When is it safe to leave these patients at home?

The number of persons with diabetes in the United States has been rising steadily over the past five decades, and the far-reaching effects of chronic hyperglycemia are staggering.

In this month’s article we will discuss the process of normal glucose metabolism, then review the pathophysiology of hypoglycemia. We will use a case-based approach to explore hypoglycemia in patients with type 1 and type 2 diabetes mellitus. In doing so, we will use the process of working through a differential diagnosis to show how to evaluate and weigh the evidence supporting or opposing hypoglycemia as the etiology of a diabetic emergency and arrive at a working diagnosis prior to obtaining a blood glucose level.

For each case we’ll use information that can be obtained with a thorough clinical exam and a detailed understanding of the history of present illness and past medical history to determine the type of diabetes present as well as precipitating factors for the emergency.

Normal Glucose Metabolism

The pancreas plays an important role in the regulation of blood glucose via the release of regulatory hormones. The pancreas is unique in that it has both exocrine and endocrine functions. The cells of the endocrine pancreas are located in groups called pancreatic islets, or the islets of Langerhans, and account for just 1% of all the pancreatic cells. Each islet contains alpha cells and beta cells. Alpha cells produce and

What the Stats Say

The CDC, in its National Diabetes Fact Sheet, reports that:

- 25.8 million people, or 8.3% of the U.S. population, have diabetes.
- Among U.S. residents 65 and older, 10.9 million, or 26.9%, had diabetes in 2010.
- About 1.9 million people 20 or older were newly diagnosed with diabetes in 2010 in the U.S., and it is estimated that 7 million people are undiagnosed.
- In 2005–08, based on fasting glucose or A1C levels (see sidebar), 35% of U.S. adults 20 or older had prediabetes. Among those 65 or older, the rate rose to 50%. Applying this percentage to the entire 2010 U.S. population yields an estimated 79 million Americans aged 20 years or older with prediabetes.
- Diabetes is the seventh-leading cause of death in the United States.
- Diabetes is a major cause of heart disease and stroke and the leading cause of kidney failure, nontraumatic lower-limb amputations and new cases of blindness among adults in the United States.
secrete the hormone glucagon, and beta cells produce and secrete the hormone insulin. Normal blood glucose levels are considered to be in the range of 70–110 mg/dL.

Insulin is released from beta cells in response to increased levels of blood glucose, as happens after meals (see Figure 1). Insulin is required for and increases the rate of glucose transport into the cells. This results in a decrease of blood glucose levels. After being transported into tissue cells, glucose is used to generate ATP, allowing that particular cell to perform its work and therefore its role in the body. Insulin also increases the rate of glucose transport into muscle and the liver, where it is stored as glycogen, ready to be used in the future when needed. In addition, insulin increases the synthesis of fat in adipose tissue, creating yet another energy store that can be tapped into when blood glucose levels fall.

As blood glucose levels start to fall, the body determines that a “fasting state” has been created and releases counterregulatory hormones in an attempt to maintain the blood glucose levels necessary for normal brain function. These counterregulatory hormones include glucagon, epinephrine, norepinephrine, cortisol and growth hormone. Glucagon has the exact opposite effect of insulin and is secreted by the pancreatic alpha cells when blood glucose levels are low. Glucagon has the effect of mobilizing glycogen stores in the liver and adipose tissues. In the liver, glucagon results in the breakdown of glycogen into glucose (a process termed glycogenolysis), which is then released into the bloodstream, increasing blood glucose levels. Glucagon also results in the synthesis of glucose from non-carbohydrate substrates such as pyruvate, lactate, amino acids and fatty acids in the liver, a process termed gluconeogenesis. In the adipose tissue, stored fats are broken down into fatty acids and released into the bloodstream. These fatty acids can be utilized as an energy source by the body’s cells.

