Chapter e95: Acute Hyperglycemia

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KEY CONCEPTS

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1. Hyperglycemia is common among patients admitted to the hospital; at least one-third of hospitalized patients experience hyperglycemia.
2. Acute hyperglycemia and hypoglycemia can lead to increases in mortality as well as complications such as surgical site infections and end-organ dysfunction.
3. Hospitalized patients are unstable, as such, a patient's treatment strategies will change as the patient moves through different levels of care.
4. Insulin is the mainstay of therapy in acutely ill patients in the hospital.
5. The three core components of a complete insulin regimen are basal, nutritional, and correctional.
6. Hyperglycemic emergencies require hospitalization and are managed through a multifaceted approach of fluid resuscitation, insulin administration, and electrolyte monitoring/repletion.

BEYOND THE BOOK

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Listen to the *Run the List* podcast, Episode 37: Inpatient Diabetes Management. Dr. Nadine Palermo, an endocrinologist and the Associate Director of the Acute Diabetes Care program at Brigham and Women's Hospital, talks with Joyce Zhou (host) and Jakub Glowala (case presenter) to discuss the management of inpatient diabetes patients.

Available at https://www.runthelistpodcast.com/endocrinology/#T2DM-inpatient.

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INTRODUCTION

1 Acute hyperglycemia is a common presentation in the ambulatory, emergency department, and inpatient hospital settings. The management of acute hyperglycemia in the emergency department and in the inpatient setting often differs from the management of diabetes in the ambulatory setting. Acute hyperglycemia is also managed differently depending on diagnosis (eg, diabetic ketoacidosis [DKA] or hyperosmolar hyperglycemic state [HHS], or acute stress hyperglycemia) and patient acuity (critically ill, acutely ill, step-down, and transitioning to outpatient). Increases in mortality and

morbidity have been observed with hyperglycemia, hypoglycemia, and glycemic variability.[1-4]

Controlling blood glucose (BG) during hospitalization has clear benefits, including improved outcomes and decreased length of stay.[4] This chapter will review the causes of dysglycemia in the hospital, as well as recommendations to manage hyperglycemia and prevent negative outcomes. Patients being admitted to the hospital may pass through several phases of care, including the emergency department, general ward, and the intensive care unit (ICU). Each of these phases poses unique challenges, different goals in treatment, and different modalities of therapeutics. This chapter will evaluate medication therapy options for patients in the hospital experiencing acute hyperglycemia, as well as patients experiencing a hyperglycemic emergency such as DKA or HHS. A multidisciplinary effort to identify, treat, and monitor glucose throughout the hospitalization is critical to achieving positive patient outcomes during the hospital stay, safely and efficiently transitioning patients home, and preventing readmission to the ICU or hospital.

EPIDEMIOLOGY

Greater than one-third of patients who are hospitalized experience hyperglycemia.[5,6] Many patients with acute hyperglycemia may not have a diagnosis of diabetes. Patients without a current diagnosis of diabetes may have stress-induced hyperglycemia or previously undiagnosed diabetes and should be evaluated for a diagnosis of diabetes. Routine monitoring of BG is the standard of care in all patients who are admitted to the hospital to identify dysglycemia. Patients with known diabetes should have a hemoglobin A1C (A1C) drawn when admitted if a result is not available from the past 2 to 3 months. Obtaining an A1C should also be done in patients with BG greater than 140 mg/dL (7.8 mmol/L) admitted to the hospital if not performed in the prior 3 months.[4] Obtaining an A1C upon admission is needed to determine whether a patient meets diagnostic criteria for diabetes, which, in turn, will dictate the discharge plan and long-term management strategy beyond the acute hyperglycemia.

ETIOLOGY/PATHOPHYSIOLOGY

Acute Hyperglycemia

Multiple mechanisms can lead to hyperglycemia in acutely ill patients. Most commonly, this may include insufficient antihyperglycemic therapy in patients with a known history of diabetes since many patients with diabetes will have non-insulin agents discontinued on admission, but not replaced with an equipotent antihyperglycemic regimen.[7] Patients in the hospital will frequently experience increases in insulin resistance in peripheral tissues, as well as increases in both hepatic and renal gluconeogenesis.[8] Acute hyperglycemia related to acute illness, commonly referred to as stress hyperglycemia, is caused by the release of the hormones norepinephrine, epinephrine, cortisol, and growth hormone and will increase inflammatory mediators leading to insulin resistance.[9] Hyperglycemia can increase pro-inflammatory cytokines, prothrombotic mediators, and increase oxidative stress.[10] External factors potentially contributing to hyperglycemia include the use of dextrose containing intravenous admixtures and maintenance fluids, medications known to increase glucose levels (glucocorticoids), and nutrition with high carbohydrate tube feedings.[7]

Hyperglycemic Emergencies

The cause of both DKA and HHS is a complex metabolic process that is the result of absolute and/or relative insulin deficiency. Episodes of DKA and HHS usually develop secondary to an underlying cause. The most frequent inciting cause of DKA and HHS is infection. Other common causes are inadequate insulin therapy (including patient non-adherence), pancreatitis, myocardial infarction, and medications. Medications that have been implicated as precipitating factors for hyperglycemic emergencies include corticosteroids, thiazide diuretics, and atypical antipsychotic agents. HHS may progress after severe dehydration in chronic illnesses where patients are experiencing decreased water intake, potentially due to being bedridden. Many patients who develop HHS have no previous diagnosis of diabetes, so the development of HHS is not recognized in a timely manner, and treatment is not initiated early. Rates of hospitalization due to DKA increased 54.9% from 2009 to 2014, a trend that is concerning given the largely preventable nature of DKA if the cause is found to be medication non-adherence.

The initiating insult can cause hyperglycemia due to increased gluconeogenesis and decreased glucose utilization by peripheral tissues, as well as an increase in counter-regulatory hormones such as glucagon. Insulin deficiency and increased hormone production will also lead to increased hepatic ketone production and lipolysis from adipose tissue, causing metabolic acidosis.

The deleterious effects of hyperglycemia are well documented in many organ systems throughout the body, and as such, it is important to address glucose status in all acutely ill patients. Persistent hyperglycemia and hypoglycemia have been associated with increased mortality in the acutely ill. Hyperglycemia has been suggested to inhibit the function of white blood cells, leading to delayed wound healing and overall blunting of the body's immune response. Hyperglycemia can impair blood flow and cause decreases in perfusion in patients with acute coronary syndrome.[11] Derangements in BG are suggested to be associated with increased mortality and may have a contributing role to the development of ICU acquired weakness.[3,12,13]

CLINICAL PRESENTATION

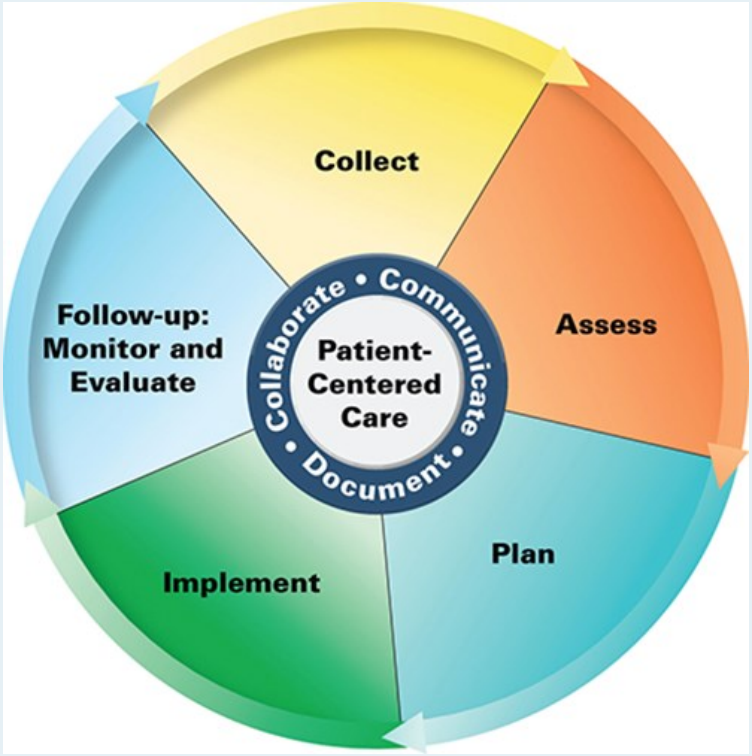
Acute hyperglycemia may present without symptoms, with non-specific symptoms, or with severe symptoms including dehydration and acid-base abnormalities symptoms. It is critical to ask the patient to provide any relevant history of medication non-adherence to help with diagnosis and explanation of the hyperglycemia.

