# Diabetic Hypoglycemia

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- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
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***Faculty***

**Diane Thompson, RN, MSN, CDE, CLNC**, has an extensive history in nursing and nursing education. She possesses a strong background in diabetes and cardiac care, starting her professional career at the cardiac care area of the Cleveland Clinic in Cleveland, Ohio. Ms. Thompson took the knowledge and experience she learned from the Cleveland Clinic and transferred it into the home health arena in rural Ohio, after which she moved to Florida and obtained further knowledge while working as a PRN nurse in all areas, including medical/surgical, intensive care, emergency, critical care, and cardiology. With a desire to have a specific area to concentrate her profession, Ms. Thompson accepted a position as a pneumonia case manager, which led into a diabetes case manager career.

Ms. Thompson has been employed in diabetes care since 2001, when she was hired as a diabetes case manager. After the completion of 1,000 hours of education to diabetes patients, Ms. Thompson earned her certification as a diabetes educator in 2003. From 2006 to 2018, Ms. Thompson was the Director of Diabetes Healthways at Munroe Regional Medical Center in Ocala, Florida. As the director of the diabetes center, Ms. Thompson was responsible for the hospital diabetes clinicians, hospital wound care clinicians, and out-patient education program. Today, she is the nurse manager of a heart, vascular, and pulmonary ambulatory clinic at Metro Health System in Cleveland, Ohio. Ms. Thompson has also lectured at the local, state, and national level regarding diabetes and the hospital management of hyperglycemia. Ms. Thompson is a member of the ADA, AADE, Florida Nurses Association, and the National Alliance of Certified Legal Nurse Consultants.

Ms. Thompson acknowledges her family as her greatest accomplishment. She is a wife of more than 30 years and a mother of a daughter and son, of which she is very proud. Ms. Thompson credits her husband for the support needed to set a goal and achieve it. He has been by her side through nursing school and completion of her Bachelor's degree and Master's degree, which she was awarded in 2015 from Jacksonville University in Florida.

***Faculty Disclosure***

Contributing faculty, Diane Thompson, RN, MSN, CDE, CLNC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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***Division Planner/Director Disclosure***

The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

***Audience***

This course is designed for nurses in any healthcare venue and dietitians with a desire to better understand the causes, recognition, and treatment of hypoglycemia in a variety of settings.



*A complete Works Cited list begins on page 22.*

### *Accreditations & Approvals*

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### *Disclosure Statement*

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### *Course Objective*

The purpose of this course is to provide nurses and healthcare professionals with a foundation of understanding hypoglycemia in order to assure the highest quality of care is provided to patients.

### *Learning Objectives*

*Upon completion of this course, you should be able to:*

1. Define hypoglycemia and its effects on community health.
2. Describe the pathophysiology of hypoglycemia.
3. Outline risk factors for hypoglycemic events, including the use of specific herbal medications.
4. List signs and symptoms of hypoglycemia.
5. Identify causes of hypoglycemia, including medications and non-medication-related factors.
6. Compare treatment options for hypoglycemia.
7. Describe education topics to incorporate into patient teaching regarding hypoglycemia prevention.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

## INTRODUCTION

Diabetes is a complex, multifaceted disease state, and healthcare providers involved in the care of patients with diabetes require in-depth knowledge of all aspects of the disease [1]. Optimal glycemic control and management for patients with diabetes has been proven to decrease both macrovascular complications (e.g., cardiovascular disease, peripheral vascular disease, cerebrovascular disease) and microvascular complications (e.g., nephropathy, neuropathy, retinopathy) [2; 68]. These findings are supported by the results of the Diabetes Prevention Program Outcomes Study and other large-scale studies [3]. Unfortunately, available diabetes treatment regimens are imperfect. Often considered a fact of the disease, iatrogenic hypoglycemia (commonly driven by insulin) is a limiting factor in successful, optimal glycemic control and management [4; 5; 6; 7]. Hypoglycemia occurs with both types of diabetes but impacts those with type 1 diabetes with lower glycated hemoglobin (HbA1c) percentages more prevalently than those with other forms of the disease [8]. This is due to specific defenses against the falling plasma glucose concentrations that continue in individuals with functioning pancreatic alpha and beta cells [9].

Patients with type 1 diabetes striving to achieve glycemic control may have symptomatic hypoglycemia up to 10 times per week, with asymptomatic events occurring more often [10]. On average, type 1 diabetes patients suffer an average of two episodes of symptomatic hypoglycemia per week, often at night [9]. An estimated 4% to 10% of deaths among individuals with type 1 diabetes are attributed to hypoglycemia [11]. Studies have revealed a wide range of episodic hypoglycemia in patients with type 1 diabetes, from 62 to 170 episodes per 100 patient-years with tight glycemic control [12]. These estimates, however, are often based on reported episodes, which may be lower than actual events because they are generally limited to severe episodes that require medical treatment. In contrast, the same studies revealed that patients with type 2 diabetes experienced between 3 and 73 hypoglycemic episodes per 100 patient-years [12].

## AN OVERVIEW OF HYPOGLYCEMIA

Identifying a definitive and concrete blood glucose level that indicates hypoglycemia has been controversial. Similar to the adjustments needed for survival with chronic acidosis or chronic anemia, the body of those with chronic hyperglycemia can adapt to regulate vital operations and maintain function [12]. Patients with uncontrolled diabetes may function with elevated blood glucose levels, causing symptoms of hypoglycemia when the levels are brought back within an acceptable range [4].

Hypoglycemia is defined as a blood glucose level of less than 70 mg/dL and the start of cognitive alteration [5]. Cognitive impairment is classically observed in patients with functioning autonomic and central nervous systems when blood glucose levels fall to less than 60 mg/dL [8]. Hypoglycemia is generally best diagnosed utilizing the Whipple triad: autonomic and/or central nervous system symptoms, a low plasma glucose concentration, and relief of symptoms with treatment [12; 13]. It is important to remember that symptoms of hypoglycemia can instigate anxiety and fear [1].

### PHYSIOLOGY OF FUEL METABOLISM

Glucose regulation is maintained by a sophisticated mechanism of regulatory and counter-regulatory reactions. When an individual consumes food, specifically carbohydrates, sugars are released into the blood circulatory system [1]. The chemical reactions to this sugar introduction help maintain homeostasis in the body.

### Phases of Insulin Response

The concentration of plasma glucose is dependent on the rate glucose enters the circulation in contrast to the rate it is removed [14]. The fuel homeostasis within the body can be explained in a five-phase approach. Phase 1, or the fed state, occurs immediately and up to 3.9 hours after consumption of food. During this phase, the circulating glucose predominantly comes from an exogenous source. Plasma insulin levels are elevated, glucagon levels are minimal, and triglycerides are synthesized in the liver. Insulin impedes the breakdown of glycogen and triglyceride reservoirs. The brain and other glucose-dependent organs utilize some of the glucose absorbed from the intestinal tract, and the excess glucose is stored in the liver, muscle, adipose tissue, and other tissues for use later.

Phase 2 occurs 4 to 15.9 hours after consumption of food and is referred to as the postabsorptive state. In phase 2, blood glucose originates from the breakdown of glycogen and hepatic gluconeogenesis. There is a decrease in plasma insulin levels, and glucagon levels begin to increase. Anabolism (energy storage) ends in this phase and catabolism (energy production) begins. There is a mobilization of carbohydrate and lipid stores. Hepatic glycogen breakdown provides maintenance of circulating plasma glucose to ensure an adequate supply of glucose to the brain and other organs. Adipocyte triglyceride begins to breakdown, and free fatty acids are released into the circulatory system for use by the liver and skeletal muscle as the primary energy source and as a substrate for gluconeogenesis. The brain continues to utilize glucose, provided mainly by gluconeogenesis, due to its inability to use free fatty acids.

