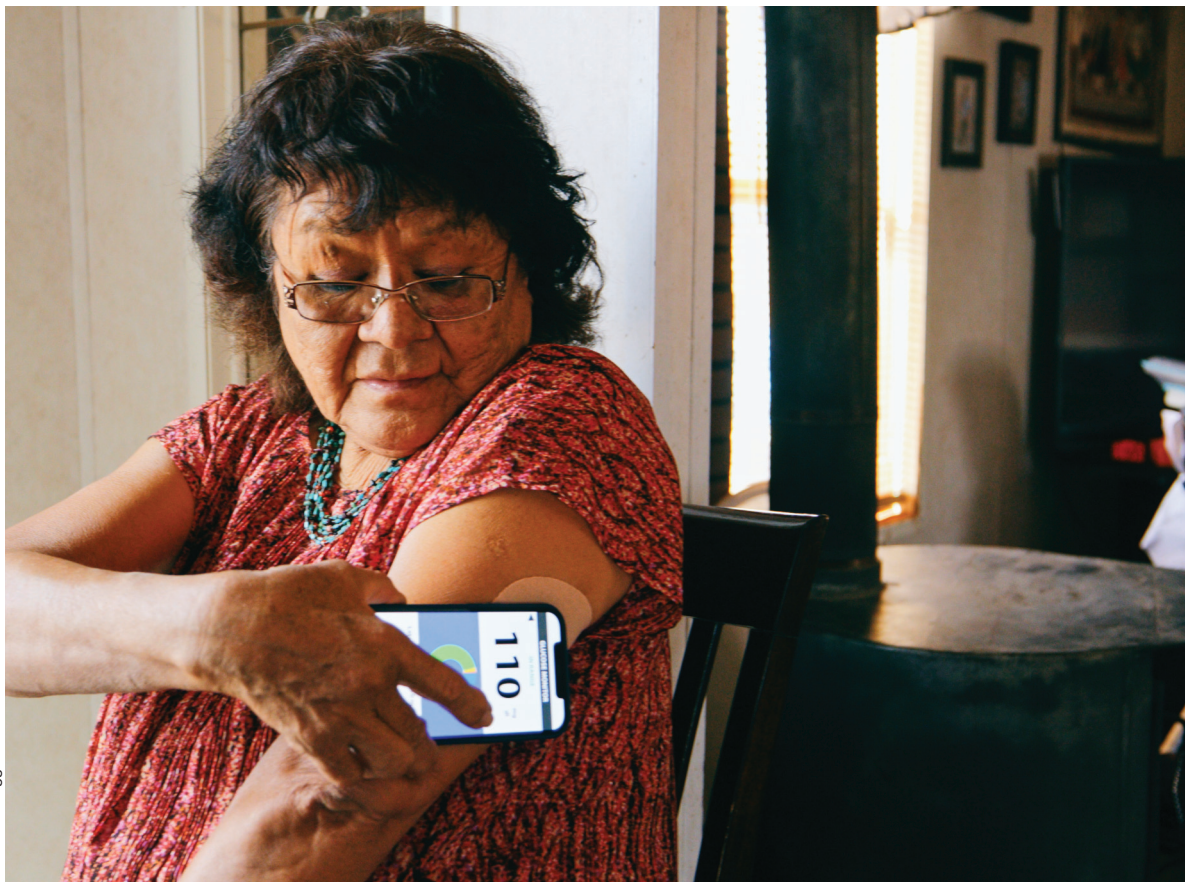


Diabetes is the most common diagnosis among home care patients. All patients with type 1 diabetes require insulin, and due to the progressive nature of type 2 diabetes, most will eventually need insulin therapy. The newer analog insulins that have been developed include long-acting, ultra-long-acting, rapid-acting, and ultra-rapid-acting. They mimic the body's natural insulin secretion and allow patients more flexibility in diet and lifestyle while achieving blood glucose control. This article provides an overview of insulin therapy and related patient care and teaching considerations.

# An Overview of Insulin Therapy in the Management of Diabetes Mellitus



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**Marla J. Hayes, MS, RPh, BCPS, BCGP, CDCES**

The year 2021 marked the 100<sup>th</sup> anniversary of the groundbreaking discovery of insulin by Drs. Banting and Best, forever changing the lives of people with diabetes. In fact, in 1925 Robert D. Lawrence stated “Now modern discoveries, particularly insulin, have completely changed the outlook. There is no reason why a diabetic [person] should not, if he can be taught to do so, lead a long normal life” (Beran et al., 2021). By the end of 1923, developments within the pharmaceutical industry resulted in the large-scale production of insulin (Hirsch et al., 2020). Since these early days, there have been monumental advances in insulin therapy starting with the purification and concentration of animal pancreas extracts (pork and beef insulin) and now with modified insulin analogs made using recombinant DNA technology. Owing to ongoing research and innovation, insulin is now available in a wide array of formulations including rapid-acting, rapid-acting inhaled, ultra-rapid, regular/short-acting, intermediate-acting, long-acting, ultra-long-acting, and premixed combinations.