Hypoglycemia may occur as an adverse effect of treatment and will present with symptoms generally in accordance with the degree of severity. Hypoglycemia at BG of 54 to 70 mg/dL (3.0 to 3.9 mmol/L) will generally have mild symptoms such as mood changes, while severe hypoglycemia (less than 54 mg/dL [3.0 mmol/L]) may present with severe mental status changes and unresponsiveness.[14]

DKA most often presents with uncontrolled hyperglycemia, metabolic acidosis, and an increase in ketone production. HHS will often clinically manifest with dehydration, hyperglycemia, and hyperosmolality, usually in the absence of a significant acidosis. Most patients presenting with DKA will have known or in some cases newly diagnosed type 1 diabetes (type 1 DM); however, patients with type 2 diabetes (type 2 DM) with a precipitating illness such as infection are also at risk of progressing into DKA.

PATIENT CARE PROCESS

Patient Care Process for Acute Hyperglycemia



Collect

- Patient characteristics (eg, age, sex, pregnancy)

- Patient medical history (personal and family) - diagnosis of diabetes
- Current medications - oral antidiabetic medications, insulin, and non-insulin injectable agents, time of the last dose
- Objective data (labs including blood glucose, A1C if not done within 90 days prior to admission)

Assess

- Presence of hyperglycemia provoking factors (infection, new corticosteroids, interruption of prehospital diabetes regimen)
- Presence of risk factors for hypoglycemia
- Dietary status (NPO, continuous tube feeds, discrete meals)
- Hemodynamic stability, patients on vasopressors or experiencing profound edema may be inappropriate for subcutaneous insulin
- Ability/willingness to self-monitor blood glucose if needed as the patient transitions to an outpatient
- Ability/willingness to self-inject insulin (if needed) as an outpatient
- Ability/willingness to pay for antidiabetic treatment options, insurance coverage of insulin pens versus vial + syringe

Plan

- Drug therapy regimen includes specific insulin(s), dose, route, frequency, and duration; (see Table e95-3)
- Monitoring parameters include efficacy (serum blood glucose as part of daily metabolic panel, point of care blood glucose testing prior to meals or standing nutritional insulin doses) and safety (eg, signs and symptoms of hypoglycemia)
- Referrals to other providers when appropriate (eg, primary care, endocrinologist, dietician)

Implement

- Best practice recommendations for the management of acute hyperglycemia given patient factors and level of acute illness (eg, emergency unit, intensive care unit, inpatient ward)
- Provide patient education regarding all elements of the treatment plan (eg, the purpose of treatment, dietary and lifestyle modification, medication administration/injection technique)
- Use motivational interviewing and coaching strategies to maximize adherence to treatment and blood glucose monitoring plan when planning to transition to outpatient

Follow-up: Monitor and Evaluate

- Blood glucose results (fasting, pre-meal), adjust insulin doses to reach goal blood glucose and avoid hypoglycemia
- Need for changes in insulin requirement given the improvement in critical illness, changing caloric intake, or tapering of corticosteroids
- A1C results every 3 months

TREATMENT

Patients Hospitalized on Antidiabetic Therapy

Many patients with a diagnosis of diabetes before hospitalization will be on an existing antidiabetic regimen. It is important to assess each patient's

outpatient regimen to ensure the correct products, doses, and patient's adherence is available to healthcare providers to aid in the assessment of hyperglycemia. It may be suggested to continue patients on their outpatient regimen upon admission to the hospital. It is important to recognize that acutely ill patients are often unstable, and as such a continuation of a patient's home regimen for hyperglycemia may not be appropriate at admission. 3 The patient's home regimens may include oral and non-insulin subcutaneous agents that may cause toxicities when organ function is compromised or may not be on an institution's formulary. The core reason why antidiabetic regimens should generally be changed when in the hospital is that inpatient situations are unstable when compared to the patient's life outside the hospital. A stable regimen outside of the hospital may be too aggressive or not aggressive enough. A patient with well-controlled type 1 DM stable on an insulin pump admitted to the hospital for an elective procedure may be most appropriately managed by continuing their insulin pump. A patient with type 2 DM on multiple oral agents and admitted for the treatment of pneumonia would be better served by discontinuing their home therapy to avoid toxicities. A patient's caloric intake is likely to be different when meals are either skipped due to illness or provided via the hospital's nutrition support services which differ from the patient's usual diet.

There is no single treatment approach suitable for all hospitalized patients. Monitoring BG values closely in the hospital is crucial, and reassessing medications during each transition between levels of care. It may be appropriate to re-initiate elements of a patient's home antidiabetic regimen prior to hospital discharge as acuity decreases.

Hyperglycemia in the Noncritically Ill Hospitalized Patient

Guideline Recommendations for Nonemergent Hyperglycemia Management

Multidisciplinary guidelines play a critical role in guiding glucose management strategies for healthcare professionals in the hospital. Recommendations on glucose management in hospitalized patients are made by several professional organizations.

American Diabetes Association/American Association of Clinical Endocrinologists Consensus Statement

In 2009, the most recent consensus statement from the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) on inpatient glycemic control was released.[15] For noncritically ill hospitalized patients, the consensus statement recommends that the premeal BG target should generally be less than 140 mg/dL (7.8 mmol/L) and random BG values less than 180 mg/dL (10.0 mmol/L), provided these targets can be safely achieved. Therapeutically, they strongly discourage the use of a sliding scale insulin regimen alone. Scheduled subcutaneous administration of insulin, with basal, nutritional, and correctional components, is the preferred method for achieving and maintaining glucose control in noncritically ill hospitalized patients with good nutritional intake.

American Diabetes Association

The ADA publishes updated standards of care for diabetes annually. While the guidelines incorporate large volumes of research into their updates each year across all domains of care for patients with diabetes, recommendations specific to the management of glucose in the hospital have not substantially changed. For patients hospitalized not in the ICU, the ADA recommends insulin therapy should be initiated for treatment of persistent hyperglycemia starting at a threshold ≥180 mg/dL (10.0 mmol/L). Once insulin therapy is started, a target glucose range of 140 to 180 mg/dL (7.8 to 10.0 mmol/L) is recommended for the majority of critically ill and noncritically ill patients (Grade A Recommendation).[4]

Noninsulin Medications

There are many limitations of noninsulin therapies in hospitalized patients including absorption, drug-disease interactions, drug-drug interactions, inconsistent diet, and acute renal and hepatic injury. Oral antidiabetic medications are generally not preferred in the institutional setting for acutely ill patients, who may be experiencing decreases in absorption from their GI tract. A summary of considerations for using noninsulin antidiabetic therapies in the hospital can be found in Table e95-1. Many oral antidiabetic medications have long half-lives, making active titration during an acute hospitalization difficult. These medications will also rely on hepatic metabolism or renal excretion. Since end-organ function may be fluctuating or be impaired in acute illness, clearance of oral agents may be impaired. This accumulation can lead to increases in adverse effects such as hypoglycemia with sulfonylureas or lactic acidosis in the case of metformin. The 2021 ADA guidelines state that the safety and efficacy of noninsulin therapies in the hospital is an area of active research. This includes the potential role of glucagon-like peptide 1 receptor agonists and dipeptidyl peptidase-4 inhibitors in specific groups of hospitalized patients. The statement does not recommend any noninsulin therapies for routine use in the hospital as non-insulin

agents are inappropriate in most hospitalized patients.[4]

TABLE e95-1

NonInsulin Therapies in the Hospital

Medication Type	Considerations in Hospitalized Patients
Sulfonylureas	• May lead to hypoglycemia if nutrition is interrupted or acute renal injury
Metformin	• Contraindicated in setting of decreased renal blood flow, surgery, and with use of iodinated contrast dye
Thiazolidinediones	• Long onset • Associated with edema and congestive heart failure
GLP-1 receptor agonists	• Impact mostly on postprandial glucose • Limited utility in patients not eating meals • Associated with nausea
DPP-4 inhibitors	• Limited utility in patients not eating meals as impact mostly on postprandial glucose

GLP-1: Glucagon-like peptide 1, DPP-4: Dipeptidyl-peptidase 4.