When blood glucose levels decrease, epinephrine is also secreted from the adrenal medulla in an attempt to stimulate numerous metabolic changes to increase blood glucose. Epinephrine binding to alpha-adrenergic receptors in the pancreas inhibits insulin secretion by the beta cells, preventing a further decrease in blood glucose levels. Beta-adrenergic binding in the pancreas increases glucagon secretion by alpha cells, resulting in an increase in blood glucose levels. In addition, epinephrine stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH), which increases lipolysis (the breakdown of lipids into fatty acids) by adipose tissue. As a result of these actions, blood glucose and fatty acid concentrations increase, providing the materials for

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**The A1C Test**

The A1C test is a blood test used to diagnose diabetes mellitus. After diagnosis, it can be used to determine how effectively a patient manages their diabetes. The A1C test reflects a patient’s average blood glucose level over the preceding 2–3 months. It measures what percentage of hemoglobin is glycated (has glucose bound to it). The higher a patient’s A1C level, the poorer their blood sugar control, and the higher their risk of complications.
energy production in cells. In addition to the specific counterregulatory effects, the release of epinephrine also results in the characteristic cool, pale, diaphoretic skin we associate with developing shock.

Diabetes Mellitus

Diabetes mellitus, often referred to simply as diabetes, is the most common disease of the endocrine system. It is actually a group of metabolic diseases in which a state of hyperglycemia (high blood sugar) exists as a result of inadequate insulin secretion from the pancreas, inadequate cellular response to the body’s natural insulin, or both.

The National Diabetes Data Group (NDDG) defines four major classifications of diabetes mellitus: type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, and other specific types. 2 Worth noting is that the other specific types include no fewer than 45 specific disease, genetic or drug- or medication-induced processes that can result in hyperglycemia.

Type 1 diabetes accounts for about 10% of all cases in the U.S. and occurs secondary to loss of insulin-producing beta cells located in the islets of Langerhans in the pancreas. It is characterized by decreased insulin secretion but a normal cellular response to insulin. It can occur in children and adults, and most often (90% of all cases of type 1 diabetes) occurs secondary to an autoimmune response during which the body’s immune system produces antigens that mistakenly target pancreatic beta cells for destruction by immune system T-cells. Once destroyed, beta cells do not regenerate. The rate of beta cell destruction can be variable, resulting in a rapid onset of the disease in some patients (mainly children) and a more gradual onset in others (mainly adults). Cellular sensitivity and responsiveness to insulin remain normal in type 1 diabetes; the issue is that there is not enough circulating insulin to maintain homeostasis. Patients with type 1 diabetes may require the administration of insulin to maintain normal glucose blood levels. These facts have led to the elimination of use of the terms insulin-dependent diabetes mellitus and juvenile-onset diabetes mellitus. 3

Type 2 diabetes is characterized by insulin resistance at the target tissues and usually also by a relative decrease in insulin secretion. Insulin resistance is a term used to describe the situation in which tissues require higher levels of insulin and therefore higher-than-normal plasma concentrations of insulin to maintain normal intracellular and blood glucose levels. Patients with type 2 diabetes typically do not require insulin treatment to survive, but do require medication to increase the secretion of insulin or decrease insulin resistance at the target tissues. As is the case with type 1 diabetes, the traditional terms non-insulin-dependent diabetes mellitus and adult-onset diabetes are no longer used to describe type 2 diabetes, as the type 2 diabetic may indeed require insulin, and it can occur in the juvenile patient. Obesity is a major risk factor for type 2 diabetes, and increasing numbers of young patients are developing the disease as obesity increases in this population.

Case 1: AMS in a Type 1 Diabetic

You and your partner, both EMTs, are dispatched to a local shopping mall for a patient with altered mental status. You arrive to find a 52-year-old male sitting in a wheelchair in the care of his wife. She reports the patient “was fine a half hour ago, but is not acting like himself now.” During your primary exam you note the patient is conscious and knows his name but is confused as to time, place and event. He is able to follow commands. He has a strong and rapid radial pulse, and his skin is cool, slightly pale and slightly diaphoretic. His respiratory rate is normal with a good tidal volume, and he is in no respiratory distress. When asked about a chief complaint, he repeatedly responds, “I don’t know what happened.” You immediately radio dispatch and request ALS support.