Diabetes is a common diagnosis among home healthcare patients. It is second only to heart failure in terms of primary diagnosis, but when both primary and secondary diagnoses are taken into consideration, it is the most common home care diagnosis (Zikos et al., 2019). Home care clinicians must be knowledgeable about insulin therapy for diabetes. This article briefly describes the pathophysiology of the two most common types of diabetes and provides an overview of insulin therapy and related patient care and teaching considerations.

## Pathophysiology of Diabetes

Diabetes is a condition that affects more than 28 million people of all ages in the United States (Centers for Disease Control and Prevention [CDC], 2022b). Diabetes develops when the pancreas does not make enough or any insulin at all, or the body does not properly respond to the effects of insulin. Most forms of diabetes are lifelong, and all forms of diabetes are manageable with medications and/or lifestyle changes. Two of the most common forms of diabetes are Type 1 (T1D) and Type 2 (T2D).

Once called insulin-dependent or juvenile diabetes, T1D is a lifelong autoimmune disease causing the pancreas to make very little or no insulin. Under normal circumstances, when glucose enters the bloodstream after a meal, it signals the pancreas to release insulin. Once released, insulin acts as a “key” that opens the cells in the body to

allow glucose to enter and be used as an energy source. As glucose enters cells, the glucose level in the bloodstream decreases, signaling the pancreas to stop producing insulin. In the absence of insulin, the body is unable to facilitate glucose uptake into the cells. As a result, glucose remains in the bloodstream leading to high blood glucose levels referred to as hyperglycemia (CDC, 2023b).

T1D typically develops in children and young adults but keep in mind it can develop in people of any age. Due to the body’s inability to produce insulin, people with T1D require lifelong insulin replacement therapy from the time of diagnosis. The goal of insulin replacement therapy is to achieve normal or near-normal blood glucose levels and prevent or minimize complications. As there are many different types of insulins available to manage T1D, the best option for insulin replacement is determined by a variety of individual factors.

T2D is the more common type of diabetes, accounting for 90% to 95% of all diabetes cases. T2D is characterized by two primary problems, 1) the pancreas does not produce enough insulin, and 2) the cells respond poorly to insulin, a condition known as insulin resistance. Although T2D is more common in older adults, an increasing number of children and young adults with obesity has led to a rise in cases of T2D in younger people. Although T2D can be successfully managed with oral medications, due to the progressive nature of T2D, most people will eventually require insulin therapy (Home et al., 2014).

Diabetic ketoacidosis (DKA) is a serious complication of diabetes that can be life-threatening. DKA develops when there is not enough insulin in the body to move glucose from the blood into cells to be used as energy. This stimulates the liver to break down fat for fuel, a process that produces acids called ketones. When too many ketones are produced too quickly, they can build up to dangerous levels. The most common underlying causes of DKA are illness, missing insulin doses, a malfunctioning insulin pump, or the wrong insulin dose. Although DKA is most common among people with T1D, people with T2D can also develop DKA (CDC, 2022a).

To prevent the development of DKA, people with T1D and those with T2D who take insulin should be instructed to test for ketones if they experience any of the following:

- Symptoms of a cold, flu, or other illness
- Nausea, vomiting, or abdominal pain
- Frequent urination

- An unpredictably high glucose level on self-monitoring
- Persistent, rapid, and marked changes in the degree of hyperglycemia

## Insulin Therapy

The goal of insulin replacement therapy is to achieve optimal blood glucose goals while avoiding hypoglycemia and other adverse effects associated with insulin use such as excessive weight gain and lipodystrophy. The variety of insulin formulations and routes of administration available today allows for individualization of insulin treatment plans, making it easier to attain these goals. However, it is important to keep in mind that insulin requirements change over a person's lifetime as well as under specific circumstances. For example, larger insulin doses are typically required during puberty, pregnancy, when steroids are prescribed, during acute illnesses or infections, and with the development of obesity.

Optimal insulin therapy requires frequent self-monitoring of blood glucose levels to make appropriate adjustments in insulin doses. Therefore, it is essential that all people taking insulin learn how to self-monitor and record their blood glucose levels and adjust insulin doses accordingly. Ideally, blood glucose levels should be checked before meals, in some cases 1 to 2 hours after meals, and at bedtime, unless the patient is using a continuous glucose monitoring device.