Subcutaneous Basal/Nutritional Insulin

The inpatient regimen of choice for most hospitalized noncritically ill patients with hyperglycemia or preexisting diabetes is scheduled subcutaneous (SC) insulin.[16,17] 4 The inpatient insulin regimen generally consists of the following three components: basal insulin to manage glucose between meals, nutritional (also known as prandial) insulin for meal-related nutritional BG spikes, and correctional insulin given in addition to the nutritional insulin dose in the event the patient might have premeal hyperglycemia (Table e95-2). 5 For most patients, the total daily dose (TDD) is split evenly with 50% of the TDD as basal insulin and 50% of the TDD as nutritional. Sliding-scale insulin alone is not recommended for glucose management in hospitalized patients.[4,18–20] The monitoring provided with a sliding scale is important information, however only utilizing a sliding scale is reactive to hyperglycemia, rather than proactive in avoiding hyperglycemia. Most insulin doses in the hospital should be accompanied by a BG check, patients with known diabetes or experiencing acute hyperglycemia without an existing diagnosis of diabetes should have BG checks before every meal if eating, and every 4 to 6 hours if not eating.[4,6,21]

TABLE e95-2

Therapeutic Options for Glycemic Control in the Medical or Stabilized Surgical Patient

	Basal Insulin	Nutritional (prandial) Insulin	Correctional (supplemental) Insulin
Place in therapy	Controls fasting and pre-meal glucose	Controls glucose from nutritional sources such as discrete meals, tube feeds, or TPN	Used to cover unexpected hyperglycemia that was not controlled by scheduled basal and nutritional insulin
Patient eating discrete meals	• Long-acting insulin once- or twice daily or • Intermediate-acting insulin (NPH) twice-daily	• Rapid-acting insulin given with a meal	• Rapid-acting insulin with meals (in addition to prandial insulin if hyperglycemic)
Patient not eating discrete meals	• Long-acting insulin once or twice-daily or • Intermediate-acting insulin (NPH) twice-daily	Not applicable	• Regular insulin every 4-6 h or • Rapid-acting insulin every 4 h
Enteral tube feeding or continuous dextrose	• Long-acting insulin once- or twice-daily or • Intermediate-acting insulin (NPH) twice-daily	• Regular insulin every 4-6 h or • Rapid-acting insulin every 4 h	• Regular insulin every 4-6 h (in addition to prandial insulin if hyperglycemic) or • Rapid-acting insulin every 4 h (in addition to prandial insulin if hyperglycemic)

When starting a new SC regimen on a treatment naïve patient, the starting estimated TDD required of SC insulin is calculated using the patient's weight. A conservative standard starting dose for an individual who has never been on insulin before is usually 0.2 to 0.7 units/kg/day.[15–18] It is best to begin at the lower end (as low as 0.2 units/kg/day) for patients at risk of hypoglycemia, such as those presenting with acute end-organ dysfunction. Doses at or above 0.7 units/kg/day should be reserved for patients with substantial risk factors for hyperglycemia, such as newly increased corticosteroids. The TDD is then divided, with one-half into the basal insulin and the other half into the nutritional insulin. Considerations in starting a new SC regimen are listed in Table e95-3.

TABLE e95-3

Initiation of Insulin Therapy on Insulin Naïve Patient

Piece of Regimen	Recommendation
Calculate starting TDD	0.2-0.4 units/kg/day - patients with hypoglycemia risk factors
	0.5-0.7 units/kg/day- standard for most patients
Adjust TDD up or down based on	Past response to insulin
	Presence of hyperglycemia-inducing risk factors, agents, stress
Basal insulin = 40%-50% of TDD	Long-acting insulin daily or twice-daily or intermediate-acting insulin twice-daily
Nutritional insulin = 50%-60% of TDD	Standing rapid-acting insulin (with discrete meals or bolus feeds) or regular insulin every 4 to 6 hours (continuous feeds)
Correctional Insulin	Insulin scale with intensity based on TDD

TDD, total daily dose.

Basal Insulin

Basal insulin refers to the patient's insulin requirements that exist regardless of the patient's caloric intake. Basal insulin should be given to patients regardless of whether they are eating or not eating. Options for basal insulin are most commonly a once-daily dose of long-acting insulin or twice daily intermediate-acting insulin NPH. Caution should be taken in patients who do not have a history of diabetes when considering initiation of long-acting basal insulin in the hospital. One retrospective analysis of surgical ICU patients without diabetes indicated an increase in the development of hypoglycemia in patients maintained with long-acting basal insulin plus sliding-scale insulin when compared to patients maintained on sliding scale insulin alone.[22] Therefore, the risks of therapy should be weighed against the potential benefits for each individual patient.

Nutritional Insulin

As discussed above, inpatient situations are often unstable, and patients can have fluctuation in their caloric intake for several reasons (NPO for the procedure, loss of feeding tube access, emesis, etc.). For these reasons, it is important to separate out nutritional insulin administration from basal insulin administration. It is important that orders are written correctly to allow for when there are acute changes in carbohydrate intake, nutritional insulin doses can be held to avoid causing episodes of hypoglycemia.

When choosing a nutritional insulin product, it is of utmost importance to distinguish the source of a patient's glucose intake and nutritional status. For patients who are on a continuous hourly rate of tube feeding or receiving total parenteral nutrition, providing a fixed dose of regular insulin every 6 hours or rapid-acting insulin every 4 hours should provide consistent coverage and avoid "stacking" of insulin doses. For patients who are eating discrete meals, or receiving bolus tube feeding, using rapid-acting insulin such as insulin aspart, insulin lispro, or insulin glulisine before meals to cover the carbohydrate intake is preferred, as the insulin analogs will offer a similar profile to the natural pancreatic insulin production in response to carbohydrate intake. Some patients may benefit from a more dynamic approach to nutritional insulin that is calculated based on the carbohydrate content of each individual meal. This is commonly referred to as "carb counting". Another strategy used by hospitals, particularly with patients who may not eat a full meal is to give the dose post-prandial (within 15 minutes after eating) depending on how much the patient ate of their meal, for example, if the patient ate only half of their meal, they would receive half of the regularly scheduled nutritional dose.

Correctional Insulin

The final piece to a successful subcutaneous insulin regimen is correctional insulin, to be administered in addition to, and at the same time as the patient's nutritional insulin. Correctional insulin is usually seen in the form of a correction or supplemental scale. Prescribers should be able to choose between different levels of the supplemental scale, based on the patient's level of insulin sensitivity, which can be determined by the patient's daily requirement of insulin or other patient characteristics such as body weight. An example of a supplemental insulin scale delivered based on scheduled insulin requirements can be found in Table e95-4.

TABLE e95-4

Example of Correctional Insulin Scales Based on Scheduled Insulin Requirement

Blood glucose (mg/dL)	Less than 40 units/day scheduled insulin"low scale" (units of insulin)	40-80 units/day scheduled insulin"medium scale" (units of insulin)	Greater than 80 units/day scheduled Insulin"high scale" (units of insulin)
150-199 (8.3 - 11.0 mmol/L)	1	1	2
200-249 (11.1 - 13.8 mmol/L)	2	3	4
250-299 (13.9 - 16.6 mmol/L)	3	5	7
300-349 (16.7 - 19.4 mmol/L)	4	7	10
Greater than 349 (19.4 mmol/L)	5	8	12

Glucose Monitoring

There are multiple methods available for glucose monitoring for patients in the hospital. Most utilized are bedside point of care testing (POCT) devices that result quickly for the bedside practitioners to act upon rather than wait for results from a central laboratory. The POCT devices usually use capillary blood from a finger stick, however venous blood or arterial blood can also be used. Variability in the glucose value will exist from each site so it is of great importance that whenever possible patients are assessed using the same source of blood to minimize this variability.

POCT monitoring is popular due to the convenience of bedside testing and the relatively fast results. POCT devices have variable accuracy, though, and the use of such instrumentation requires training and continual competency assessment of nursing and nursing support staff to ensure proper technique. The International Organization for Standardization criteria requirement for accuracy is that displayed values be within 20% of the actual BG level for all readings greater than 75 mg/dL (4.2 mmol/L).[23,24]

Blood samples collected by venipuncture, venous line, or arterial line and sent to a central laboratory are typically processed with a whole-blood analyzer or an arterial blood-gas analyzer. These methods should produce the most accurate results; however, the results can take considerably longer, limiting utility for patients when results are needed in a timely fashion, particularly around meals or if patients may be experiencing symptoms of hypoglycemia. Blood analyzers are more expensive than POCT devices; therefore, they are typically not used in at the bedside with frequency. Patients who are active in the management of their diabetes may want to self-monitor their BG while in the hospital using a home device. In these cases, the hospital should consider a policy on how these cases should be handled, and additionally require testing of BG values at the same time with a hospital-approved device.

Patients receiving insulin in the hospital should have their BG checked throughout the day. For many patients this will be driven by a whole BG reading as part of their regular basic metabolic panel of laboratory values is the morning, and throughout the day as part of their correctional scale driven based on nutritional intake. Patients eating discrete meals should have their BG checked before meals, and patients who are NPO or continuous feeds should have their BG checked every 4 to 6 hours.

Hyperglycemia in the Intensive Care Unit

Guideline Recommendations

In the critically ill population, there are several multidisciplinary organizations that have made recommendations on how BG should be managed. It is important for healthcare professionals to recognize the variability that may exist between these groups and specific guidance provided for subgroups of patients.

Society of Thoracic Surgeons

The Society of Thoracic Surgeons (STS) Practice Guideline for Blood Glucose Management During Adult Cardiac Surgery provides guidance for the management of hyperglycemia in patients undergoing cardiac surgery.[25] STS guidelines provide evidence to support targeting BG values less than 180 mg/dL (10.0 mmol/L) including reduced mortality, reduced morbidity, lowered incidence of wound infections, reduced hospital length of stay, and enhanced long-term survival. STS recommends that cardiac surgery patients with BG values greater than 180 mg/dL (10.0 mmol/L) receive intravenous insulin to maintain BG values below 180 mg/dL (10.0 mmol/L) for the duration of their ICU stay (Level A recommendation). STS also recommends that patients who will require three or more days in the ICU should have intravenous insulin infusion to keep BG values less than or equal to 150 mg/dL (8.3 mmol/L)(Level B recommendation).