The patient’s wife informs you he is a type 1 diabetic and he ate his normal breakfast this morning and took his usual dose of insulin. She further states that
he is routinely compliant with his diet and insulin treatments and has not had “any issues with his sugar for a couple of years.” Your physical exam does not reveal any signs of trauma. You note that his pupils are slightly dilated bilaterally, equal and reactive to light. His lung sounds are clear and equal bilaterally. He has no facial droop, his speech is not slurred, and he has no neurologic deficits. While examining his lower extremities, you determine he has cellulitis on his left lower leg extending from his foot to midway up the calf. You also note an ulcer on the dorsal surface of his foot that appears to be infected, with a purulent discharge from the wound. The patient’s wife says the ulcer is chronic but that the infection and cellulitis “have gotten worse over the past couple of days.”

His vital signs are heart rate 102/min, strong and regular; blood pressure 132/84 mmHg; respiratory rate 12/min with good tidal volume; and pulse oximetry 97% on room air.

Your local scope of practice as an EMT does not include the use of a glucometer to determine the patient’s blood glucose level, but local protocol allows administration of oral glucose. You determine the patient is able to both protect his airway and follow commands, then have him self-administer 15 g. Within five minutes you note he is now alert to person, place and time. You explain to the patient that he had an episode of hypoglycemia and suggest he go to the emergency department for evaluation. He thanks you for responding and correcting it, but says he does not wish to be transported at this time.

Questions:

- Prior to the patient’s improvement with the administration of glucose, what would have been your best guess as to which was more likely, hypoglycemia or hyperglycemia?
- What is the prehospital management of the conscious patient with hypoglycemia?
- What criteria should be met in order to support this patient’s wish to refuse transport?

DISCUSSION

Hyperglycemia and hypoglycemia are both complications associated with type 1 diabetes. Hyperglycemia often occurs when a diabetic does not take their insulin or takes a dose inadequate to properly control blood glucose levels. A number of particulars in this case strongly suggested that hypoglycemia, not hyperglycemia, was the cause of this diabetic’s altered mental status. Specifically, the patient was a type 1 diabetic who had been compliant with his insulin, had a recent onset of infection, experienced an acute onset of...
Hypoglycemia is a frequent problem in patients with type 1 diabetes and should immediately be considered in all patients with altered mental status and a history of type 1 diabetes. Hypoglycemia can occur secondary to a number of factors, including missing a meal, an overdose of insulin or oral antihyperglycemics, other drug overdoses (Table 1), increased energy demands or disease (Table 2).4

This patient’s foot infection and cellulitis would cause increased metabolism and subsequent increased energy demand, resulting in increased glucose utilization and the risk of hypoglycemia. In such cases, maintaining a normal dietary intake and insulin regimen may prove insufficient to maintain adequate blood glucose levels. Infections are common for patients with Type 1 diabetes. Maintain a high index of suspicion and look for infection sources.

Prehospital providers should attempt to identify a source of infection in the diabetic patient with hypoglycemia.

Foot ulcers and cellulitis are common complications of diabetes and occur secondary to both the peripheral vascular insufficiency and peripheral neuropathy common with it. The peripheral neuropathy results in decreased pain sensation in the feet, allowing minor trauma and ulcer formation to occur unidentified. Peripheral vascular insufficiency then leads to a decreased ability to fight infection. Other infections that can precipitate hypoglycemia and should be identified include pneumonia and sepsis.

