Both hypoglycemia and hyperglycemia are true medical emergencies. As we discussed last month, hypoglycemia often has a rapid onset and can impact any patient whose body is not provided an adequate glucose supply. While anyone can experience hypoglycemia, it is most common in patients who have been diagnosed with diabetes and whose natural insulin does not function normally.

Patients with diabetes also risk developing hyperglycemia, a complex and dangerous metabolic derangement that can be fatal without proper care. The American Diabetes Association says that in 2011 there were a staggering 25 million patients with diabetes and 79 million with pre-diabetes across the United States.

This month’s CE article explores the consequences of hyperglycemia on the body and the life-threatening emergencies it can cause.

Diabetic Disease Progression

Recall that insulin secretion is stimulated by eating. Insulin secretion is not stimulated between meals, and a decline in the body’s blood glucose levels inhibits the pancreatic islets’ insulin secretion and stimulates the secretion of glucagon, which allows glucose levels to remain in a normal range. Figure 1 demonstrates the relationship between blood glucose levels and the pancreas.

With the exception of very few organs, such as the brain and the kidneys, the body’s tissues require insulin for glucose to pass through the cell walls. For patients with diabetes mellitus (DM), either their pancreas doesn’t produce enough insulin or their insulin is not functioning...
properly; without oral medications or injected insulin, the body's tissues are unable to move glucose from the bloodstream into the cells, and dysfunction can ensue.

Glucagon is also released as the cells release chemical signals indicating they are not getting enough glucose. The patient may experience hunger because the cell's signals indicate a lack of glucose despite the fact that there really is an adequate supply; it just cannot be moved into the cells. For patients with DM, this perceived lack of glucose can lead to blood glucose levels rising dangerously high without the body being able to use or benefit from its presence.

Regularly experiencing rising glucose levels is harmful to the body. Diabetic retinopathy is the leading cause of blindness for individuals aged 25–74, with an annual incidence of 65,000. When patients regularly experience abnormal glucose metabolism and elevated blood glucose levels, chronic increased blood viscosity and a shunting of excess glucose into intracellular pathways result in the production of harmful alcohol-based byproducts. In the retinal capillaries these byproducts degrade the capillary walls, leading to "outpouching" or micro-aneurysms, as well as a breakdown of the capillaries' cell walls. Weakening the cell walls causes fluid shifts within the retina and a thickening of the cell walls. Over time blood flow can become inadequate, and the retina and nerves within the eye can experience hypoxia and eventually necrosis. This can manifest anywhere on the spectrum from blurred vision to vision loss.

Nearly 50% of patients with diabetes mellitus experience some form of diabetic neuropathy, which is progressive nerve fiber function loss and peripheral nerve dysfunction in the presence of diabetes. Nerve dysfunction impairs a patient's
sensory and motor functions and can also impair autonomic nervous system functions. Neuropathy is exacerbated by peripheral vascular disease. The irregular fluctuations in blood glucose levels harm distal capillaries and break down the cell walls over time, resulting in poor perfusion of the distal tissues. Diabetic-induced peripheral vascular disease (PVD) is a particular problem in the hands and feet. Larger vessels are also affected by PVD, becoming stiff as the vessel walls thicken from years of transporting blood viscous from increased glucose levels. Combined, neuropathy and PVD lead to an overall decreased quality of life and put patients at risk for falls, ulcers, dysrhythmias and ileuses.

The exact mechanism for diabetic neuropathy is unclear but appears to be exacerbated by hyperlipidemia, hypertension, smoking and obesity. Prehospital providers are unlikely to diagnose diabetic neuropathy but are likely to see its manifestations as patients present with impaired fine motor function, extremity tremors, tripping and toe dragging, and complaints of progressive limb weakness over extended periods of time.2

Asymmetrical diabetic neuropathy is not uncommon and presents with one extremity weaker than its pair. Do not confuse this with stroke-like symptoms that have a sudden onset and are likely to affect an entire side of the body rather than just one extremity.