American Diabetes Association/American Association of Clinical Endocrinologists Consensus Statement

For the subset of critically ill patients, it is recommended to initiate insulin therapy at a BG threshold of 180 mg/dL (10.0 mmol/L), and that a goal BG value of 140 to 180 mg/dL (7.8 to 10.0 mmol/L) is recommended for most critically ill patients. They recommend using intravenous infusions as the preferred method of delivering insulin, as well as a validated intravenous insulin protocol with demonstrated efficacy and low rates of hypoglycemia.[15]

American Diabetes Association

In the 2021 recommendations for critically ill patients, the ADA recommends the initiation of insulin therapy at a BG level of 180 mg/dL, and a goal BG range of 140 to 180 mg/dL (7.8 to 10.0 mmol/L) for the majority of critically ill patients (Grade A recommendation).[4] The guidelines concede, however, that tighter BG goals may be appropriate for selected patients if the intervention used to achieve them will not lead to increases in hypoglycemia (Grade C recommendation). The guidelines do not make a recommendation on the specific insulin infusions to be used, stating only that intravenous insulin infusions should be administered based on validated written or computerized protocols that allow for predefined adjustments in the infusion rate, accounting for glycemic fluctuations and insulin dose.

American College of Critical Care Medicine/Society of Critical Care Medicine

Further guidelines on the use of intravenous insulin in the critically ill population are offered from the American College of Critical Care Medicine (ACCM) and Society of Critical Care Medicine (SCCM) guidelines published in 2012.[26] These guidelines recommend initiation of insulin therapy when BG values are greater than 150 mg/dL (8.3 mmol/L) (level of evidence low), and that most ICU patients should be treated to a BG goal of less than 150 mg/dL (8.3 mmol/L) and absolutely less than 180 mg/dL (10.0 mmol/L) using a protocol that demonstrates low rates of hypoglycemia, suggesting that BG values less than or equal to 70 mg/dL (3.9 mmol/L) are associated with increased mortality, that even brief BG values ≤ 40 mg/dL (2.2 mmol/L) are independently associated with a greater risk of mortality (quality of evidence: low).

These guidelines weigh in on certain specific populations of patients with regards to how their glucose should be managed. The guidelines suggest for patients who have undergone trauma and are in the ICU, BG greater than or equal to 150 mg/dL (8.3 mmol/L) should trigger initiation of insulin therapy and titrated to keep BG values less than 150 mg/dL (8.3 mmol/L).[26] While less than 150 mg/dL (8.3 mmol/L) is the goal, the patient's BG should absolutely be maintained less than 180 mg/dL (10.0 mmol/L) using a protocol that achieves a low rate of hypoglycemia. This is important in trauma

patients to achieve lower rates of infections and shorter stays in the ICU.

For patients experiencing certain neurologic conditions, specifically ischemic stroke, intraparenchymal hemorrhage, aneurysmal subarachnoid hemorrhage, or traumatic brain injury, the guidelines again suggest that a BG ≥ 150 mg/dL (8.3 mmol/L) serves as a trigger for initiation of insulin therapy.[26] The goal in this patient population is to keep the BG consistently less than 180 mg/dL (10.0 mmol/L) while avoiding hypoglycemia less than 100 mg/dL (5.6 mmol/L) to minimize adverse neurological outcomes.

Surviving Sepsis Campaign

More targeted recommendations are put forth in the 2021 Surviving Sepsis Campaign guideline for initiation of therapy and BG target.[27] These Guidelines recommend the initiation of a protocol for glucose management at a BG level greater than 180 mg/dL (10.0 mmol/L) in patients with sepsis, and remark that following the initiation of insulin therapy a typical target range is 144 to 180 mg/dL (8.0 to 10.0 mmol/L)(strong recommendation, moderate quality of evidence).

ASPEN (American Society for Parenteral and Enteral Nutrition)

As nutritional support is not only an important issue throughout acute illness but also a major contributor to hyperglycemia in critically ill patients, official recommendations from nutritional support and organizations have also been put forth. ASPEN in accordance with SCCM recommends a goal BG range of 140 or 150 to 180 mg/dL (7.8 or 8.3 to 10.0 mmol/L) for the general ICU population (strong recommendation), noting no clinical trial has established outcomes for different BG targets in patients receiving nutritional support.[28]

There is no clear consensus among professional organizations for goal BG in critically ill patients, or recommendations on intravenous insulin protocols to achieve specific BG targets. The recommendations put forth in these guidelines are summarized in Table e95-5. This increases the need for vigilance at the institutional level to implement and rigorously evaluate glucose management in the acutely ill population utilizing the multidisciplinary team approach.

TABLE e95-5

Summary of Recommendations of National/International Guidelines

	Goal BG in ICU	Goal BG in Non-ICU Hospitalized Patients	Definition of Hypoglycemia	Guidance on Insulin Therapy
STS[25]	Less than 180 mg/dL (10.0 mmol/L) for cardiac surgery patients in the first 24 hours of admission	• Premeal: Less than 110 mg/dL (6.1 mmol/L) • Post-prandial: Less than 180 mg/dL (10.0 mmol/L)	None provided	Before intravenous insulin infusions are discontinued, patients should be transitioned to a subcutaneous insulin schedule using institutional protocols
ADA/AACE Consensus Statement[15]	140-180 mg/dL (7.8 - 10.0 mmol/L)	• Premeal less than 140 mg/dL (7.8	None provided	• Use of validated insulin infusion protocols with demonstrated • safety and efficacy, and with low rates of occurrence of hypoglycemia

		mmol/L) • Random less than 180 mg/dL (10.0 mmol/L)		
ADA Annual Standards of Care[4]	140-180 mg/dL (7.8 - 10.0 mmol/L)	140-180 mg/dL (7.8 - 10.0 mmol/L)	• Level 1: 54- 70 mg/dL (3.0-3.9 mmol/L) • Level 2: less than 54 mg/dL (3.0 mmol/L) • Level 3: clinical event requiring assistance from another person to recover	• A regimen with basal, nutritional, and correctional is the preferred treatment for noncritically ill hospitalized patients with good nutritional intake • Avoid hypoglycemia
ACCM/SCCM[26]	Less than 150 mg, absolutely less than 180 mg/dL (10.0 mmol/L)	Not discussed	Less than 70 mg/dL (3.9 mmol/L)	Avoid hypoglycemia, monitor BG every 1-2 hours
Surviving Sepsis Campaign[27]	Typical target BG 144-180 mg/dL (8.0-10.0 mmol/L)	None provided	None provided	None provided
ASPEN[28]	140 or 150-180 mg/dL (7.8 or 8.3-10.0 mmol/L)	140 or 150-180 mg/dL (7.8 or 8.3-10.0 mmol/L)	Less than 70 mg/dL (3.9 mmol/L)	None provided

BG, blood glucose; ICU, intensive care unit; STS, Society of Thoracic Surgeons; ADA, American Diabetes Association; AACE, American Association of Clinical Endocrinologists; ACCM, American College of Critical Care Medicine; SCCM, Society of Critical Care Medicine; ASPEN, American Society for Parenteral and Enteral Nutrition.

Goal BG Level Based on Diagnosis of Diabetes

Patients who carry a diagnosis of diabetes may benefit from a different goal BG level in the hospital compared to patients who do not carry the diagnosis of diabetes. It is theorized that in patients with diabetes, adaptation to a chronic hyperglycemic state may occur, and thus patients with diabetes will not benefit from tighter BG targets in the 80 to 110 mg/dL (4.4 to 6.1 mmol/L) range because a normoglycemic range for these patients may be higher. One retrospective cohort analysis evaluated 3,529 patients using the same protocol, allowing for providers to choose between 80 and 110 mg/dL (4.4 to 6.1 mmol/L) or 90 and 140 mg/dL (5.0 and 7.8 mmol/L) for a goal BG level, in 12 ICUs across eight hospitals.[29] After multivariate analysis, there was no significant difference in 30-day mortality between the groups demonstrated based on glucose target. When stratified based on diabetic status, it was demonstrated that the 90 to 140 mg/dL (5.0 to 7.8 mmol/L) glucose target was independently associated with increased risk of mortality in patients without diabetes when compared to an 80 to 110 mg/dL (4.4 to 6.1 mmol/L) target range but decreased risk of mortality in patients

with diabetes.

Another retrospective analysis of 5,567 patients evaluating the relationship between preadmission A1C, glycemic metrics in the ICU, and mortality in the critically ill found that A1C values over 8% (64 mmol/mol) were associated with lower mortality in patients with mean BG values greater than or equal to 180 mg/dL (10.0 mmol/L) compared to patients with lower A1C values. Increasing mortality was seen in patients with an A1C lower than 6.5% (48 mmol/mol) who experienced increasing glucose variability compared to patients with a higher A1C.[30] These two analyses demonstrate the necessity for providers and institutions to consider how to incorporate more patient-specific factors into their standards of care for glucose management in the hospital. No multidisciplinary guideline has offered different inpatient BG goals based on the patient's diabetic status.

