. People with type 2 diabetes can produce insulin, but either the pancreas does not make enough insulin or the body cannot use the insulin properly.⁶

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References:

1. White JR. Dipeptidyl Peptidase-IV Inhibitors: Pharmacological Profile and Clinical Use. *Clinical Diabetes* 2008; 26:2: 53-57.
2. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care* 2008;28:S12-S54.
3. Hundal RS, Krssak M, Dufour S, Laurent D, Lebon V, Chandramouli V, Inzucchi S, Schumann W, Petersen K, Landau B, Shulman G. Mechanism by Which Metformin Reduces Glucose Production in Type 2 Diabetes. *Diabetes* 2000; 49: 2063-2069.
4. Henry RR. Glucose Control and Insulin Resistance in Non-Insulin-dependent Diabetes Mellitus. *Ann Intern Med* 1996; 124:1: 97-103.
5. Nathan DM, Buse JB, Davidson MB, Heine RJ, Holman RR, Sherwin R, Zinman B. Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy. *Diabetes Care* 2006; 29:8: 1963-1972.

6. Centers for Disease Control and Prevention. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2007. Rev ed. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2007.

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