Phase 3 is the early starvation state. About 16 to 47.9 hours after the consumption of food, the blood glucose is generated from hepatic gluconeogenesis and glycogenolysis. Gluconeogenesis continues to generate most of the hepatic glucose. In this phase of starvation, lactate makes up half of the gluconeogenesis substrate along with amino acids (specifically alanine) and glycerol. The secretion of insulin is suppressed and counter-regulatory hormone (glucagon, cortisol, growth hormone, and epinephrine) secretion is stimulated.

Phase 4 begins 48 hours to 23 days after food consumption. During this preliminary prolonged starvation state, blood glucose originates from hepatic and renal gluconeogenesis. Within 60 hours of starvation, gluconeogenesis provides more than 97% of hepatic glucose output. The secretion of insulin is distinctly diminished and counter-regulatory hormone secretion is stimulated.

Phase 5, or the secondary prolonged starvation state, begins 24 days after food consumption. Blood glucose during this phase originates from hepatic and renal gluconeogenesis, just as in phase 4. However, in phase 5 the rate of glucose being utilized by the brain and the rate of gluconeogenesis diminishes.

The relationship between the glucoregulatory and counter-regulatory hormones and the many factors that contribute to the fuel metabolism should be considered. There is a sophisticated relationship between the metabolic-regulatory hormones insulin (a glucoregulatory hormone), glucagon, and epinephrine (counter-regulatory hormones). When insulin is elevated, glucagon and epinephrine are suppressed [15]. This process occurs to prevent the continued rise of endogenous glucose levels. Conversely when insulin levels decline in response to diminished circulating glucose levels, glucagon and epinephrine respond by increasing. These relationships are maintained when normal homeostasis is maintained. In the presence of diabetes, there is a disruption of this homeostasis [16].

## PATHOPHYSIOLOGY OF HYPOGLYCEMIA

Hypoglycemia is a result of one of two different issues: hyperinsulinemia (resulting from too much exogenous insulin, an insulin-secreting pancreatic tumor, or excessive oral diabetes medication) or iatrogenic issues (alteration in glucose counter-regulation) [12]. Hypoglycemia can be a complication of insulin therapy in both type 1 and type 2 diabetes or of oral medications that stimulate the pancreatic beta cells in the islets of Langerhans [17]. Symptoms of hypoglycemia tend to have a greater severity when they are the result of hyperinsulinemia due to the prevention in the formation of alternative fuels, such as free fatty acids or ketones [8].

Iatrogenic hypoglycemia is the consequence of the relationship of relative insulin surplus (also referred to as absolute insulin surplus) and compromised physiologic and behavioral responses to falling plasma glucose levels in patients with type 1 diabetes and patients with insulin-deficient type 2 diabetes [4; 13]. Normally, a decrease in insulin release is the first physiologic defense. An increase in glucagon production is the second, and the third physiologic defense is epinephrine [15]. Epinephrine limits the clearance of glucose in insulin-sensitive tissues. The result of each of these defenses is a sympathoadrenal response, primarily a sympathetic neural response, to hypoglycemia initiating neurogenic symptoms. As a result, behavioral protections, such as hunger, take effect [1]. In some cases, these natural defenses may be compromised.

Chronic hypoglycemia can result in hypoglycemia-associated autonomic failure (HAAF), a syndrome characterized by both defective glucose counter-regulation and hypoglycemia unawareness. This response is common in patients with type 1 diabetes, but can also occur in patients with advanced type 2 diabetes. In patients with HAAF, the epinephrine response to ensuing hypoglycemia is decreased, with adjustments in insulin and glucagon absent [18]. These patients will also experience fewer symptoms of low blood glucose levels due to a decrease in the sympathoadrenal response, resulting in an unawareness of the condition or the need to correct it [12]. Tight control of blood glucose levels and avoidance of hypoglycemia can reverse HAAF within two to three weeks [18].

Research has also indicated that recurrent hypoglycemia can result in increased nitric oxide production by the ventromedial hypothalamus, a mechanism that triggers response to hypoglycemia in patients with HAAF [19]. However, prolonged or excessive nitric oxide production causes an impaired counter-regulatory response. In an animal study, blocking this action with the use of the antioxidant *N*-acetylcysteine prevented the development of an impaired counter-regulatory response [19].

### Nocturnal Hypoglycemia

Nocturnal hypoglycemia is another concern for some diabetes patients. Sleep impairs the counter-regulatory response to hypoglycemia in individuals with or without diabetes [20]. This impairment is caused by a decreased epinephrine response to dropping blood glucose levels during sleep. The result is an increased susceptibility to asymptomatic nocturnal hypoglycemia, particularly for patients with type 1 diabetes. Because it has been established that recurrent hypoglycemia can result in further deficits in counter-regulatory hormone responses, regular nocturnal hypoglycemia can trigger a cycle of hypoglycemia, impaired counter regulatory responses, and decreased awareness of low blood glucose levels while awake or asleep. Patients who experience recurrent asymptomatic nocturnal hypoglycemia are at increased risk for more frequent and severe hypoglycemia [8].

Some patients will experience a rebound reaction to hypoglycemia known as the Somogyi phenomenon [21]. This condition almost exclusively occurs in patients who take long-acting insulin and occurs most often following nocturnal hypoglycemia [21]. Untreated hypoglycemia or a rapid decrease in blood glucose triggers a release of counter-regulatory hormones, resulting in an episode of hyperglycemia and a period of insulin resistance that can persist for hours to days. The insulin resistance and hyperglycemia can lead to ketonuria or ketonemia [1].

Recognition and diagnosis of the Somogyi phenomenon is difficult, and it is important that healthcare providers thoroughly assess signs and symptoms of nocturnal hypoglycemia. This can be done nicely by utilizing continuous glucose monitoring [5]. This option involves placing a small sensor under the skin that monitors interstitial fluid [22]. The sensor device transmits an electronic signal to a monitor every five minutes. These levels are stored for up to 72 hours.

## RISK FACTORS

The first step in developing a plan for the prevention and treatment of hypoglycemia is having a solid knowledge of risk factors and strategies to avoid or address those factors [5]. Reduction of hypoglycemia risk factors is an important aspect of the education process for patients with either type 1 or type 2 diabetes. Hypoglycemia risk reduction involves addressing the issues of hypoglycemia at every patient contact [5]. The principals of aggressive glycemic control are necessary to prevent hypoglycemia and include patient education, frequent self-monitoring of blood glucose (SMBG), flexible insulin (or other medication) regimens, individualized glycemic goals, and continuous professional guidance [23]. Finally, healthcare providers should consider both conventional risk factors and those indicative of compromised defenses against hypoglycemia and adjust treatment accordingly [9].

### INSULIN

Inaccurately timed, an incorrect type, or excessive doses of insulin can result in hypoglycemia. In addition, there can be a diminished exogenous glucose source as a result of a missed meal, skipped snack, extended fast, or exercise [1; 5]. The duration of insulin therapy may also be a risk factor for hypoglycemia [24].

### WEIGHT LOSS

When patients with diabetes experience weight loss, there is a corresponding increase in insulin sensitivity. Along with weight loss, improved fitness enhances insulin sensitivity by increasing muscle mass and optimizing glucose utilization. If these patients continue on a pre-weight-loss medication or insulin regimen, there is a greater potential of hypoglycemia [9].