Intravenous Insulin Infusions

Achieving goal glucose levels and outcomes in the ICU often requires the use of an intravenous insulin protocol. Ideally a protocol with demonstrated efficacy and safety in achieving desired glucose goals without increasing risk for severe hypoglycemia.[26] There is not a gold standard intravenous insulin protocol that is widely adopted, and many institutions have had to develop their own. An institutional standardized trigger point should be set for the initiation of intravenous insulin in critically ill patients. Generally, initiation of an insulin infusion is recommended in an ICU patient with at least one of the following:

- BG greater than 180 mg/dL (10.0 mmol/L) and expected ICU stay greater than 3 days
- Known history of type 1 DM
- Unstable clinical condition (such as on corticosteroids, vasopressors, variable nutrition) and at high risk for hyperglycemia
- BG persistently elevated and not controlled with SC insulin therapy

Intravenous insulin protocols may be initiated with or without a bolus dose. If electing to use a bolus dose, the bolus and initial rate of insulin should be based on the patient's BG level. If not using a bolus dose, the initial rate of insulin should still be based upon the patient's initial BG level.

Institutions will generally have developed protocols for how to titrate an insulin infusion to achieve goal glucose level and avoid hypoglycemia. These protocols will generally require frequent input of BG values to guide nursing staff to increase or decrease the insulin being administered. These protocols are often reliant on accounting for the rate of change between the patient's previous BG levels and current, requiring a calculation to be done by the nurse administering the infusion. Electronic protocols are becoming more frequently utilized by institutions to attempt to mitigate this manual calculation as a source of human error. If electronic protocols are not readily achievable, data related to the efficacy and safety of the institution's paper-based protocol should be captured and changes to the protocol should be made as necessary to optimize outcomes for patients.[31]

Glucose Monitoring in the Intensive Care Unit

Monitoring principles in the ICU are like noncritically ill patients, although the frequency of testing is often increased in patients requiring insulin therapy. Intravenous insulin has a short half-life and will require BG tests at a minimum of every 1 to 2 hours, and more frequently if changes in how nutrition is being delivered, to prevent patients from developing hypoglycemia.

It remains vital for BG values to be collected from consistent sites for interpretation by healthcare providers. Patients receiving care in the ICU may be on vasoactive therapy or fluid overloaded causing decreases in SC blood flow. Due to this decrease, checking BG from SC sites may not accurately reflect the patient's true BG, so regular use of an arterial or venous source will help healthcare providers accurately assess and manage their patient's BG.

Continuous Glucose Monitoring

Continuous glucose monitoring (CGM) devices have become more popular. In theory, these devices would provide several advantages compared with POCT testing, especially in the ability to rapidly identify hypoglycemia. These devices are placed in a variety of sites depending on the model, ranging from arterial or venous sampling to subcutaneous or proprietary interstitial space monitoring.[32–35] Currently, there are insufficient data demonstrating improved outcomes, cost-effectiveness, or safety when using CGM devices in acutely ill patients.[4] Research on these technologies in the

critically ill population continues, and a CGM coupled with an intravenous insulin protocol could lead to a paradigm shift in the management of glucose in hospitals.

Transitions of Care

Each different level of care during an acute hospitalization needs to be met with different levels of monitoring and standards for the treatment of hyperglycemia. While a patient may be on multiple oral antidiabetic mediations at home those may not be appropriate throughout their acute illness. This patient may come into the hospital via the emergency department and be managed with a combination of intravenous and subcutaneous insulin therapy. This patient then may require admission to an ICU where they will be maintained on an intravenous infusion. When the patient's acute state is recovering, they will be transitioned to subcutaneous therapy for the general ward.

When the patient leaves the hospital, if it is deemed appropriate, they may then again be placed back on their noninsulin antidiabetic agents. However, this hospitalization may be a time for the healthcare provider to revisit the home regimen and depending on many factors may have the home regimen changed. If the A1C drawn at admission is elevated, an investigation should be done to determine what has led to sub-optimal treatment. Factors the healthcare provider and the patient should discuss include medication adherence, home dietary changes, and the patient's home monitoring plan. Engaging the patient in their perceived barriers may improve their adherence and engagement going forward, slowing the progression of their disease as well as preventing complications. If the patient reports an excessive pill burden as a barrier, combination products may be available as an outpatient. If the patient reports forgetting doses, the use of a pillbox, alarm, or app may help remind patients when doses are due. If the patient reports difficulty in utilizing a vial and syringe to administer insulin, insulin pens may be a more convenient option to provide the patient when they are discharged.

Follow-up appointments with the patient's ambulatory providers are vital to check in on the medication regimens. Each of these changes introduces opportunities for error if the regimen does not match with the patient's level of care

Transition from Intravenous to SC

For patients initially managed according to an intravenous insulin infusion, a transition to a subcutaneous regimen should be considered when one of the following criteria is met:

- The patient is ready for transfer out of the ICU
- The patient has been on a stable dose of the insulin infusion for greater than 24 hours, the glucose is well controlled, and the patient is no longer critically ill
- The patient is consistently requiring doses less than 0.5 units/hr

Transitions from intravenous infusion to subcutaneous regimens can lead to the development of hypoglycemia in some patients so a thorough dosing and monitoring plan is vital.[36] To safely transition patients from intravenous to subcutaneous insulin, the healthcare provider should:

1. Determine the TDD of insulin based on the average hourly insulin infusion rate for the past 6 hours. The TDD = (average hourly insulin drip rate for past 6 hours) X 24 hours.
2. Calculate 80% of the previous TDD as the new TDD (TDD × 0.8).[37]
3. Order 50% of new calculated TDD as basal insulin, and 50% as nutritional insulin to match intake (eg, separated evenly between three meals for patients eating discrete meals)
4. Give correctional insulin scale based on TDD
5. Stop insulin drip 1 to 2 hours after the first dose of nutritional insulin or 2 to 3 hours after the first dose of basal insulin is administered.

Management of Hypoglycemia in the Hospital Setting

The ADA defines hypoglycemia as a BG level of less than 70 mg/dL (3.9 mmol/L). Both the AACE and the ADA agree that insulin therapy should be

adjusted when the BG level is less than 70 mg/dL (3.9 mmol/L) and re-evaluated when levels are less than 100 mg/dL (5.6 mmol/L).[4,38] Re-evaluating insulin dosing or product selection when a level less than 100 mg/dL (5.6 mmol/L) occurs may prevent a future hypoglycemic event. Due to the negative consequences of hypoglycemia, all efforts should be made to limit the incidence of hypoglycemia. Incidence of hypoglycemia should be anticipated, and a plan put in place to systematically allow nurses to treat without delay, rather than waiting for orders from a prescriber.[11,39,40]

Hospitalized patients are at a unique risk of hypoglycemia because the nutritional status may change frequently, including the patient alternating on and off NPO status, inconsistent nutritional intake while eating, and some altered mental status. A protocolized plan is warranted to monitor for, prevent, and treat hypoglycemia. This plan should involve a clear definition of and plan to manage patients at risk of hypoglycemia in the hospital environment.

One preventive strategy is to use a glucose value as a signal to reassess insulin therapy before hypoglycemia occurs. For example, a fasting BG level of less than 100 mg/dL (5.6 mmol/L) for patients on insulin therapy can be used as a signal to systematically reassess the patient's regimen. This type of proactive approach for the prevention of hypoglycemia should be a part of the guidelines of each institution's protocols and guidelines.

The standing hypoglycemia management protocol/guideline should encompass the explicit route, dose, and form of glucose administration, depending on the patient's level of cognition. Insulin infusions should be discontinued (or reduced, if the patient has type 1 DM), and glucose should be administered. Repetition of BG monitoring and administration of glucose are required until the patient is stabilized. Assessing causality and adjusting treatment is then necessary. Look for the cause of hypoglycemia and determine whether other treatment modifications are needed.

Treatment of Hyperglycemic Emergencies

The most serious and common acute complications of hyperglycemia are DKA and HHS, both of which require immediate treatment and, typically, hospitalization.[41,42] The most recent consensus statement from the ADA on the management of DKA and HHS was published in 2009. The ADA put forth treatment strategies including monitoring, correction of fluid and electrolyte status, as well as insulin therapy for patients with DKA and HHS.