The acute onset of this patient’s AMS, reported by his wife, is another indication that hypoglycemia, not hyperglycemia, is the cause. Both hypoglycemia and hyperglycemia can result in AMS. The onset of AMS associated with hypoglycemia tends to be rapid, taking place over minutes to hours. This is because the AMS associated with hypoglycemia is a result of the rapid depletion of glucose, and the brain is often the first organ affected. The onset of AMS associated with hyperglycemia tends to be more gradual, taking place over days or even weeks.
logic symptoms characteristic of hypoglycemia include bizarre, uncharacteristic or combative behavior, seizures and coma.

The signs of sympathetic nervous system activation, specifically the patient’s tachycardia, dilated pupils and cool, pale, diaphoretic skin, are also characteristic of hypoglycemia. Recall that epinephrine is released in response to decreased blood glucose concentrations. Epinephrine is not released in response to hyperglycemia, so the signs and symptoms of epinephrine release strongly suggest that hypoglycemia is present. Other signs of epinephrine release include tremors, nervousness and palpitations.

Treatment for this patient can be achieved at the BLS level with the administration of oral glucose, as he is conscious and able to follow commands, reducing the risk of aspiration. This can be accomplished by administering a commercially available oral glucose preparation, typically 15 g of glucose in gel preparations or 4 g in tablet form, or by having the patient consume a sugar-containing beverage or food. Note that in many areas the presence of AMS in a known diabetic is an indication for the administration of oral glucose; an exact blood glucose determination with a glucometer is not necessary.

Very often a patient who has their hypoglycemia treated in the field will refuse transport to the ED for evaluation. In fact, many of these patients are at relatively low risk for a recurrence as long as some criteria are met. First, determine that the patient is indeed conscious, alert and oriented to person, place, time and event. A patient with AMS cannot make an informed decision regarding transport to the ED and should be transported under the principles of implied consent.

Then determine if a nonpathologic explanation exists for the episode of hypoglycemia. For example, did the patient take their normal dose of insulin or oral antihyperglycemic medication and skip a meal or eat less than normal? Doing so will often result in hypoglycemia. Did the patient exert themselves more than normal, increasing metabolic demand and depleting their blood glucose? These scenarios do not necessarily require transport to the ED. A precipitating factor for the patient in this case appears to be an infection on his foot and leg, which is a very good reason he should be evaluated in the ED. He will need treatment for his infection.

In addition, any patient who refuses transport should be encouraged (if not required), preferably in front of the EMS crew, to eat a meal or snack consisting of protein, carbohydrates and fats, such as a sandwich. This will help prevent rebound hypoglycemia that can develop after administration of glucose. Eating a snack or meal containing complex carbohydrates, protein and fat will ensure a steady digestion and supply of blood glucose. Examples of such foods are an energy bar, leftover meal or peanut-butter-and-jelly sandwich.

An analogy can be drawn between nutrients and blood glucose and fuel for a fire. Oral glucose and carbohydrates, fats and proteins are to blood glucose levels what gasoline and logs are to a fire. Pour gasoline onto a fire, and it burns very hot and quick. Administer oral or IV glucose, and blood glucose levels rise quickly but then lower quickly as the simple sugar is used up. Place logs on a fire, and it burns more slowly, maintaining blood glucose levels for a longer time.

To summarize, always ensure the patient who refuses transport to the ED after the administration of glucose eats a nutrient-rich snack or meal. In addition, try to ensure that the patient who has experienced an episode of hypoglycemia and refused transport has someone with them who can call for EMS should the problem recur. They should not be left alone.

**Case 2: Hypoglycemia in a Type 2 Diabetic**

You, a paramedic, and your partner, an EMT, are dispatched to an unconscious person at a residential address. A 42-year-old female presents lying supine on a couch with snoring respirations, unresponsive to verbal stimuli. She opens her eyes and looks at you when you apply...
painful stimuli, but promptly becomes unresponsive if not kept stimulated. Your partner opens her airway with a head-tilt chin-lift and jaw thrust, and you insert a nasopharyngeal airway (NPA) to help keep it open. You note that her respiratory rate and tidal volume are normal, and she has a strong, rapid, regular radial pulse. Her skin is cool, slightly pale and slightly diaphoretic. Your administer oxygen via nasal cannula at 2 lpm. Her husband says she’s “not been feeling well and has an appointment to see her physician tomorrow.”