### ALCOHOL USE

Use of alcohol also increases the risk of experiencing hypoglycemia. Ethanol impedes gluconeogenesis and inhibits cortisol and hormone responses to hypoglycemia. Severe hypoglycemia can occur when ethanol consumption is coupled with lack of food or overnight fast, resulting in glycogen depletion [8]. Hypoglycemia can be prevented in this case by eating while ingesting any alcohol and limiting alcohol intake [25].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Academy of Nutrition and Dietetics, alcohol consumption may place adults with diabetes at increased risk for delayed hypoglycemia, especially if using insulin or insulin secretagogues. Therefore, adults with diabetes should be advised that if they choose to drink alcohol, they should do so in moderation (i.e., one drink per day or less for adult women and two drinks per day or less for adult men).

(https://www.andeal.org/topic.cfm?menu=5305&cat=5595. Last accessed February 19, 2023.)

**Level of Evidence/Strength of Recommendation**: Weak, Conditional

## HAAF

As discussed, iatrogenic hypoglycemia is the result of the interplay of relative insulin excess and compromised physiologic and behavioral defenses against dropping plasma glucose concentrations. Risk factors for HAAF include insulin deficiencies, a history of severe hypoglycemia or hypoglycemia unawareness, and aggressive glycemic control therapy [9].

## HORMONES AND PREGNANCY

Women with diabetes who are of child-bearing age should be acutely aware of potential hypoglycemic episodes. Women are at an increased risk of hypoglycemic events at specific points in their lives, such as at the start of each menstrual cycle, as a result of decreased levels of progesterone. After conception and early in the first trimester, the risk of hypoglycemia is amplified as a result of increases in peripheral utilization and storage of glucose. Late in the third trimester, nocturnal hypoglycemia becomes a concern, as a bedtime snack may be insufficient to meet the intensified fetal demands for glucose. Lastly, during the postpartum phase, the risk of hypoglycemia results from the loss of placental hormones [1].

## AGING

As the aging process progresses, an individual's risk of hypoglycemia increases as a result of various behavioral and physical changes. The production of counter-regulatory hormones that are so important to preventing hypoglycemia begins to slow [12]. Additionally, elderly patients frequently are prescribed many medications for various conditions, making polypharmacy a concern. Polypharmacy is relatively common among patients with type 1 and type 2 diabetes due to the multiple comorbidities associated with the disease. However, drugs may interact and increase the risk for hypoglycemia [26].

Behavioral changes, including cognitive decline and changes in eating habits, can also affect hypoglycemia risk [27; 28]. Elderly patients often have erratic nourishment or caloric intake, and this coupled with oral medications that increase insulin secretion or exogenous insulin significantly increases the potential for hypoglycemia [1]. Even when adequate calories are consumed, the older adult's intestinal absorption of those calories is slowed. As a patient ages, the adrenergic response to low blood glucose diminishes or disappears [12]. Additionally, the preliminary symptoms of hypoglycemia, for instance lack of motor skills or confusion, may be misdiagnosed or unrecognized [26].

## DEPRESSION

In one study of more than 4,000 patients, individuals with diabetes and major depressive disorder were found to be more likely to experience frequent episodes of hypoglycemia than those without depression [29]. In addition, the time to first severe episode of hypoglycemia is shorter in depressed patients.

## COMPLEMENTARY AND ALTERNATIVE THERAPIES

It is imperative to investigate individuals' use of any alternate therapies due to concerns associated with the usage. Research has demonstrated that less than 40% of individuals inform their primary care providers of their use of complementary or alternative therapy [30; 71]. Furthermore, patients with diabetes who used some form of complementary or alternative therapy in the past year for treatment and/or wellness varies; the majority of research shows that between 25% and 40% of patients with diabetes use complementary and alternative modalities, while some smaller studies have shown use as high as 88% [31; 69; 72; 73]. Therefore, inquiring about the use of these therapies, particularly the use of herbal medications, should be incorporated into each instance of patient contact.

The use of some complementary or alternative therapies can increase the risk of hypoglycemia and may be a concern for many reasons. Some concerns include:

- Potential side effects
- Drug interactions
- Product variability
- Lack of product standardization
- Possibility of contamination
- Possibility of misidentification

Side effects and drug interactions are the two most significant areas of concern. Serious side effects have been experienced by patients taking complementary therapies, and the risk of drug interactions is a particular concern for patients with existing conditions, such as diabetes. Concomitant use of complementary therapies in these patients may result in toxicity secondary to exaggerated or subtherapeutic effects of their medication [32].

There are 10 botanical or complementary therapies that pose a specific risk of hypoglycemia in patients with diabetes. These include cinnamon, fenugreek, bitter melon, ginseng, nopal, aloe, banaba, caiapo, bilberry, and milk thistle [33].

### Cinnamon

Cinnamon is derived from the bark of an evergreen tree that grows in tropical climates. This product has an active compound, hydroxychalcone, that may lower blood glucose and lipid levels in patients with diabetes, although research has been mixed [34; 35]. Some patients will take cinnamon to help control blood glucose levels despite the lack of proof of efficacy. It is possible that the effects of hydroxychalcone may potentiate the effects of secretagogue agents, increasing the risk of hypoglycemia [32].

### Fenugreek

Fenugreek is a member of the *Leguminosae* family along with chickpeas, green peas, and peanuts. Historically, this herb was used to induce labor, but today it is used for diabetes, loss of appetite, and stimulation of milk production in breastfeeding women [36]. The active compounds of fenugreek include saponins and glycosides, and the seeds contain alkaloids, 4-hydroxyisoleucine, and fenugreekine, which delay gastric emptying, resulting in slow carbohydrate absorption, glucose transport inhibition, increased insulin receptors, improved peripheral glucose utilization, and possible stimulation of insulin secretion [32]. In diabetes patients, these effects may result in hypoglycemia [33].

### Bitter Melon

Bitter melon is a vegetable cultivated in India, Asia, South America, and Africa and may also be known as bitter gourd, bitter apple, bitter cucumber, karolla, or karela. It is the most widely used diabetes treatment in Ayurveda, a form of traditional medicine originating in India [37; 38]. The active compounds in this vegetable include momordin, charantin, polypeptide P, and vicine. Use of bitter melon, usually in the form of juice or tea, can cause hypoglycemia, hypoglycemia-induced coma, increased tissue uptake of glucose, inhibition of enzymes involved in glucose production, and enhanced glucose oxidation of glucose-6-phosphate-dehydrogenase pathways [32]. Specific attention is required and intensive education is necessary when bitter melon is taken in conjunction with an insulin secretagogue [1].

### Ginseng

Ginseng is a popular botanical product traditionally used to support overall health and the immune system [39]. The active ingredient in ginseng is ginsenoside, which decreases carbohydrate absorption in portal circulation and may increase glucose transport and modulation of insulin secretion when taken with an insulin secretagogue [33]. However, it is important to note that there is no conclusive evidence supporting any health benefits of ginseng [39].

### Nopal

Nopal, also known as prickly pear, is a member of the cactus family and is a food source in Mexico. It is also used as an antihyperglycemic in Mexican culture [40]. The active compounds in nopales are mucopolysaccharide fibers and pectin, which slow the absorption of carbohydrate, decrease lipid absorption, and increase insulin sensitivity [32; 40]. As a result, there may be an improvement in blood glucose levels without hypoglycemia, but further research is necessary to confirm the efficacy and safety of this use. In the United States, the use of nopal is usually limited to Mexican and Native American populations [1].

### Aloe Vera

Aloe vera is a common desert plant belonging to the family *Liliaceae*. The gel of aloe leaves has traditionally been used topically to soothe and heal wounds [41]. The active chemical constituent of aloe is glucomannan, a polysaccharide similar to guar gum and glycoprotein. Glucomannan has the potential to increase and promote glucose uptake. As a result, hypoglycemia can occur when aloe is consumed, particularly when used in combination with a secretagogue [32].