Because the body requires insulin even in the absence of food intake, management of diabetes, particularly T1D, requires both basal (background) and prandial (bolus at mealtime) insulin (Table 1) delivered as either multiple daily injections or via continuous subcutaneous insulin infusion (insulin pump). The purpose of using basal-bolus insulin therapy is to mimic the body's natural insulin secre-

tion. As recommended by various guidelines, the starting total daily insulin dose is typically weight based, ranging from 0.4 to 1.0 units per kilogram body weight. However, in newly diagnosed patients with T1D, insulin requirements may be less because of a temporary recovery in beta-cell function occurring early after the initiation of insulin, often referred to as the "honeymoon phase." Due to this phenomenon, a lower initial dose of between 0.3 and 0.4 units per kilogram body weight may be used to prevent the risk of hypoglycemia early in the course of the disease (Janež et al., 2020).

As a rule, approximately 40% to 50% of the total daily insulin dose is administered as basal insulin, which generally remains constant day to day. The other 50% to 60% of the total daily insulin dose is divided into meal-time doses based on carbohydrate intake and to a lesser extent on protein and fat content to prevent postprandial hyperglycemia. Bolus insulin dosing is adjusted by measuring blood glucose levels before and 2 hours after meals and snacks (Janež et al., 2020).

Insulin pumps use only rapid-acting insulin to provide both basal needs and to deliver boluses of insulin to control mealtime excursions and correct hyperglycemia. Insulin pumps are programmed with adjustable basal rates, insulin-to-carbohydrate ratios, correction factors, and target glucose ranges (Lucier & Weinstock, 2023). Patients who use insulin pumps are highly trained on the management of these devices.

Because T2D is a progressive disease, many patients with T2D eventually require and benefit from insulin therapy. Basal insulin alone is the most convenient initial insulin treatment and can be added to oral and other noninsulin injectable medications. Starting doses of insulin can be estimated based on body weight (0.1–0.2 units/kg/day) and the degree of hyperglycemia. Insulin dosing should then be individually titrated over days or weeks as needed to meet blood glucose goals (ElSayed et al., 2023).

Insulin types are classified by how quickly they work, when they peak, and how long they last. It is important to remember, however, factors such as body temperature, exercise, insulin sensitivity, and lipodystrophy at the injection site can cause variations in the time of action.

Long-acting insulin is preferred for basal insulin injection therapy. The long-acting insulins U-100 and U-300 glargine (Lantus ©) and degludec (Tresiba ©) can be administered once a day, whereas detemir

**Table 1. Terms to Know**

<b>Bolus Insulin</b>
Short- or rapid-acting insulin taken at or before mealtimes to control blood sugar levels.
<b>Basal Insulin (background insulin)</b>
Intermediate- or long-acting insulin taken to keep blood sugar levels steady between meals and overnight.
<b>Basal-Bolus Regimen</b>
Rapid-acting insulin taken at mealtimes and long-acting insulin taken once or twice a day.

Source: Centers for Disease Control and Prevention (2023a).

(Levemir ©) and U-100 glargine may require twice-daily administration. Glargine does not have a pronounced peak and lasts approximately 20 to 24 hours. U-300 glargine lasts more than 24 hours, and degludec has a longer duration of action, up to 42 hours. Intermediate insulin (NPH, NPL) is the least expensive basal insulin, but it is associated with more hypoglycemia. NPH insulin has onset in 2 to 4 hours, peak action at 4 to 12 hours, duration of 12 to 24 hours, and is usually given before breakfast and bedtime (Lucier & Weinstock, 2023).

Rapid-acting insulins such as lispro (Humalog ©), aspart (Novolog ©), and glulisine (Apidra ©) generally have an onset of 12 to 30 minutes, peak in 1 to 3 hours, and a duration of action of 3 to 6 hours. Ultra-rapid-acting insulin (lispro or aspart) has a slightly quicker onset of action and somewhat shorter duration of action. Short-acting insulin (regular insulin) has an onset in 30 minutes to 1 hour, with peak action in 2 to 4 hours, and a duration of 5 to 8 hours (CDC, 2022c).

### Barriers to Diabetes Management

Identification of barriers that may impair safe insulin self-administration is a critical component of a successful insulin therapy plan. This includes ensuring individuals and caregivers understand correct insulin injection technique. Using open-ended, nonjudgmental questions allows individuals to address their concerns and develop effective problem-solving strategies. Concerns that insulin therapy will be complicated and inconvenient, as well as anxieties about pain and needles are common when starting insulin therapy.

Hypoglycemia (a blood glucose level <70 mg/dL) is the most frequent adverse effect associated with insulin therapy. Slowly increasing insulin doses during treatment initiation is critical to minimize hypoglycemia. All people with diabetes should be educated on how to recognize, treat, and avoid hypoglycemia, including the importance of meal planning. Some people who have had diabetes for a long time may not experience the symptoms of hypoglycemia such as a tachycardia, shaking, sweating, nervousness, irritability or confusion, dizziness, and hunger. This is known as hypoglycemia unawareness and is more common in T1D. Consequently, it is critical that friends and caregivers can recognize the warning signs and be knowledgeable about how to treat hypoglycemia (American Diabetes Association, 2023).