In reality, diabetes impacts every one of the body’s organ systems. Diabetic neuropathy impairs nerve function and the patient’s ability to sense injury. One consequence is that wounds can go unnoticed, unmanaged and risk infection as PVD results in decreased blood flow to the extremity and thereby delays healing. Foot infections are the single most common problem diabetic patients experience.3 These can impact the bones, skin and soft tissues of the foot, and when combined with peripheral vascular disease and kidney dysfunction can lead to complications ranging from amputation to severe sepsis.3 Infections stress the body’s metabolism and in both diabetic and nondiabetic patients can lead to hyperglycemic emergencies. In one study of patients with sepsis, hyperglycemia developed in 20% of nondiabetic patients and 70% of those with diabetes.4

**Hyperglycemic Emergencies**

Patients with diabetes mellitus must manage their blood sugar levels daily. When they fail or suffer another illness, they risk developing one of two serious metabolic derangements: hyperosmolar hyperglycemic state (HHS) or diabetic ketoacidosis (DKA). They are similar in presentation, with their biggest differences...
being the severity of their dehydration and the patient’s level of acidosis.

Patients without diabetes can still develop hyperglycemic emergencies. As many as 40% of patients diagnosed with HHS will have no prior diabetic history. Diabetic ketoacidosis presents in newly diagnosed and previously unknown diabetic patients in 15% of cases. A recent study also demonstrated the benefit of routinely determining blood sugars in patients with suspected infections, particularly pneumonia. In this 2,124-patient study, 67% developed stress/illness-associated hyperglycemia requiring treatment. Additional studies have demonstrated that severe body stresses, including severe sepsis, surgery and trauma, can all trigger hyperglycemia, and this hyperglycemia predicts an increased mortality.

Both HHS and DKA are fairly common, with HHS affecting roughly 1 in 500 patients with DM and DKA accounting for 50% of diabetic-related hospital admissions for patients under 19. The latter demonstrates that DKA is more common in younger patients; it most commonly presents in patients younger than 20, while the median age of a patient with HHS is 60. More attention is given to DKA in most prehospital and emergency medicine settings, though its 2% mortality is significantly lower than the 20% with HHS.

When a patient with diabetes becomes ill, such as with an infection, their body is stressed worse than other patients’ because the illness-induced increased metabolic demand alters their insulin and glucose needs. Specifically their body needs additional glucose and insulin, and the amount by which the need changes is difficult to anticipate. This increased metabolic demand is also complicated by increased fluid loss, placing the diabetic patient at risk for blood glucose elevation.

For diabetic patients, challenges eliminating glucose via the kidneys complicate their illness. When blood glucose levels are normal, the kidney filters and reabsorbs glucose as a normal part of renal function. As glucose levels exceed 180 mg/dL, the renal tubules become saturated with glucose, and additional reabsorption is not possible. Glucose remains in the renal tubules, which causes additional water and electrolytes to diffuse into the renal system and be excreted as urine. This process is known as osmotic diuresis. Osmotic diuresis leads to excessive urine production and a profound decrease of the total body water level; patients can be dehydrated by up to 9 liters. With the excessive urine production patients also experience electrolyte loss, and their dehydration exacerbates the hyperglycemia.

**Hyperosmolar Hyperglycemic State**

This complex cascade of events leads to a hyperosmolar hyperglycemic state where patients have dangerous hyperglycemia and their blood serum is dangerously hyperosmolar. Hyperglycemia is present whenever blood glucose levels rise above 250 mg/dL. Hyperosmolarity describes a state of increased osmotic pressure. Osmotic pressure refers to the amount of “pull” fluids experience between the two sides of a semipermeable membrane. There is always some osmotic pressure between these sides, and fluids shift from areas of lower osmotic pressure to areas of higher osmotic pressure. As osmotic pressure increases, fluids shift in greater volumes and with greater force.

Osmotic diuresis is an example of what happens in a hyperosmolar state. Because of excess glucose in the renal tubules, there is a greater force pulling fluids out of the bloodstream and into the renal system than the body would normally experience. Excessive
glucose in the bloodstream also creates an increased osmotic pressure compared to the intracellular and extracellular spaces and causes fluids to shift from the cells into the bloodstream, dehydrating the cells. When the osmotic pressure is normal, fluids can shift freely back and forth between the bloodstream and these other spaces. In hyperosmolar conditions fluids only shift into the bloodstream, leaving the extracellular and intracellular spaces fluid-deprived.

HHS was previously known as hyper-osmolar hyperglycemic non-ketotic coma (HHNC). This phrasing was dropped, as fewer than 20% of patients with HHS experience a decreased level of consciousness. The most important feature distinguishing HHS from diabetic ketoacidosis is that acidosis does not develop; the reasons for this are unknown.