### Banaba

Banaba is a type of crape myrtle commonly found in the Philippines, India, Malaysia, and Australia [32]. Commonly used as a tea to treat diabetes and promote weight loss, banaba has the chemical components corsolic acid and ellagitannin, which stimulate glucose uptake [33]. Banaba also has an insulin-like activity secondary to activation of insulin receptor tyrosine kinase or inhibition of tyrosine phosphate. Concurrent use of banaba and oral diabetes medication or insulin may result in an increased risk for hypoglycemia [32].

### Caiapo

Caiapo is a form of white sweet potato cultivated in the mountains of Japan and South America. The botanical product is commonly used by Native Americans to decrease thirst and promote weight loss [32]. The active compound in caiapo is acidic glycoprotein, which decreases insulin resistance and improves insulin sensitivity. As a result, there is an increased potential for hypoglycemia, particularly when used with a secretagogue.

### Bilberry

Bilberry is a plant related to the American blueberry, huckleberry, and cranberry. Two forms of bilberry may be used: the berry and the leaf. The fruit is used for circulatory problems, diarrhea, eye disorders, and menstrual cramps, while the leaf is used for other conditions, including diabetes [42]. The active compounds of bilberry leaf are anthocyanosides and chromium [32]. These components increase the potential for hypoglycemia due to the decreased vascular permeability and redistribution of microvascular blood flow. Research is still being completed to determine the exact mechanism by which bilberry lowers blood glucose [33].

### Milk Thistle

Milk thistle is related to daisies and other thistles and has been used extensively for various hepatic disorders [43]. The active components are silybin, silychristin, and silydianin. These compounds inhibit the hepatotoxin-binding hepatocyte membrane receptors and decrease glutathione oxidation [32]. The resultant blood glucose-lowering effects and potential for hypoglycemia are being studied [1].

### Case Study

Patient A arrives at her primary care provider's office for a routine examination. She is a Native American woman, 45 years of age, who is 5 feet 4 inches tall and weighs 205 pounds, with a body mass index of 35.3 kg/m$^2$. Her physician is concerned because of her family history of type 2 diabetes, heart disease, and stroke. Patient A has a past medical history of hypertension and hyperlipidemia. Her blood work reveals an HbA1c of 8.0% (estimated average glucose: 183 mg/dL) and a fasting blood glucose level of 173 mg/dL. A diagnosis of type 2 diabetes is confirmed by further blood work. Patient A is reluctant to start medications and asks her primary care provider if he knows of any alternative therapies she could use instead. After a thorough explanation regarding the benefits of glycemic control in respect to her family and personal past medical history, Patient A agrees to start taking metformin. She is also referred to a diabetes self-management education program recognized by the American Diabetes Association (ADA) for information regarding SMBG, medication management, exercise, blood glucose goals and behavior change, and culturally sensitive meal planning.

Patient A returns in three months for a follow-up evaluation of her progress. Her HbA1c remains 8.0% (estimated average glucose: 183 mg/dL), and she states her fasting blood glucose levels are 185–220 mg/dL. She states she has been adherent to her meal plan and has been working outside more often to increase her activity level. She appears frustrated with the lack of improvement.

Her primary care provider decides to add a sulfonylurea to the patient's therapy to increase insulin production. Patient A is started on glipizide 10 mg twice per day. Additional education is completed regarding the action of glipizide as well as the potential side effects and the importance of eating meals on a consistent schedule to prevent hypoglycemia. The patient and her daughter were both instructed on recognition of signs and symptoms of hypoglycemia and treatment options. Patient A is able to verbalize all instructions given.

One month later, Patient A's daughter calls the primary care provider in the mid-morning to report that her mother was working out in the yard and became dizzy, shaky, sweaty, and confused. She is instructed to check Patient A's blood glucose level and treat for possible hypoglycemia. After the patient's blood glucose levels are stabilized, the daughter is told to bring the patient to the clinic. The initial blood glucose level is 43 mg/dL. After Patient A consumes 6 ounces of orange juice, the blood glucose is rechecked in 15 minutes. The result is 87 mg/dL.

At the clinic, the certified diabetes educator assesses Patient A's medication understanding and adherence. No adverse practices are identified, so further information gathering is completed.

***Rationale and comments***: *From the information gathered so far, it is unclear what caused Patient A's hypoglycemia. Additional areas should be explored, including:*

- *Timing of medication and meals*
- *Breakfast intake*
- *Blood glucose level prior to working in the yard*
- *Other episodes of hypoglycemia*
- *Fasting blood glucose levels*

The diabetes educator requests Patient A recall her breakfast, which reveals the intake of two scrambled eggs, one slice of whole-wheat toast with butter, half of a banana, 8 ounces of fat-free milk, and a cup of tea. The educator also inquires about any use of holistic or herbal remedies. Patient A becomes quiet and is hesitant to answer, but finally reveals she has been drinking bilberry tea every morning and using nopal and bitter melon in most of her meals. The patient indicates she did not share this with her primary care provider because she did not feel it was important. The diabetes educator informs Patient A about the potential interactions of many herbal medications and the impact they could be having on her diabetes and other conditions. The importance of including these medications in her conversations with all of her healthcare providers is stressed. As a result, Patient A's primary care provider decides to decrease her glipizide to 5 mg twice a day. The patient is also instructed to call the diabetes nurse with a week of blood glucose levels to determine the success of the change in therapy.

## SIGNS AND SYMPTOMS OF HYPOGLYCEMIA

Hypoglycemia is a serious and real threat to diabetes patients. Patient education must emphasize the early recognition of hypoglycemic states to assure the condition is treated promptly [44].

Symptoms of hypoglycemia are categorized by the acute response and progress in severity of the reaction. Initially, symptoms of hypoglycemia are a result of adrenergic effects that occur secondary to the release of catecholamine. These symptoms include sweating, weakness, shakiness, tremors, anxiety, faintness, tachycardia, and palpitations [45].

As hypoglycemia progresses and plasma blood glucose levels continue to decrease, the reaction to the lack of glucose becomes more severe. Symptoms in this stage are the result of the deficit of glucose in the central nervous system and include confusion, irritability, diplopia, inappropriate affect, motor incoordination, headache, abnormal behavior, weakness, and convulsions. The most severe of the central nervous system symptoms are diabetic coma and death [45].

More than half of all severe hypoglycemia episodes occur during sleep, when symptoms are less likely to be detected or recognized [21]. Nocturnal hypoglycemia most typically is caused by excessive insulin therapy and, with great cause for concern, usually does not awaken the person. Patients should be aware of symptoms that may indicate nocturnal hypoglycemia, such as morning headaches, feeling "foggy" in the morning, difficulty awakening, psychological changes, exhaustion, restlessness while sleeping, night sweats, nightmares, and loud respirations [8]. Additionally, unusually high blood glucose levels after breakfast or lunch or detection of a small amount of ketones but no glucose in the morning urine are signs of nocturnal hypoglycemia [21].

### CASE STUDY

Patient B is a White adolescent, 15 years of age, with a five-year history of type 1 diabetes. He is on multiple daily injections of insulin glargine for his background insulin and a rapid-acting insulin analog for meal and correction boluses. Patient B has experienced a roller-coaster effect with his glucose levels, and he has had difficulty in school recently due to fatigue and headaches. Patient B states he has not been sleeping well at night and wakes up exhausted. When asked to recall his blood glucose levels, he states his morning glucose levels have ranged between 189 mg/dL and 215 mg/dL. The primary care physician suspects nocturnal hypoglycemia and possible Somogyi phenomenon.