Classification of Severity

Classification of severity of episodes of DKA and HHS can be important when determining optimal treatment strategies, as well as the level of care patients will require upon admission to the hospital. Table e95-6 describes the classification of severity of DKA and HHS. The severity of DKA is classified into mild, moderate, and severe DKA based on laboratory findings. Some patients may present with a mixed picture of both DKA and HHS. Patients with mild DKA who are cognitively alert and capable of taking fluids orally may be treated under observation and sent home without admission.[43] The ADA recommends admission for patients who are experiencing plasma BG greater than 250 mg/dL (13.9 mmol/L) with an arterial pH below 7.30, a serum bicarbonate level of less than 15 mEq/L (mmol/L), and a moderate or greater level of ketones in the serum or urine.[44] Patients being admitted to the hospital with mild to moderate DKA will generally be admitted to a general ward, while patients with severe DKA should be admitted to the intensive care unit.[45]

TABLE e95-6

Classification of Severity of DKA and HHS

	DKA			HHS
	Mild	Moderate	Severe	
Arterial pH	Less than 7.30	7.00-7.24	Less than7.0	Greater than 7.3
Serum bicarbonate (mmoL/L)	15-18	10-14	Less than 10	Greater than 18
Urine ketone	1-3+	1-3+	1-3+	Trace
β-Hydroxybutyrate (mmol/L)	Greater than 1	Greater than 1	Greater than 1	Trace
Serum osmolality	Normal to elevated	Normal to elevated	Normal to elevated	Greater than 320 mOsm/kg (mmol/kg)
Anion gap (mmol/L)	Greater than 10	Greater than 12	Greater than 12	Variable

DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state.

While DKA is not a diagnosis of exclusion, other disease states can produce similar laboratory abnormalities. Alternative causes of ketoacidosis include starvation ketosis and alcoholic ketoacidosis; however, these cases will often not also present with uncontrolled hyperglycemia. A severe anion gap metabolic acidosis can present from toxic ingestions such as ethylene glycol, salicylates, and methanol. For these reasons, it is important to conduct a thorough history including previous drug use to ensure an appropriate diagnosis.

Fluids

Initially, the goal of fluid therapy should be to expand the patient's intravascular and interstitial volume since both are reduced in a patient with a hyperglycemic emergency. The resuscitation fluid of choice in a hyperglycemic emergency is 0.9% sodium chloride, initially infused at a rate of 15 to 20 mL/kg/hr. As some patients are obese and the weight-based dose may be difficult to administer in the first hour, 1 to 1.5 L during the first hour is also acceptable. Patient-specific adjustments should be considered in patients with known cardiac or renal dysfunction to avoid causing dramatic fluid overload. After the initial bolus maintenance fluid rate should be based on physiologic parameters to maintain hemodynamic stability as well as the intravascular and extravascular volume. Providers should also calculate a corrected sodium (Corrected sodium = measured sodium + 0.016 × (BG -100 mg/dL)) or when expressed in SI units (Corrected sodium = measured sodium + 0.288 × (BG -5.6 mmol/L)). If the corrected sodium is high or normal, the use of 0.45% sodium chloride at a rate of 250 to 500 mL/hr is appropriate. If the corrected sodium is low, maintenance fluid resuscitation should continue to be done with 0.9% sodium chloride. The hyperglycemia will likely resolve before the ketoacidosis has resolved, as such providers should consider adding dextrose 5% in water in DKA patients with a BG less than 200 mg/dL (11.1 mmol/L) or an anion gap less than 12 mmol/L, and HHS patients with a BG less than 300 mg/dL (16.7 mmol/L) or until osmolality is less than 315 mOsm/kg (mmol/kg) and until patients are mentally alert or receiving carbohydrates in the form of enteral nutrition. Monitoring of serum chloride is also important, as large volumes of sodium chloride-containing resuscitation fluids are often given to patients undergoing a DKA/HHS episode.[46] Excessive chloride administration can lead to a prematurely closed anion gap, complicating the assessment of the patient's acid/base status. If the anion gap closure is due to high chloride levels, and not to sufficient clearance of ketones, and fluid therapy is discontinued, patients may be at risk of having the anion gap reopen. In these patients, it may be appropriate to change to a more balanced resuscitation fluid. While the 2009 guidelines have endorsed the fluid resuscitation strategy described above, research is being published exploring the role of initial resuscitation with balanced crystalloids rather than normal saline.[47,48]

Electrolytes

Beyond sodium and chloride, electrolyte abnormalities that will need to be managed in patients experiencing a hyperglycemic emergency include

potassium, bicarbonate, and phosphate.

Potassium management in a patient with DKA/HHS can prove the most complicated. Patients may experience mild-moderate hyperkalemia upon presentation. Upon initiation of fluid resuscitation, insulin therapy, and correction of the ketoacidosis, a shift towards decreased potassium will occur. To prevent the occurrence of severe hypokalemia, potassium supplementation is recommended to begin when serum potassium levels fall below 5 mEq/L (mmol/L). This can be achieved by using a potassium chloride-containing maintenance fluid. If severe hypokalemia occurs, patients may require the placement of a central venous catheter to allow for infusion of concentrated potassium chloride. If patients require greater than 10 mEq (mmol) of potassium chloride per hour, cardiac monitoring should be initiated. If patients experiencing a hyperglycemic emergency are severely hypokalemic (potassium value less than 3.3 mEq/L(mmol/L) on presentation, insulin therapy should be delayed until a potassium value greater than 3.3 mEq/L (mmol/L) is obtained.

The use of sodium bicarbonate in DKA is controversial, current recommendations only favor the addition of intravenous sodium bicarbonate in patients with severe acidosis (pH less than 6.9) who are hypotensive and not responsive to intravenous fluids.

Similar to potassium, serum phosphate levels will also decrease after the initiation of insulin therapy. There has not been any benefit on clinical outcomes displayed with phosphate supplementation of patients in DKA. Due to concern of excess phosphate supplementation causing hypocalcemia, routine phosphate supplementation is not recommended for patients with a phosphate level greater than 1.0 mmol/dL.

Insulin

Intravenous Insulin therapy is the mainstay of therapy in patients with DKA and HHS in the emergency department and ICU, though patients with an uncomplicated mild-to-moderate episode of DKA or HHS may be able to be managed safely and effectively via a subcutaneous regimen. Patient-specific factors such as hemodynamic status and etiology of DKA/HHS should be considered when selecting the route of administration for insulin, since severely ill patients may have decreased subcutaneous absorption.

An example of a weight-based intravenous insulin regimen is described in Table e95-7. Debate exists about whether to initiate therapy using an intravenous bolus of insulin. If using an intravenous insulin bolus, the dose recommended is 0.1 units/kg of actual body weight, and the initial rate of insulin should be 0.1 units/kg/hr. If therapy is not initiated using an insulin bolus, it is recommended to initiate therapy at 0.14 units/kg/hr. Hourly monitoring of BG is recommended, and strategies for adjustment of the rate of insulin infusion can be found in Table e95-7. It is important to not reduce the patient's BG too rapidly, particularly in patients experiencing HHS as too rapid a reduction in BG may result in cerebral edema.

TABLE e95-7

Intravenous Regular Insulin Management of Hyperglycemic Emergencies

Step of Treatment	Recommendation
Initial bolus dose (optional)	0.1 units/kg
Initial rate of insulin infusion	0.1 units/kg/hr in patients who receive bolus
	0.14 units/kg/hr in patients who do not receive bolus
If BG decreases by less than 10% in the first hour	Administer intravenous bolus of 0.14 units/kg and continue the previous rate
If BG decreases by greater than 75 mg/dL/hr (4.2 mmol/L/hr)	Decrease infusion rate to 0.05 units/kg/hr
DKA: If BG is less than 250 mg/dL (13.9 mmol/L)	0.05 units/kg/hr until anion gap is less than 12 mmol/L
HHS: if BG is less than 300 mg/dL (16.7 mmol/L)	0.05 units/kg/hr until osmolality is less than 315 mOsm/kg (mmol/kg)

BG, blood glucose; DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state.

The transition from intravenous insulin to subcutaneous insulin should take place once the DKA/HHS episode has resolved. Resolution of DKA is described as BG less than 200 mg/dL (11.1 mmol/L) and two of the following: Serum bicarbonate greater than 15 mEq/L (mmol/L), venous pH greater than 7.3, and an anion gap less than 12 mmol/L. Resolution of HHS is described as BG less than 300 mg/dL (16.7 mmol/L), a plasma osmolality less than 315 mOsm/kg (mmol/kg), and the patient is mentally alert. It is critical to overlap the first dose of subcutaneous insulin with the infusion by 1 to 2 hours before discontinuation of the infusion. Patients who were on a stable regimen of insulin prior to the DKA/HHS episode may be restarted on their previous regimen if the underlying cause of the emergency has been resolved. Patients who are insulin naïve can be initiated on a weight-based subcutaneous regimen on 0.5 to 0.8 units/day, split approximately evenly between a basal insulin and a nutritional insulin. A correctional insulin scale tailored to the patient's TDD of insulin with BG monitoring multiple times daily is also critical for a complete subcutaneous regimen.

For patients with mild DKA who are determined to be appropriate candidates for subcutaneous administration of insulin, patients should receive an initial dose of a rapid-acting insulin at a dose of 0.3 units/kg, and subsequently, receive 0.2 units/kg every 2 hours. When BG is less than 250 mg/dL (13.9 mmol/L), the dose should be reduced to 0.1 units/kg every 2 hours until the patient is ready to transition to a maintenance regimen. A similar rate of ketone reduction should be expected among patients who are managed with intravenous or subcutaneous insulin, however until further research is available, subcutaneous insulin may not be ideal for patients with severe DKA, anasarca, or hemodynamic instability.