The patient has a history of type 2 diabetes, and her husband says she’s been compliant with her glipizide. He noticed this morning that she was developing an altered mental status, and he called EMS when he was unable to easily wake her from sleep. A secondary exam reveals that her mucous membranes are dry and she has poor skin turgor. Vital signs are heart rate 112/min, strong and regular; blood pressure 104/60 mmHg; respiratory rate 14/min with good tidal volume; and pulse oximetry 94% on room air. It increases to 100% on 2 lpm via nasal cannula.

You perform a finger stick and find her blood glucose to be 32 mg/dL. The cardiac monitor reveals a sinus tachycardia, and you initiate IV access with an 18-gauge angiocath to her left antecubital region and hang a 500 mL bag of normal saline with a macrodrip set flowing KVO. You also give 25 g of D50W and remove the NPA as the patient starts to regain consciousness.

By the time you’ve finished administering the D50W, the patient wakes up and is conscious, alert and oriented to person, place and time. A repeat BGL shows a value of 324 mg/dL. The patient informs you that she’s had a two-day history of pain with urination and suspects she has a urinary tract infection. She also says she’s not been drinking as much water as she should and is “probably a bit dehydrated.” You note her mucous membranes are dry. She confirms she has an appointment with her physician at 0900 the next day. Repeat vital signs are heart rate 100/min, strong and regular; blood pressure 108/62 mmHg; respiratory rate 12/min with good tidal volume; pulse oximetry 97% on room air.

You offer to transport the patient to the ED for evaluation, but she refuses. She says she believes this was an isolated incident. She realizes her illness will increase her risk of hypoglycemia due to increased metabolic demand, so she will eat more than usual. She also points out that her husband will be with her until she sees her physician tomorrow, and he can call EMS should problems recur.

Questions
• What is the prehospital management of the unconscious patient with hypoglycemia?
• Can you think of a strong argument as to why this patient should be transported to the ED for evaluation?

DISCUSSION
Creating and maintaining a patent airway and ensuring adequate ventilation and oxygenation are priorities in patients who present with an altered level of consciousness.

This patient presented with hypoglycemia that resulted in a decreased LOC that subsequently interfered with her ability to maintain an open airway. Her snoring indicated her tongue was acting as an airway obstruction. This was corrected with a combination of a manual airway maneuver and BLS airway adjunct.

The use of the NPA was a good idea, as patients who are arousable with painful stimuli often have an intact gag reflex, which is a contraindication for use of an oropharyngeal airway (OPA). In addition, an NPA is particularly handy in a patient (such as a diabetic with hypoglycemia) in whom you expect the level of consciousness to improve. If an OPA had been used with this patient, her gag reflex would have been stimulated at some point as her LOC improved, and she may have gagged or even vomited, potentially compromising the airway. This was avoided with the use of an NPA, which will not stimulate the gag reflex.

Ventilation assistance with a bag-valve mask was not necessary, as her ventilation was adequate. Administer oxygen to all patients with a diminished LOC or AMS; here the administration of 2 lpm of oxygen via nasal cannula was enough to improve her oxygen saturation.

If a patient with hypoglycemia has a decreased level of consciousness, cannot follow commands or is a risk for aspiration for any other reason, give D50W IV at a dose appropriate for the age group (Table 3). Take care to ensure the IV line is patent and no extravasation is present. Glucose preparations, especially D25W and D50W, are hyperosmolar and can cause significant ischemia and necrosis if allowed to infiltrate surrounding tissue.