***Rationale and comments***: *Nocturnal hypoglycemia is indicated by several signs and symptoms. The patient has experienced:*

- *Headaches and fatigue*
- *High blood glucose levels in the morning*
- *Waking up exhausted*

*These are all signs of nocturnal hypoglycemia.*

The physician instructs Patient B to assess his blood glucose level at 3 a.m. to identify if Somogyi phenomenon is an issue. She also prescribes the use of a continuous glucose sensor to assess blood glucose patterns and hyperglycemia/hypoglycemia events that may be occurring without being noticed.

## CAUSES OF HYPOGLYCEMIA

The frequency of hypoglycemia in patients with diabetes is due primarily to abnormalities in glucose counter-regulation. There is a multitude of potential causes of hypoglycemia, including, but not limited to, excessive oral and injectable medications, physical activity, illness, and inappropriate patient practices [1].

## ORAL MEDICATIONS

The appropriate use of diabetes medications requires an understanding of the mechanisms of action of each agent. This understanding should decrease incidents of hypoglycemia. Patients taking oral medications for diabetes who may be at an increased risk for hypoglycemia are often thin, are taking an insulin secretagogue, and/or have erratic eating patterns. This is especially true when a patient is taking medications with a rapid onset of action.

Sulfonylurea medications, such as glyburide, glipizide, and glimepiride, are associated with an increased risk for hypoglycemia due to their mechanisms of action. Sulfonylurea preparations appear to acutely lower blood glucose levels by stimulating the release of insulin from the pancreas, an effect dependent upon functioning beta cells in the pancreatic islets [46; 70]. These agents close the energy-sensitive potassium channel in the cell membrane of the pancreatic beta cell. By accomplishing this, there is an increased amount of available insulin [44]. It is important to note that individuals with impaired first-phase insulin release will experience a diminished effect from sulfonylurea therapy [1].

The nonsulfonylurea secretagogues, or glinides, are hypoglycemic agents with the potential to reduce blood glucose levels to below normal. Within this classification of hypoglycemic agents there are two medications: repaglinide and nateglinide [47; 70]. These agents lower blood glucose levels by stimulating the release of insulin from functioning beta cells in the pancreas. Insulin release is glucose-dependent and diminishes at low glucose concentrations. These agents are most effective when taken just prior to the first intake of a meal [47]. This results in a greater insulin release during the first phase.

## INSULIN

Insulin can be divided into two categories: basal and bolus. Healthy pancreatic beta cells release insulin into the blood stream throughout the day. This basal or background insulin enables stored fat and glucose to be released in the correct amounts to enable adequate metabolism during times when a person is not eating. This steady insulin level throughout the day regulates glucose production by the liver, the production and release of fat as fuel, and the entry of particular amino acids into cells for the creation of enzymes and structural proteins. Individuals without diabetes release about half of their total daily insulin requirements as background insulin to fulfill these needs [21]. As food is consumed, it is converted to glucose and other energy precursors by the digestive system. In response to rising blood glucose levels, the beta cells of the pancreas are stimulated to produce and release insulin. This is known as bolus insulin release [1].

When an individual's pancreatic beta cells are no longer proficient in producing enough or any insulin, exogenous insulin is required [1]. This can be accomplished utilizing many differing preparations. Previous therapies were formulated from beef or pork insulin, which were the only available synthetic forms of human insulin. Today, recombinant human insulin is available and is used by most persons requiring insulin therapy. The modern human recombinant insulin differs from the pork insulin by only one amino acid and beef preparations by three amino acids [21]. Insulin injections, in small amounts, provide the body with the needed hormone to adjust to plasma glucose levels. However, unregulated and sustained hyperinsulinemia is common with exogenous insulin [9].

Unfortunately, hypoglycemia is the most important limiting factor for insulin adjustments to improve glycemic control. The risk of hypoglycemia depends on multiple factors, including age, weight, degree of insulin resistance, duration of the disease process, duration of insulin therapy, degree of glycemic control, and past history of episodes. In addition, there are casual factors that can instigate an episode of hypoglycemia, such as over administration of insulin, dietary transgressions, unplanned strenuous exercise while taking insulin, excessive alcohol intake, and hypoglycemia unawareness [5]. According to various studies, the annual incidence of severe hypoglycemia in the person with type 2 diabetes is 2% to 13% [48; 49]. Although the severe hypoglycemia experienced by the insulin-treated type 2 diabetes group is not trivial, the rate of severe hypoglycemia demonstrated by the type 1 diabetes individual during the Diabetes Control and Complication Trial was far greater. Of individuals treated with intensive insulin therapy during this study, 65% suffered severe hypoglycemic reactions requiring assistance from another individual for recovery [12].

Patients using insulin for the treatment of diabetes require extensive education regarding preparation and administration, as inaccurate dosing is a significant threat. If a patient is unable to fully visualize the small incremental markings on the syringe, the chance of dosing error is increased. The result of medication errors can be severe hypoglycemia, seizures, and possibly even death. For patients with poor vision, the insulin pen may be a better option and may increase the safety for the individual. Patients should demonstrate their techniques for preparation, site selection and preparation, and administration. This allows for a thorough assessment of potential risk factors for hypoglycemia [1].

The development of hypoglycemia is a concern for all individuals on an insulin therapy regimen. Education should include information regarding oral and injectable combination medication management, exercise considerations, and specific patient-centered issues to maintain safe use of medications in daily life [1].

Insulin alone or in combination with another antihyperglycemic agent increase the potential for an adverse hypoglycemia reaction [50]. Preventative measures include not skipping meals, eating prior to exercise, and appropriately timing insulin bolus therapy [50; 51].

EVIDENCE-BASED PRACTICE RECOMMENDATION

For individuals using fixed insulin doses (or insulin secretagogues), the Academy of Nutrition and Dietetics asserts that consistent carbohydrate intake with respect to time and amount can result in improved glycemic control and reduce risk for hypoglycemia.

(https://www.andeal.org/topic.cfm?menu=5305&cat=5595. Last accessed February 19, 2023.)

**Level of Evidence/Strength of Recommendation:** Fair, Conditional

Accurate and frequent SMBG is recommended for all patients who use insulin. SMBG can help prevent hypoglycemia and provide information relevant to adjusting food intake, activity level, and medication [5]. Patients should report frequent blood glucose levels below 70 mg/dL to their primary care provider [52]. This will allow for the fine tuning of the insulin regimen, which should result in optimized glycemic control and reduction of adverse outcomes [1]. Nocturnal hypoglycemia can be an issue for patients taking insulin, and those who have or who are suspected to have nocturnal hypoglycemia as a result of insulin therapy should monitor their blood glucose levels [1].

For patients on an insulin regimen, exercise can significantly increase the potential for hypoglycemia [53]. Education related to exercise should focus on the assessment of pre-exercise blood glucose levels and determination if additional carbohydrates are needed. The risk for hypoglycemia increases as the duration or intensity of the activity increases. SMBG also can be used to monitor how psychological and physical stressors influence glycemic responses [54]. Correlating SMBG results with the presence of stressors can help the patient manage them better for glycemic control.

### Case Study

Patient I is an African American man, 72 years of age, with a 15-year history of type 2 diabetes. He has experienced diabetes-related complications, including a transient ischemic attack, angioplasty for coronary heart disease, renal impairment, and hypertension. His glycemic control has diminished steadily over the past two years to a current HbA1c of 8.9% (estimated average glucose: 209 mg/dL). Patient I has been very hesitant to start insulin therapy because of the experiences of past family members. He states, "As soon as I start on the needle, my life is over." After multiple educational opportunities regarding the benefits of good glycemic control and how it can diminish the adverse effects of his diabetes, Patient I ultimately agrees to a change in treatment therapy to include insulin injections. The physician prescribes neutral protamine Hagedorn (NPH) insulin 10 units twice per day due to cost factors over the more expensive long-acting insulin.