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As glucose enters cells, the glucose level in the bloodstream decreases, signaling the pancreas to stop producing insulin. In the absence of insulin, the body is unable to facilitate glucose uptake into the cells.

General recommendations for treating hypoglycemia are to follow the “rule of 15.” If blood glucose is below 70 mg/dL, the person should eat or drink something with 15 grams of fast-acting carbohydrates such as 3 glucose tablets, half cup (4 ounces) of fruit juice or regular soda, 6 or 7 hard candies, or 1 tablespoon (15 grams) of sugar. They should then wait 15 minutes and recheck their blood glucose level. If it is still below 70 mg/dL, they should repeat another 15 grams of carbohydrate then wait 15 minutes and recheck blood glucose. Once the blood glucose is above 70 mg/dL, they should be instructed to eat a meal or snack within an hour to keep blood glucose levels from dropping again. Note: chocolate contains fat which can slow carbohydrate absorption, so it is not a good choice for the treatment of hypoglycemia (American Diabetes Association, 2023).

Treatment of severe hypoglycemia may require assistance from another person. Glucagon is an emergency medicine that can be injected to raise blood glucose levels when the person is unable to ingest carbohydrates orally. Family and friends should be familiar with when and how to use glucagon. It is important to store glucagon in a designated place so it can be accessed and given promptly.

Improper storage of insulin can result in its breakdown, potentially reducing its effectiveness



Because T2D is a progressive disease, many patients with T2D eventually require and benefit from insulin therapy. Basal insulin alone is the most convenient initial insulin treatment and can be added to oral and other noninsulin injectable medications.

and predictability in reducing blood glucose levels. Although there may be some slight differences depending on insulin type, the following are general best practices for proper insulin storage:

- **Keep It Cool:** According to the product labels from all three U.S. insulin manufacturers, insulin should be stored in a refrigerator at approximately 36°F to 46°F. Avoid freezing insulin. Do not use insulin that has been frozen (Bahendeka et al., 2019).
- **Know Its Expiration Date:** Unopened insulin refrigerated in the recommended temperature range maintain potency until the expiration date on the package.

All insulin products packaged in vials or cartridges supplied by the manufacturer (opened or unopened) may be left unrefrigerated at temperatures between 59°F and 86°F for up to 28 days. Note: depending on the insulin type, some insulins may have longer stability at room temperature. Any insulin that has been

removed from the manufacturer's original vial, for example prefilled syringes, should be discarded within 2 weeks (Bahendeka et al., 2019). Insulin contained in the infusion set of a pump device (reservoir, tubing, catheter) should be discarded after 48 hours. Insulin contained within the infusion set of a pump device exposed to temperatures exceeding 98.6°F should be discarded (Bahendeka et al., 2019).

- **Avoid Extreme Temperatures**

Insulin loses effectiveness when exposed to extreme temperatures. The longer insulin is exposed to extreme temperatures, the less effective it becomes. Insulin should be kept away from direct heat and out of direct sunlight. Insulin exposed to extreme temperatures should be discarded and replaced as soon as possible (Bahendeka et al., 2019).

- **Inspect Insulin Before Each Use**

Look for changes in color or clarity, including clumps, solid white particles or crystals in the bottle or pen. Insulin that is clear to begin with should always be clear, and never look cloudy (Bahendeka et al., 2019).

The goal of insulin replacement therapy is to mimic the action of insulin in the body as closely as possible to reach blood glucose goals while avoiding hypoglycemia. Over the past century, innovation and the use of biotechnology have brought about significant advancements toward achieving this goal. Today there are a variety of insulin treatment options and delivery methods making insulin safer and more effective. Despite these advances, insulin use is still associated with some risks and errors in dosing that can cause harm or even death. In fact, the Institute for Safe Medication Practices considers insulin a high-alert medication. Unfortunately, mistakes with insulin can happen at home. One resource available to patients and caregivers to access information regarding safe insulin use is The Insulin Safety Center (Consumer MedSafety.org, 2023) which can be accessed at: <https://www.consumermedsafety.org/insulin-safety-center/insulin-safety-home>. The site includes common errors associated with insulin. For example, different types of insulin have similar names and similar-looking vials can cause prescription or dispensing errors. Teach patients to carefully check insulin before leaving the pharmacy. The site also advises patients on prevention and treatment of hyper- and hypoglycemia.

## Conclusion

Diabetes is the most common diagnosis among home care patients. Research within the pharmaceutical industry has resulted in advances in insulin therapy, making achievement of glycemic control more attainable for people with diabetes. Home health clinicians play a critical role in assisting patients with diabetes to become proficient at insulin therapy and must be knowledgeable about insulin therapy and management of barriers to achieving blood glucose goals. ■

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