Typically HHS develops slowly over several days and may take many weeks before symptoms become apparent. This slow onset promotes the slow and profound dehydration patients can experience. During this time both hyperglycemia and hyperosmolality drive a fluid shift that leads to intracellular dehydration and loss of electrolytes. The two most significant electrolytes depleted are sodium and potassium. Their elimination is accelerated by increased osmotic diuresis, or excessive urination.

Patients with HHS experience blood glucose levels in excess of 600 mg/dL and can exceed 1,000 mg/dL. The relative slow onset of HHS permits the slow development of profound dehydration. This can lead to focal and global neurologic deficits, including loss of fine motor skills, tremors and in severe cases seizures and mental status changes.

Table 1 highlights the neurological changes common in HHS. The body’s serum osmolarity shifts during HHS from the normal baseline of 280–290 mOsm/kg (a narrow range) to more than 320 mOsm/kg. This is a significant change that causes a strong pull of fluids from the extra- and intracellular spaces into the bloodstream, thus enhancing fluid availability for elimination via the kidneys.

Laboratory data is not typically available to prehospital providers but is available for most teams completing interfacility transports. A review of the lab data for patients with HHS should demonstrate that their pH is greater than 7.30 (normal is 7.35–7.45), which is only slightly more acidic than normal. This
is because patients tend to compensate well in HHS, and profound acidosis does not develop. Bicarbonate, a key part of the body's buffer system, is normally 22–26 mEq/L and in HHS can be low (because it is being used to maintain the patient's pH) but will be greater than 15 mEq/L. Hold on to these values for now, and compare them to the values found in patients with DKA. Finally, patients with HHS present with hyponatremia and hypokalemia.³

It is extremely important to identify the underlying illness that triggered HHS. While prehospital providers may not always be able to accomplish this, it is still important to be a detective and look. Infections such as pneumonia, upper respiratory system infections and sepsis, GI distress, and drug abuse can all cause HHC, as can the illnesses listed in Table 2. Stroke and myocardial infarction are both on the list; always consider these as contributing factors to hyperglycemic states until they can be ruled out. Always perform a 12-lead EKG and stroke assessment on patients with hyperglycemia.

**Diabetic Ketoacidosis**

Diabetic ketoacidosis is an acute life-threatening emergency most common in patients with diabetes mellitus. It is diagnosed with uncontrolled hyperglycemia and the presence of ketoacidosis and defined by a serum ketone level greater than 5 mEq/L and a blood sugar over 300 mg/dL. One of the significant differences between DKA and HHS is the onset: DKA's is rapid and develops within just a few days. DKA is most commonly caused by poor compliance with prescribed insulin administration. The causes of DKA are highlighted in Table 3.

Physiologically DKA is a complex metabolic state that begins when a patient has a relative or absolute insulin deficiency as well as an increased presence of the counterregulatory hormones glucagon, cortisol and epinephrine. In this respect, and in the hyperosmotic state created by elevated blood sugar, DKA is quite similar to HHS. However, while the body's pH in HHS is relatively normal, acidosis rapidly sets in during DKA as liver metabolism transitions to using free fatty acids as an alternative energy source. When free fatty acids are

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**Table 2: Common Hyperosmolar Hyperglycemic State Triggers**³

- Alcohol and drug abuse
- Anesthesia
- Burns
- GI hemorrhage
- Hypothermia
- Infections (UTIs, pneumonia, etc.)
- Intracranial hemorrhage
- Myocardial infarction
- Pancreatitis
- Pulmonary embolism
- Stroke
- Medications, including:
  - Antiepileptics
  - Antihypertensives
  - Antipsychotics
  - Beta blockers
  - Corticosteroids
  - Diuretics

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metabolized, ketogenesis leads to an accumulation of ketones and keto acids. The body can regulate and break down ketones and keto acids for a finite period, but if there is still an insulin shortage as this period passes and ketones are still being produced, they then rapidly accumulate in the bloodstream. The accumulation triggers nausea and vomiting and produces the fruity-odor breath characteristic of patients with DKA. Osmotic diuresis develops similar to in HHS and is exacerbated by the vomiting. Because the onset of this state is more rapid in DKA, dehydration is not as profound as in HHS but can still exceed 6 liters of fluid loss.