One morning, Patient I's wife calls emergency services reporting that Patient I is combative, confused, sweating, and beginning to lose consciousness. She is able to pour a large glass of orange juice in his mouth. She states, "I wanted to make sure it worked, so I put 5 tablespoons of sugar in it." When the patient arrives in the emergency department his blood glucose level is 357 mg/dL and he is complaining of chest pain. The decision is made to admit Patient I for further observation and glucose management. He is ordered weight-based insulin correction for glucose control. His NPH insulin is put on hold. The next morning, Patient I has a blood glucose level of 313 mg/dL. His glucose is covered, and the physician orders his home dose of NPH insulin 10 units. Patient I refuses his dose because it made him, "sicker than I was before. I was brought here because it doesn't work." The nurse explains the action of the insulin in relationship to his blood glucose levels and the action of the NPH, again stressing the benefits of adequate glucose control and the detrimental effects of hyperglycemia. The patient remains adamant that he is not going to take insulin again. His primary care provider discusses the need for the insulin therapy, and Patient I agrees to take the insulin while he is in the hospital and staff is around in case he "gets into trouble." After 24 hours, the patient has blood glucose levels less than 150 mg/dL and states he is feeling better than he has in many months. Through education regarding insulin, the connection is made between the increased perception of health and the decrease in blood glucose levels.

Patient I agrees to try insulin at home again. When it is time for his next dose of NPH, the nurse brings in the vial and a syringe to assess his ability to successfully draw up the 10 units of insulin. Observation reveals that the patient is struggling to complete the task competently and has actually drawn up 16 units of insulin opposed to 10 units. When his attention is drawn to the excessive amount of insulin in the syringe, he states, "Those little lines are so hard to see even with my glasses on. I figured the amount is so small it shouldn't hurt me." Patient I also struggles to manipulate the vial and syringe to the extent of the needle bending within the bottle.

***Rationale and comments***: *There are several options available to Patient I to ensure he is receiving the correct amount of insulin. A Magni-Guide may be helpful to increase visualization of the syringe markings. A refrigerator vial stabilization device may also be considered to allow for greater stabilization of the needle when preparing the insulin syringe. The wife's willingness to learn how to draw up insulin into the syringe should be assessed. Once taught, her ability to accurately prepare the insulin syringe should be observed. Finally, the best option may be utilizing an insulin pen, which can increase patient safety.*

The treatment options are discussed with Patient I and his wife, and they decide to investigate the use of an insulin pen. The patient calls his insurance company to evaluate the coverage and is happy to hear the insulin pen is covered due to his recent hypoglycemia experience. Patient I and his wife are both taught how to dial the correct amount of insulin units, how to change insulin pen needles, and how to appropriately dispose of needles. Both individuals are able to perform all vital components taught regarding insulin pen usage and safely return home.

## INSULIN PUMP THERAPY

Some patients may use a form of insulin delivery known as continuous subcutaneous insulin therapy, or insulin pump therapy. Insulin pumps are small, battery-operated microcomputers that resemble a standard pager device in size and appearance. This therapy is used most often for individuals with type 1 diabetes, although it is an option for some patients with type 2 diabetes. In contrast to multiple daily injections of rapid- and long-acting insulins, the insulin pump delivery system works to mimic normal pancreatic function [21]. This is accomplished by the steady release of precise amounts of insulin from the pump to achieve the basal or background insulin the body requires and optimize metabolic homeostasis. Likewise, when food is consumed, the individual or care provider enters the amount of carbohydrate and the pump calculates the correct dose and recommends a bolus dose. The individual can accept or enter an alternate bolus. Insulin pumps only use rapid-acting insulin to increase the ability of the pump to imitate normal pancreatic functioning [1].

In 2016, the U.S. Food and Drug Administration (FDA) approved the first automated insulin-delivery device for individuals 14 years of age and older with type 1 diabetes [55]. The device is a hybrid closed-looped system that automatically monitors glucose and provides appropriate basal insulin doses. It measures glucose levels every five minutes and automatically administers or withholds insulin, depending on the level of glucose measured. The device requires little to no input from the user.

A major advantage of insulin pumps is the opportunity for tight blood glucose control. This is possible because insulin delivery becomes very similar to the normal physiologic pattern. Pumps also offer the benefit of a more normal lifestyle, allowing users more flexibility with meal and activity patterns.

Although patients utilizing insulin pump therapy have been proven to achieve better glycemic control, they are not immune to hypoglycemia, and even with the introduction of this technology, hypoglycemia rates have been relatively unchanged for decades. Inappropriate carbohydrate counting or overriding the recommended bolus dose can lead to overdosing and ultimately hypoglycemia. Furthermore, if a meal bolus is programmed and delivered and the meal is interrupted or missed, hypoglycemia may result. As when any form of insulin is injected into the body, the potential of hypoglycemia is increased with planned or unexpected exercise. Lastly, stress can increase the release of adrenocorticotropic hormone and corticotrophin-releasing hormone, resulting in an increase in circulating blood glucose [17]. This stress can be the result of positive or happy events or as a response to negative events. If the pump was programmed for deliveries to meet known stress needs, hypoglycemia may develop when the stressors are removed without adjusting the total insulin delivery [21].

The ADA provides guidelines for the selection of patients appropriate for pump use [56]. Candidates should be highly motivated to take a great deal of responsibility for the care of their diabetes on a day-to-day basis. This includes the ability to count carbohydrate grams, to calculate appropriate bolus dosing, to make adjustments for varying activity patterns, and to monitor blood glucose four to seven times per day.

### Case Study

Patient K is a defense attorney in a busy, prestigious law firm. She has dealt with type 1 diabetes since her diagnosis at the age of 13 years. She was started on an insulin pump in order to level out her blood glucose control and improve her overall health and has been happy with the results. Patient K is invited to play in a softball game prior to the barbeque at the annual neighborhood picnic. She feels it would be a good idea to get a little exercise because she has spent much of the day sitting and relaxing while talking with her friends. In the middle of the game, the patient suddenly becomes weak, diaphoretic, shaky, and confused—clear signs of hypoglycemia.

***Rationale and comments***: *Several factors most likely contributed to Patient K developing hypoglycemia, the most significant being her engagement in exercise (unplanned) prior to eating her meal. In addition, the patient is away from the stress of her job and is relaxing, which is lowering her stress hormones. Together, these conditions are to blame for her hypoglycemic episode.*

## EXERCISE

Individuals on an insulin therapy regimen should have a clear understanding of the risk of hypoglycemia related to exercise. Strenuous or aerobic exercise raises the blood glucose levels initially, but these levels will decrease as the body re-establishes its stores [57]. Although an initial increase in blood glucose levels will be seen, the potential for hypoglycemia can last up to 72 hours after stopping exercise. This is due to the physiologic reaction of fuel mobilization for energy release. When an individual is exercising at maximal levels, the body's energy level demands increase up to 20-fold in comparison to the resting state. In an attempt to maintain homeostasis and prevent hypoglycemia, several regulatory mechanisms are activated. Initially, skeletal muscles break down their own stores of glycogen, triglycerides, and free fatty acids from adipose tissue. In order to mobilize extramuscular stores, hormonal adjustments are essential. In the early phase of exercise, hepatic glucose production is increased by a reduction of insulin levels and unchanged glucagon levels. In subsequent stages, glucagon and catecholamine levels are elevated. As a result, glucose levels in healthy individuals remain fairly constant during exercise. When individuals with diabetes engage in moderate- or high-intensity exercise on a regular basis, however, the result is a decrease in blood glucose levels and increased insulin sensitivity [57]. Helping patients with diabetes to understand this sophisticated balance of fuel and energy metabolism is vital in the prevention of hypoglycemia [1].