Follow-up and Diabetes Education

Consultation with an available local clinical management team, such as an endocrine or a diabetes management service should be considered for complicated DKA/HHS patients or for patients with a new diagnosis of diabetes to provide a continuity of care for when the patients go to the general ward and are eventually discharged. Diabetes education to enforce medication adherence as well as how to recognize the signs and symptoms of hypoglycemia and hyperglycemia may also be appropriate for patients who may be able to avoid progression to DKA/HHS in the future. Follow-up with existing or new diabetes outpatient providers should be ensured before discharge to prevent readmission.

Team Approach to Glucose Management in the Hospital

With insulin being a high-risk medication and the primary medication for inpatient management of hyperglycemia, implementing a safe and effective environment for glucose management in the hospital requires resources across multiple disciplines. Implementation of treatment protocols to optimize patient care outcomes and minimize adverse events, a standardized, multidisciplinary team approach should be employed.

There are two main types of dedicated glucose management teams: (1) the "Multidisciplinary steering committee" with a focus on global oversight of glucose management for an institution and (2) the best practice "clinical management team" with a focus on bedside clinical management of patient's glucose.[49]

Multidisciplinary Steering Committee

The multidisciplinary steering committee's role is to provide global oversight of the institution's development and implementation of policies, order sets, protocols, and guidelines. The goals of the multidisciplinary committee should be individualized to the needs of the institution, these goals should be established and agreed upon at the time of formation and maintained through future works. The multidisciplinary steering committee focuses on protocol development, implementation, and performance improvement.

Designated champions from each involved discipline may be necessary to implement initiatives put forth by the multidisciplinary team on a departmental basis. Disciplines that should be involved in glucose management teams include pharmacists, physicians, nursing, data analysts, and nutritionists, among others. Guidelines and protocols are essential as they have been shown to improve outcomes in BG management. A new policy, order set, protocol, or guideline may not always be the best option if existing guidance exists at the institution; however existing protocols often need to be revised as more information becomes available from internal analyses. The goal of a committee should be to provide encompassing direction without over-burdening staff with excess policies and guidelines.

The steering committee should anticipate and plan for barriers to successful implementation; as well as have a system in place to monitor for success or opportunities for improvement once the change has been implemented. A stepwise approach to process improvement is described in Table e95-8.

TABLE e95-8

Stepwise Approach to Developing and Implementing Institutional Protocols and Guidelines

Phase 1: Development	Phase 2: Implementation	Phase 3: Monitoring/continuous Quality Improvement
• Creation/identification of "physical champion" • Multidisciplinary committee • Data synthesis • Protocol drafting	• Pilot analysis: efficacy, safety, adherence • Endorsement of protocol from institutional credible bodies • Education to all clinicians • Integration with electronic documentation and clinical monitoring systems	• Periodic metric assessments • Guideline updates with current literature as available • Publication of efficacy, safety, and compliance data • Benchmarking against other institutions

Clinical Management Team

In addition to the steering committee, some healthcare systems may have a "clinical management team" performing consultative services for individual patients. The order sets, protocols, and guidelines developed by the steering committee should aid multidisciplinary providers in the management of most patients. Complex patient cases in the acute care setting may require assistance beyond what is offered by these guidelines, and in these cases, the clinical management team serves to offer expert guidance. Clinical management teams can include endocrinologists, endocrine fellows, hospitalists, nurse practitioners, physician assistants, and clinical pharmacists. In addition to bedside practice, the clinical management team can also be involved in staff education, discharge planning and counseling, and facilitating change in culture.

In addition to improvements in patient care, the clinical management service model may generate revenue if advanced practice clinicians are able to bill for consultation services. An unfortunate potential cultural shift to instituting a clinical management team for glucose management is the perception that interns and residents may be less engaged in managing glucose therapy and start to refer the uncomplicated patient to the clinical management team.

Glucose management in the inpatient setting requires a multidisciplinary team approach. The creation of a steering committee or task force focused

on development, oversight, implementation, and quality assessment and improvement can standardize and coordinate glucose management measures within an institution. Clinical glucose management teams with a focus on direct patient care may also help improve patient outcomes.

Acute Hyperglycemia and Sick-Day Management in the Outpatient Setting

Acute hyperglycemia can occur in the outpatient setting for a variety of reasons, and if detected early, can often be adequately treated at home to prevent DKA or HHS and hospitalization. Acute illness, infection, or inadequate insulin therapy are primary reasons for acute hyperglycemia at home.[37] Acute self-limited illness rarely presents a major problem for patients with type 2 DM but instituting a sick day plan can avoid urgent care visits from dehydration. Type 2 DM patients should perform blood glucose monitoring more often, especially if they take medications that may cause hypoglycemia. Sick day management for patients with type 1 DM is more challenging.[50] While caloric intake generally declines when people feel sick, insulin sensitivity often decreases. Thus, patients often require greater amounts of insulin to control BG during periods of acute illness. Patients with type 1 DM should increase the frequency of blood glucose monitoring, check urine ketones, and consume 120 to 150 g of carbohydrates per day. Patients should continue their usual insulin regimen and use supplemental rapid-acting insulin based on glucose results. Basal insulin should be continued regardless of nutritional intake, while mealtime insulin use should be based on the nutritional intake of the patient. Additional insulin may be needed if ketonuria develops. Ketone testing should be done if two consecutive plasma glucose readings are above 250 mg/dL (13.9 mmol/L) or if vomiting occurs, as this may be a sign of ketosis. Sugar and electrolyte solutions, such as sports drinks, can be used to maintain hydration and provide electrolytes if there are significant GI or urinary losses. They also provide glucose to keep the patient from developing hypoglycemia. However, if the BG remains consistently elevated, the patient should abstain from sugary drinks and increase the intake of sugar-free liquids.

CONCLUSION

Acute hyperglycemia is common in hospitalized patients and presents many challenges to healthcare providers. Variations in clinical conditions, level of care, and local guidelines will all impact the management of patients experiencing dysglycemia.

ABBREVIATIONS

A1C	hemoglobin A1c
AACE	American Association of Clinical Endocrinologists
ACCM	American College of Critical Care Medicine
ADA	American Diabetes Association
ASPEN	American Society for Parenteral and Enteral Nutrition
BG	blood glucose
CGM	continuous glucose monitoring
DKA	diabetic ketoacidosis
DM	diabetes mellitus
HHS	hyperosmolar hyperglycemic state
ICU	intensive care unit
POCT	point of care testing
SC	subcutaneous
SCCM	Society of Critical Care Medicine
STS	Society of Thoracic Surgeons
TDD	total daily dose

REFERENCES

1. Estrada CA, Young JA, Nifong LW, Chitwood WR Jr. Outcomes and perioperative hyperglycemia in patients with or without diabetes mellitus undergoing coronary artery bypass grafting. *Ann Thorac Surg.* 2003;75(5):1392–1399. [PubMed: 12735552]

2. Krinsley JS. Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients. *Mayo Clin Proc.* 2003;78(12):1471–1478. [PubMed: 14661676]

3. Mamtani M, Kulkarni H, Bihari S, et al. Degree of hyperglycemia independently associates with hospital mortality and length of stay in critically ill, nondiabetic patients: Results from the ANZICS CORE binational registry. *J Crit Care*. 2020;55:149–156. [PubMed: 31731174]

4. American Diabetes A. 15. Diabetes care in the hospital: Standards of medical care in diabetes-2021. *Diabetes Care*. 2021;44(Suppl 1):S211–S220. [PubMed: 33298426]

5. Tamez-Perez HE, Quintanilla-Flores DL, Proskauer-Pena SL, et al. Inpatient hyperglycemia: Clinical management needs in teaching hospital. *J Clin Transl Endocrinol.* 2014;1(4):176–178. [PubMed: 29159098]

6. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: An independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab.* 2002;87(3):978–982. [PubMed: 11889147]

7. Smith WD, Winterstein AG, Johns T, Rosenberg E, Sauer BC. Causes of hyperglycemia and hypoglycemia in adult inpatients. *Am J Health Syst Pharm.* 2005;62(7):714–719. [PubMed: 15790798]

8. Turina M, Fry DE, Polk HC Jr. Acute hyperglycemia and the innate immune system: Clinical, cellular, and molecular aspects. *Crit Care Med.* 2005;33(7):1624–1633. [PubMed: 16003073]

9. Mizock BA. Alterations in carbohydrate metabolism during stress: A review of the literature. *Am J Med.* 1995;98(1):75–84. [PubMed: 7825623]

10. McCowen KC, Malhotra A, Bistrian BR. Stress-induced hyperglycemia. *Crit Care Clin.* 2001;17(1):107–124. [PubMed: 11219223]