Some of the differences between HHS and DKA become evident when comparing the patient’s anticipated lab value findings. Diabetic ketoacidosis presents with a pH of less than 7.30 and a bicarbonate less than 15 mEq/L. These values signify that the body is becoming depleted of bicarbonate, a valuable acid buffer, and is unable to maintain a normal pH. Moderate DKA develops when the pH drops below 7.2 and the bicarbonate below 10 mEq/L. Severe life-threatening DKA is present when the pH is less than 7.1 and the bicarbonate is less than 5 mEq/L. These last patients are on the precipice of death.

In many respects DKA and HHS present similarly. It is reasonable to anticipate weakness, fatigue and malaise. Mental status changes are common, including confusion and disorientation. However, a decreased level of consciousness is rare. In addition, patients with DKA are likely to experience nausea and vomiting as well as diffuse abdominal pain. Because profound dehydration is common, anticipate poor skin turgor. Finally, look for the hallmark symptoms of DKA: polyuria (excessive urination), polydipsia (excessive thirst), a fruity odor on the breath (from ketones) and tachypnea.

Anticipate profound tachypnea in patients with DKA, it is a compensatory mechanism to regulate acidosis. If the patient’s respirations are slowed and returned to a normal rate, their acidosis could rapidly worsen.

Examining the Hyperglycemic Patient

The assessment of any patient with an acute illness requires a holistic approach. Avoid being sucked into only focusing on one complaint or body region.

Begin with a thorough history. Valuable information can be obtained here, including the presence of a diabetic

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**Table 3: Triggers for Diabetic Ketoacidosis**

| • Bacterial infection       | • Pneumonia       |
| • Idiopathic               | • Poor insulin compliance (25% of cases) |
| • Medications (corticosteroids) | • Surgery |

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history. Remember, though, that a history of diabetes is not required for a patient to develop hyperglycemia. If the patient has diabetes, determine what form and if they are compliant with their medications.

A typical OPQRST assessment can help you understand the progression of your patient’s current complaints. An increased length of illness may lead toward HHS if blood glucose is later found to be elevated. While interviewing the patient, be sure to determine the frequency of their urine output, not just when they went last; also determine how their fluid intake has compared to urine loss. Good detective work can help predict the amount of loss. Inquire about recent weight loss; every 1 kg or 2.2 lbs of body mass loss equals roughly 1 liter of total body fluid loss. Pay particular attention to signs of underlying illness or infection. With any cardiac-associated complaint, be sure to also perform a 12-lead EKG when allowed. Also, never hesitate to complete a neurological examination.

Early and regular vital sign monitoring is essential. Expect tachycardia and tachypnea, as they are compensatory mechanisms of hyperglycemia and dehydration. When a patient experiences hyperglycemia, additional metabolic acids are produced, and the body wants to eliminate these as quickly as possible. Increased respirations are the fastest method, as carbon dioxide is exhaled and eliminated with each breath. Tachycardia develops as the dehydrated cardiovascular system works harder to continue transporting oxygen and nutrients to the body’s tissues with a decreased volume. Both develop early in illness progression.

While tempting, orthostatic vital signs are not predictive of volume status and will not help you in your differential diagnosis. An important yet often forgotten vital sign is core temperature. Be sure to obtain one if possible whenever evaluating a patient with a diabetic-related complaint. Elevated temperatures suggest an infectious etiology of underlying illness. Decreased core temperatures also suggest an underlying illness but carry a grave prognosis.

While orthostatic vital signs do not help predict fluid volume status, there are symptoms to look for. Evaluate skin turgor by pinching the patient’s skin lightly. If it has a healthy fluid level, it should return to its normal position within about a second. When dehydrated, elasticity is lost, and the skin will experience a delayed return to its resting position. If the pinched skin stays elevated for longer than 2 seconds following release, it is said that skin turgor is poor.

Blood glucose determination is essential in hyperglycemic emergencies. The glucometers used at patient bedsides are regulated by the FDA and CLIA as waived point-of-care testing devices. Waived devices do not require the same preci-
sion as laboratory devices. An awareness of this is important because these "waived" glucometers are typically calibrated to be within 20 mg/dL. This means that a BGL of 72 could really be between 52 and 92 mg/dL. Additionally most waived glucometers can only provide results for blood sugars up to 600–700 mg/dL. Patients with HHS often have blood sugars over 800 mg/dL and it is not uncommon to see values exceeding 1,000 mg/dL in severe cases. DKA tends to present with lower, though elevated, blood sugars from 300 mg/dL up.