EVIDENCE-BASED PRACTICE RECOMMENDATION

Individual glycemic response patterns can differ markedly with exercise; therefore, the Academy of Nutrition and Dietetics recommends that persons with diabetes taking insulin or insulin secretagogues use glucose monitoring and recognition of glucose patterns to make decisions to exercise safely.

(https://www.andeal.org/topic.cfm?menu=5305&cat=5595. Last accessed February 19, 2023.)

**Level of Evidence/Strength of Recommendation**: Consensus, Conditional

## PATIENT ISSUES

Other significant causes of hypoglycemia are patient behaviors and choices. Patient-related risk factors, such as meal timing and accurate administration of medications, are particular concerns when insulin or oral antihyperglycemic agents that increase the production of insulin from the pancreatic beta cells are used [58]. Meal timing is a key component of insulin, sulfonylurea, and nonsulfonylurea insulin secretagogue therapy. Also, vision and manual dexterity are necessary to administer injectable medications and should be assessed in all individuals new to insulin therapy. Likewise, cognitive function is a consideration when caring for persons utilizing any medication, oral or injectable. Rapid-acting oral agents, such as repaglinide and nateglinide, are taken just prior to the first bite of a meal; if short-term memory is an issue, special caution and instructions are required [1]. In many cases, clear and complete patient education may alleviate these factors. However, if cognitive or physical deficits are an issue, involvement of a caregiver and/or the use of adaptive tools may be necessary.

**Case Study**

Patient G is a White man, 85 years of age, with a long history of type 2 diabetes. The nurse conducts a home health care visit for home assessment and medication evaluation. The patient indicates that his blood glucose levels are consistently in the high 200s, including in the mornings and at night. The nurse reviews the medications remaining in his weekly pill box to assess medication adherence and notes that he has been missing multiple medications throughout the week, including the medication to help control his blood glucose levels. Patient G states that when he realizes he has missed the medication, he is afraid to take it. The nurse informs the patient's physician of the findings, and the patient's regimen is changed to repaglinide 2 mg just prior to each of the three biggest meals. The instructions are given to Patient G, and he states understanding and is able to verbalize when to take the medication.

The nurse returns to Patient G's home three days later to assess his tolerance to the new medication. When the nurse arrives at 9 a.m., the patient is in a state of confusion, diaphoresis, and shakiness. His blood glucose level is 48 mg/dL. The nurse provides adequate treatment, and Patient G is then able to help determine what precipitated the episode of hypoglycemia. The patient reports that he took the repaglinide pill at 7:15 a.m., but he had not consumed breakfast. The nurse works with Patient G to develop a plan to avoid skipping meals. They decide that the patient will make his breakfast each day and elicit the assistance of his daughter to remind him to take the repaglinide when she talks to him each morning. The daughter also agrees to check in after lunch and dinner to assure that the patient is taking the repaglinide as he should at all meals.

## TREATMENT OF HYPOGLYCEMIA

Treatment of hypoglycemia is fairly straightforward when the cause is known. When symptoms are mild-to-moderate and the patient is able to communicate and swallow, treatment is usually administered via the oral route. In most cases, hypoglycemia may be reversed by adhering to the 15:15 rule [1]. The 15:15 rule is simply defined as utilizing 15 grams of carbohydrate and rechecking the blood glucose in 15 minutes. If the blood glucose level is less than 70 mg/dL, with or without the presence of hypoglycemia symptoms, another 15 grams of carbohydrate should be administered and the blood glucose level should be checked again [58; 59]. When the blood glucose level is greater than 70 mg/dL, treatment should be stopped. Examples of foods that provide 15 grams of carbohydrate include three glucose tablets (sold in most pharmacies), one-half can of regular soda, 4 ounces of fruit juice, 2 tablespoons of raisins, 1 tablespoon of sugar, or 8 ounces of non-fat milk [1].

It may take up to 30 minutes for complete resolution of hypoglycemia symptoms following treatment. A common mistake when treating hypoglycemia is continuing the administration of glucose regardless of blood glucose levels because symptoms persist. This can lead to overtreatment and rebound hyperglycemia. When the blood glucose level is greater than 70 mg/dL, the individual should consume a snack consisting of a carbohydrate and a protein to prevent rebound hypoglycemia. This snack could include half of a peanut butter sandwich, crackers and cheese, or half of a ham or turkey sandwich [58].

Episodes of severe hypoglycemia, in which the individual has the potential of becoming comatose, combative, and/or unable to swallow, require more direct and immediate treatment [1]. In cases when a person may be combative but still able to swallow, treatment options include administering a tube of glucose gel or 1 to 2 tablespoons of honey into the cheek to raise blood glucose levels [21]. When the individual is no longer able to cooperate or is unconscious, the options decrease significantly. In cases when the individual is in an acute care facility and has an intravenous access line, the treatment is 50% dextrose. The dose of dextrose is calculated using the formula (100 - blood glucose level) x 0.4. This equation will indicate the amount of 50% dextrose in milliliters to be administered intravenously [1].

Although this treatment is very effective, hypoglycemia does not always occur within the hospital or when intravenous access is available. In these instances, the option for treatment is glucagon [58]. Glucagon is a polypeptide hormone typically secreted by the alpha cells of the pancreas. It increases the blood glucose level by stimulating the liver to change stored glycogen to glucose. Glucagon opposes the action of insulin, and it is used as an injection to reverse hypoglycemia and insulin shock in patients with diabetes. Glucagon also increases the use of fats and excess amino acids for energy production [60]. Glucagon can be given intramuscularly, intravenously, or subcutaneously. For individuals who weigh 20 kg or more, the appropriate dose is 1 mg. For children weighing less than 20 kg, the appropriate dose is 0.5 mg or 20–30 mcg/kg. Treatment can be repeated if unsuccessful but should not exceed a maximum of 1 mg for children [50]. In 2019, the FDA approved the first non-injection glucagon therapy for the treatment of severe hypoglycemia in persons 4 years of age or older [67]. The new product is a nasal powder packaged in a single-use dispenser. Glucagon can be kept at room temperature, and it is suggested that it should be available at all times [1].

Treatment of mild, moderate, or severe hypoglycemia in patients who use insulin pumps is similar to the treatment of all patients. However, because insulin pumps administer a rapid-acting insulin analog with a short half-life, removal of the pump may resolve mild-to-moderate hypoglycemia symptoms independent of any other intervention, depending on severity. In cases of severe hypoglycemia, treatment should be provided as described, with the additional need to immediately remove the insulin pump to prevent resistance to hypoglycemia treatment [21].

## PATIENT EDUCATION

Prevention is the best and most effective intervention for hypoglycemia. Hypoglycemia prevention is a key patient education topic and should be discussed at every interaction with the individual. Education should include information regarding oral medication management, insulin therapy, exercise considerations, SMBG, and specific patient-centered issues to maintain safe use of medications in daily life [1]. Many healthcare providers believe self-management education is best completed by a certified diabetes educator prepared to do this type of formal education. This is true, but consistent reinforcement is needed and is best done by each healthcare provider in the form of teachable moments while interacting with the patient [61]. Individuals who actively manage their own diabetes care have better outcomes than those who do not. For these reasons, an educational approach that facilitates informed decision making on the part of the patient is widely advocated [62]. It is important to tailor teaching to an individual's specific literacy and comfort level. This will guide the educational interaction. Encompassing a variety of theories and teaching styles is paramount [63]. Patient education is a vital aspect in preventing adverse effects and detrimental outcomes related to medication therapy with diabetes. Each category of medication is associated with specific instructions to prevent hypoglycemic episodes [1].