If a hypoglycemic patient cannot take oral glucose and IV access cannot be established, glucagon can be administered via the intramuscular or subcutaneous routes. The onset of action is fairly rapid, about 10–20 minutes, and peak blood glucose levels are reached in about 30–60 minutes.3 Glucagon can also be administered IV, and 1 mg has an effect on blood glucose levels equivalent to about 25 g ampule of D50W.3 As discussed above, glucagon increases blood glucose levels by stimulating

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<thead>
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<th>Medication</th>
<th>Age group</th>
<th>Dose/concentration</th>
<th>Route</th>
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<tbody>
<tr>
<td>Glucose</td>
<td>Adult</td>
<td>25–75 g</td>
<td>D50W IV</td>
</tr>
<tr>
<td></td>
<td>Child</td>
<td>0.5–1 g/kg</td>
<td>D25W IV</td>
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<tr>
<td></td>
<td>Neonate</td>
<td>0.5–1 g/kg</td>
<td>D10W IV</td>
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<tr>
<td>Glucagon</td>
<td>Adult</td>
<td>1–2 mg</td>
<td>IV, IM, SC</td>
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<tr>
<td></td>
<td>Child</td>
<td>0.025–0.1 mg/kg</td>
<td>IV, IM, SC</td>
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Criteria for Allowing Hypoglycemic Patients to Refuse Transport/Follow-up

• The patient is conscious, alert and oriented x 4.
• There is an identifiable nonpathologic cause of the hypoglycemic episode.
• The patient does not take oral antihypoglycemics.
• There is no concurrent illness or infection.
• The patient is able to eat a meal.
• The patient will not be left alone.

Table 3: TREATMENT FOR HYPOGLYCEMIA

<table>
<thead>
<tr>
<th>Age group</th>
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glycogenolysis in the liver. As such, glucagon would be ineffective at correcting hypoglycemia in any patient who has diminished glycogen stores, as in patients with alcohol-induced hypoglycemia.

IV access was obtainable in this patient, 25 g of D50W was administered, and the patient regained consciousness. When the question of transport to the ED arose, she offered a valid argument for not going. However, the patient should be advised that diabetics who use sulfonylurea antihyperglycemic agents are at particular risk for prolonged, severe and recurring episodes of hypoglycemia.⁴

Sulfonylureas are a class of medication widely used in the treatment of type 2 diabetes and promote the increased secretion of insulin from the pancreas. Medications in this class include chlorpropamide, glipizide and glibenclamide (glyburide). Any impairment of liver or kidney function will decrease clearance of the drug, increasing plasma concentrations and the risk of hypoglycemia. The patient in this case had a UTI and reports drinking less water than she should. In addition, her elevated heart rate, low blood pressure and dry mucous membranes are characteristic of dehydration. Both a UTI and dehydration could by themselves affect kidney function sufficiently to result in decreased clearance of her glipizide. Consequently, her blood levels of glipizide could increase and result in episodes of hypoglycemia.

In addition to impaired liver or kidney function, an overdose of a sulfonylurea will result in an oversecretion of insulin, elevated blood insulin levels and hypoglycemia. In addition to glucose administration, these patients require treatment with a medication to inhibit further insulin secretion (such as octreotide, a somatostatin analog) and subsequent lowering of blood glucose levels. Metformin (Glucophage) and oral agents in the thiazolidinedione class, common medications used in the treatment of type 2 diabetics, have a different mechanism of action than the sulfonylureas and rarely cause significant or prolonged hypoglycemia.

While in many cases it is relatively safe to support a patient’s desire to refuse medical care, in this case providers should strongly advocate for evaluation in the ED. The risk of recurring, severe and prolonged episodes of hypoglycemia must be made perfectly clear. If a patient does not meet the criteria for declining transport (see sidebar) and you feel they should be evaluated by a physician, contact medical control, give a report and produce documentation that clearly demonstrates the patient refused transport against medical advice.

REFERENCES

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