Management

Whenever treating hyperglycemia the primary intervention goals are the same: stabilize and normalize blood glucose; rehydrate; maintain electrolyte homeostasis; and treat the underlying condition. The management of diabetic ketoacidosis has additional treatment goals of acid-base normalization and early insulin administration.

Suspected or known hyperglycemia is an advanced life support call. BLS management is supportive in nature and includes oxygen via nasal cannula, early access to ALS and rapid transport to an emergency department. Advanced providers need to initiate cardiac monitoring early during patient care. Perform a 12-lead EKG to rule out STEMI. Additionally, continuous cardiac monitoring is essential to monitor for profound electrolyte abnormalities, particularly hypokalemia.

Manage the airway and breathing carefully. It is common to observe hyperventilation in patients with hyperglycemic emergencies, as the patient’s body is eliminating excess carbon dioxide to try to maintain a normal pH. These increased respiratory rates are a critical compensation mechanism and need to be supported. As necessary, provide oxygen to maintain an SpO₂ between 92%–96%.

As early as possible, advanced providers should establish IV access and initiate a fluid bolus of normal saline. Remember, patients can be dehydrated by as many as 9 liters, and in-hospital care will strive to replace at least half the fluid deficit within 12 hours, and up to 2 liters in the first 2 hours. When patients are experiencing HHS, aggressive fluid
replacement may be enough to correct hyperglycemia. When DKA is suspected, first-hour fluid administration can be increased to 3 liters of normal saline. Keep in mind that most patients in DKA are children; for children, initiate 20 mL/kg of normal saline to be administered over the first hour.

The potential benefit of prehospital insulin by paramedics has been long discussed and rarely implemented. In HHS, all patients will eventually need IV insulin. However, IV insulin is initially contraindicated because if insulin is administered prior to fluid replacement, it is likely to drive glucose, potassium and water into the cells at a rate that can cause circulatory collapse and life-threatening hypokalemia. Insulin is administered earlier in DKA than in HHS, typically within an hour of initial fluid therapy. In both emergencies insulin is not initiated prior to determining the patient’s potassium. Several studies have demonstrated that earlier insulin in DKA does not hurt patient outcomes; however, it does not benefit patients either and therefore is not generally recommended in the field.

For teams that participate in interfacility transports, insulin may regularly be seen. For these transports, check the patient’s blood sugar regularly and keep in mind that when insulin is administered, the rate of blood glucose decline should be limited to a maximum of 100 mg/dL per hour. If the blood sugar is decreased at a faster rate, patients risk developing cerebral edema.

When profound acidosis is suspected or known, administration of sodium bicarbonate may be tempting. Sodium bicarbonate is only indicated when the acidosis appears life-threatening or when associated with severe sepsis or lactic acidosis. Typically this is not done during prehospital care unless the patient is seizing or unresponsive, or if the team is able to perform an arterial blood gas.

Programs managing patients during interfacility transports will have the added benefit of lab data identifying the patient’s electrolyte levels. Patients with hyperglycemia will likely have low potassium and sodium levels. These cannot be managed without known accurate lab data, but when known, it’s common to provide potassium replacement while managing the elevated blood glucose. When profound hypokalemia is present, many emergency departments also assume simultaneous hypomagnesemia and initiate IV magnesium replacement.

**Summary**

Diabetes mellitus is an incredibly complex disease and impacts millions of Americans. The pancreas and insulin are both key to normal glucose metabolism and glucose control. Nearly any body stressor that alters a patient’s metabolism can impair normal insulin function and trigger hyperglycemia. It is prudent to check blood sugar in all patients with suspected serious illness, whether or not they have diabetic histories. Hyperglycemia can affect any patient and is a predictor of increased mortality if not treated early. Diabetic ketoacidosis has a more rapid onset than a hyperosmolar hyperglycemic state and often presents with a comparably lower blood sugar and the presence of acidosis. HHS does not present with profound acidosis and has a slower onset, yet more profound dehydration and a higher blood sugar. Do not underestimate the need for early prehospital intervention with hyperglycemia. Early and aggressive IV fluid administration can improve patient outcomes and speed recovery.

**REFERENCES**