For patients receiving medication therapy for diabetes, strategies to prevent hypoglycemia include not skipping meals and eating prior to exercise. Additionally, patients should be advised regarding the proper steps if a medication dose is missed. Most medication preparations should be taken as soon as the missed dose is realized, but there are a few exceptions. If the medication is either repaglinide or nateglinide or if it is too close to the time of the next dose, the missed dose should be skipped [50].

Patients should also receive thorough education related to the signs and symptoms of hypoglycemia [5]:

- Dizziness/lightheadedness
- Numbness or tingling around the mouth
- Palpitations
- Confusion
- Shaking
- Sweating
- Irritability/nervousness
- Hunger
- Headache
- Weakness

These signs and symptoms of hypoglycemia should be stressed at each patient education session.

Patient education regarding the treatment of hypoglycemia consists mainly of reinforcement of the 15:15 rule. It is critical that each patient, as well as the support person or caregiver, is aware of the steps to be taken in cases of severe hypoglycemia, when the individual is unable to swallow and has a potential of choking. In these situations, the only treatment available is an intramuscular injection of glucagon [12].

## ORAL MEDICATIONS

Fundamental topics for all individuals taking a medication to prevent and/or correct hyperglycemia include [1; 50; 58]:

- Adherence to the medication regimen
- Adherence to the meal and exercise regimen
- Importance of wearing medical identification at all times
- Physician notification of frequent hypoglycemia or continued, unresolved hyperglycemia

Sulfonylurea medications should be taken with breakfast or the first main meal of the day to maximize effect and safety [50]. Patients taking a sulfonylurea should also space meals no more than four hours apart and avoid situations when meals have the potential of being missed [1]. Patients may carry a rapid-acting glucose source, such as glucose tablets or gel, in order to swiftly treat the onset of hypoglycemia in the initial stages [50]. Safe alcohol consumption practices are also essential when a treatment regimen includes a sulfonylurea agent [58].

As with the sulfonylureas, timing is essential for the prevention of hypoglycemia when utilizing nonsulfonylurea secretagogues (i.e., repaglinide and nateglinide). Patients should be instructed to take the medication no more than 30 minutes prior to the meal; often, the medication is taken with the first bite of the meal [50; 58]. If a meal is to be skipped, the patient should also skip the prescribed dose of the medication [50].

Patients prescribed acarbose or miglitol require special consideration. These patients (and/or caregivers) should receive instruction regarding the need to take the medication with the first bite of each main meal [50]. Instruction regarding the action of these alpha-glucosidase inhibitors and the prompt treatment of hypoglycemia with simple sugar sources is imperative. Patients also benefit from carrying glucose tablets or gel at all times [58].

## INSULIN

When an individual is being treated with insulin, patient education needs include the signs and symptoms of hypoglycemia, treatment of hypoglycemia, safe preparation of insulin syringes, and meal planning [58]. Healthcare professionals should assess each patient's ability to adequately see the markings on the small insulin syringe. If this cannot be satisfactorily met, visual aids (e.g., magnifiers) or insulin pens should be considered.

Caregivers and close family members or friends should receive information regarding prevention and treatment of hypoglycemia and providing a safe environment for the individual should hypoglycemia occur [1]. Instructions should be provided regarding preparation of glucagon, including how to inject the saline from the prefilled syringe into the glass vial of powdered hormone and appropriate injection sites (e.g., the upper arm, leg, or buttock) [21].

Emphasis on accurate and frequent SMBG and reporting frequent blood glucose levels less than 70 mg/dL to a primary care provider is an essential tool in the education process [22]. Communication between the individual, the certified diabetes educator, and the primary care provider is an optimal approach to incorporate into the education plan [58].

## PHYSICAL ACTIVITY

The greatest potential for exercise-related hypoglycemia occurs when a person is receiving insulin therapy, although it may occur in patients taking oral glucose-lowering medications as well [64]. For these patients, education related to exercise should focus on the assessment of pre-exercise blood glucose levels, consumption of additional carbohydrates as needed, and having a carbohydrate source available if symptoms of hypoglycemia develop. It is also important to note that hypoglycemia risk increases as the duration or intensity of the activity increases. If assessment of blood glucose prior to exercise reveals a level less than 100 mg/dL, the individual should consume 25–50 grams of carbohydrate before engaging in physical activity. If the blood glucose level is 100–180 mg/dL, the patient should consume 10–15 grams of carbohydrate [1]. Patients should avoid exercise when their insulin or medication therapy is at peak effect. Lastly, patients should be advised to inject insulin away from muscles that will be the focus of exercise, as when a muscle is used, blood flow and utilization of glucose transport to the skeletal muscle increase [1].

## NOCTURNAL HYPOGLYCEMIA

Patients who experience or who are suspected of having nocturnal hypoglycemia should be advised to monitor blood glucose levels prior to going to bed. When the blood glucose is less than 110 mg/dL, the patient should consume a snack that includes a carbohydrate and a protein. The specific signs and symptoms of nocturnal hypoglycemia should be explained, including the need to notify the primary care provider of suspected episodes. If an episode of nocturnal hypoglycemia occurs, the patient will be instructed to measure blood glucose levels at 3 a.m.; these levels are useful when creating a treatment plan [1].

## PATIENT BEHAVIORS

Behavioral issues should be an aspect of patient education as well. Meal planning, particularly the need to count carbohydrates and adhere to dietary limitations, should be assessed. A food diary can assist in determining areas of focus for the individual and caregiver when hypoglycemia is occurring and cause is in question [65].

An additional area of educational focus is the issue of safety while driving [66]. The use of appropriate self-care skills and safety precautions should be taught and frequently reinforced in patients who drive. Emphasis should be placed on blood glucose monitoring prior to operation of a vehicle and frequent monitoring (every two hours) while on extended trips. Patients should be advised to refrain from driving when signs and symptoms of hypoglycemia are present [65]. Finally, a rapid-acting glucose source should always be available in the vehicle to treat any signs of hypoglycemia, although tablets should not be stored in the vehicle [66]. As always, wearing medical identification indicating that the patient has diabetes is important [65].

## CONCLUSION

Hypoglycemia is a serious complication of diabetes and is most commonly experienced by patients who use oral medication or insulin to control the disease. In healthy people, hypoglycemia is prevented by a sophisticated interaction of the fuel metabolism and regulation of the body's counter-regulatory hormones. Causes of homeostatic imbalance include overdose of oral medication therapy, excessive insulin therapy, exercise, and inappropriate patient practices.

Recognition of hypoglycemia and knowledge of the treatment are critical concepts for healthcare providers to incorporate into the education plan of all diabetes patients, especially those who have just initiated medication therapy or have been newly prescribed an insulin regimen. Strategically placed assessment questions allow healthcare providers to illicit critical information regarding symptoms and signs the individual or caregiver may not recognize as hypoglycemia.

Finally, communication is essential to the prevention and understanding of hypoglycemia. In addition to the primary care team (i.e., the individual, support person or caregiver, the primary care provider, and the certified diabetes educator), other members may be added to improve care, including an exercise physiologist, registered dietitian, and pharmacist. All members of the education team should provide consistent information regarding the prevention, recognition, and treatment of hypoglycemia at each patient contact. This approach will provide the best possible level of understanding in order to obtain optimal glycemic control and minimize the adverse effects of hypoglycemia.

**Implicit Bias in Health Care**

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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