11. Kosiborod M, Inzucchi SE, Krumholz HM, et al. Glucometrics in patients hospitalized with acute myocardial infarction: Defining the optimal outcomes-based measure of risk. *Circulation*. 2008;117(8):1018–1027. [PubMed: 18268145]

12. Witteveen E, Wieske L, Sommers J, et al. Early prediction of intensive care unit-acquired weakness: A multicenter external validation study. *J Intensive Care Med.* 2020;35(6):595–605. [PubMed: 29716425]

13. Wernly B, Jirak P, Lichtenauer M, et al. Hypoglycemia but not hyperglycemia is associated with mortality in critically ill patients with diabetes. *Med Princ Pract.* 2019;28(2):186–192. [PubMed: 30544102]

14. Agiostratidou G, Anhalt H, Ball D, et al. Standardizing Clinically Meaningful Outcome Measures Beyond HbA1c for Type 1 Diabetes: A Consensus Report of the American Association of Clinical Endocrinologists, the American Association of Diabetes Educators, the American Diabetes Association, the Endocrine Society, JDRF International, The Leona M. and Harry B. Helmsley Charitable Trust, the Pediatric Endocrine Society, and the T1D Exchange. *Diabetes Care*. 2017;40(12):1622–1630. [PubMed: 29162582]

15. Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Endocr Pract.* 2009;15(4):353–369. [PubMed: 19454396]

16. Umpierrez GE, Smiley D, Jacobs S, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 surgery). *Diabetes Care*. 2011;34(2):256–261. [PubMed: 21228246]

17. Umpierrez GE, Smiley D, Zisman A, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial). *Diabetes Care*. 2007;30(9):2181–2186. [PubMed: 17513708]

18. Clement S, Braithwaite SS, Magee MF, et al. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care*. 2004;27(2):553–591. [PubMed: 14747243]

19. Hirsch IB. Insulin analogues. *N Engl J Med.* 2005;352(2):174–183. [PubMed: 15647580]

20. Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: An algorithm for glycemic control. *Endocr Pract.* 2009;15(6):540–559. [PubMed: 19858063]

21. Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care*. 2009;32(6):1119–1131. [PubMed: 19429873]

22. Masse J, Giuliano CA, Brown S, Paxton RA. Association between the use of long-acting insulin and hypoglycemia in nondiabetic patients in the surgical intensive care unit. *J Intensive Care Med.* 2018;33(5):317–321. [PubMed: 27821581]

23. Inoue S, Egi M, Kotani J, Morita K. Accuracy of blood-glucose measurements using glucose meters and arterial blood gas analyzers in critically ill

adult patients: Systematic review. *Crit Care*. 2013;17(2):R48. [PubMed: 23506841]

24. Guimont MC, Desjobert H, Fonfrede M, et al. Multicentric evaluation of eight glucose and four ketone blood meters. *Clin Biochem.* 2015;48(18):1310–1316. [PubMed: 26232287]

25. Lazar HL, McDonnell M, Chipkin SR, et al. The Society of Thoracic Surgeons practice guideline series: Blood glucose management during adult cardiac surgery. *Ann Thorac Surg.* 2009;87(2):663–669. [PubMed: 19161815]

26. Jacobi J, Bircher N, Krinsley J, et al. Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients. *Crit Care Med.* 2012;40(12):3251–3276. [PubMed: 23164767]

27. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock 2021. *Crit Care Med.* 2021;49(11):e1063–e1143. [PubMed: 34605781]

28. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr.* 2016;40(2):159–211. [PubMed: 26773077]

29. Lanspa MJ, Hirshberg EL, Phillips GD, Holmen J, Stoddard G, Orme J. Moderate glucose control is associated with increased mortality compared with tight glucose control in critically ill patients without diabetes. *Chest*. 2013;143(5):1226–1234. [PubMed: 23238456]

30. Krinsley JS, Rule P, Pappy L, et al. The interaction of acute and chronic glycemia on the relationship of hyperglycemia, hypoglycemia, and glucose variability to mortality in the critically ill. *Crit Care Med.* 2020;48(12):1744–1751. [PubMed: 33031146]

31. Gibson GA, Militello MA, Guzman JA, Bauer SR. Evaluation of an updated insulin infusion protocol at a large academic medical center. *Am J Health Syst Pharm.* 2016;73(11 Suppl 3):S88–93. [PubMed: 27208145]

32. Long MT, Rice MJ, Coursin DB. Glucose monitoring in the ICU: What is really needed? *Crit Care Med.* 2018;46(8):1372–1374. [PubMed: 30004967]

33. Krinsley JS, Chase JG, Gunst J, et al. Continuous glucose monitoring in the ICU: Clinical considerations and consensus. *Crit Care*. 2017;21(1):197. [PubMed: 28756769]

34. Preiser JC, Lheureux O, Thooft A, Brimioulle S, Goldstein J, Vincent JL. Near-continuous glucose monitoring makes glycemic control safer in ICU patients. *Crit Care Med.* 2018;46(8):1224–1229. [PubMed: 29677007]

35. Salinas PD, Mendez CE. Glucose management technologies for the critically ill. *J Diabetes Sci Technol.* 2019;13(4):682–690. [PubMed: 30638048]

36. Zhou K, Williams MF, Esquivel MA, et al. Transitioning from intravenous to subcutaneous insulin in the medical intensive care unit. *Diabetes Res Clin Pract.* 2017;134:199–205. [PubMed: 29154154]

37. Weber C, Kocher S, Neeser K, Joshi SR. Prevention of diabetic ketoacidosis and self-monitoring of ketone bodies: An overview. *Curr Med Res Opin.* 2009;25(5):1197–1207. [PubMed: 19327102]

38. Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2012;97(1):16–38. [PubMed: 22223765]

39. Bagshaw SM, Egi M, George C, Bellomo R, Australia New Zealand Intensive Care Society Database Management C. Early blood glucose control and mortality in critically ill patients in Australia. *Crit Care Med.* 2009;37(2):463–470. [PubMed: 19114915]

40. Investigators N-SS, Finfer S, Liu B, et al. Hypoglycemia and risk of death in critically ill patients. *N Engl J Med.* 2012;367(12):1108–1118. [PubMed: 22992074]

41. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32(7):1335–1343. [PubMed: 19564476]

42. Delaney MF, Zisman A, Kettyle WM. Diabetic ketoacidosis and hyperglycemic hyperosmolar nonketotic syndrome. *Endocrinol Metab Clin North Am.* 2000;29(4):683–705, V. [PubMed: 11149157]

43. Kitabchi AE, Umpierrez GE, Murphy MB, et al. Hyperglycemic crises in diabetes. *Diabetes Care*. 2004;27(Suppl 1):S94–S102. [PubMed: 14693938]

44. American Diabetes A. Hospital admission guidelines for diabetes. *Diabetes Care*. 2004;27(Suppl 1):S103. [PubMed: 14693939]

45. Trachtenbarg DE. Diabetic ketoacidosis. *Am Fam Physician*. 2005;71(9):1705–1714. [PubMed: 15887449]

46. Goad NT, Bakhru RN, Pirkle JL, Kenes MT. Association of hyperchloremia with unfavorable clinical outcomes in adults with diabetic ketoacidosis. *J Intensive Care Med.* 2020;35(11):1307–1313. [PubMed: 31342846]

47. Hammond DA, Lam SW, Rech MA, et al. Balanced crystalloids versus saline in critically ill adults: A systematic review and meta-analysis. *Ann Pharmacother.* 2020;54(1):5–13. [PubMed: 31364382]

48. Self WH, Evans CS, Jenkins CA, et al. Clinical effects of balanced crystalloids vs saline in adults with diabetic ketoacidosis: A subgroup analysis of cluster randomized clinical trials. *JAMA Netw Open*. 2020;3(11):e2024596. [PubMed: 33196806]

49. Szumita PM RD. Team approach for glucose management. In: R HM Garg, ed. *Hyperglycemia in the Hospital Setting*. Philadelphia: Jaypee Brothers; 2014:100–108.

50. Brink S, Joel D, Laffel L, et al. ISPAD Clinical Practice Consensus Guidelines 2014. Sick day management in children and adolescents with diabetes. *Pediatr Diabetes*. 2014;15(Suppl 20):193–202. [PubMed: 25182314]

SELF-ASSESSMENT QUESTIONS

1. Which of the following is a common cause of acute hyperglycemia in hospitalized patients?
   A. Anti-inflammatory mediators in acute illness
   B. Nothing by mouth (NPO) status
   C. Decreased gluconeogenesis
   D. Glucocorticoid usage
2. Which of the following is true about intravenous insulin protocols?
   A. There is a nationally accepted “gold standard” protocol
   B. Electronic intravenous insulin protocols decrease human error
   C. Paper-based protocols are preferred compared to electronic protocols
   D. The initial rate of insulin should be a fixed dose, regardless of the patient’s initial blood glucose
3. Which of the following is a reason why insulin is generally recommended for the management of acute hyperglycemia instead of non-insulin medications in the hospital setting?

A. Insulin has a lower risk of hypoglycemia compared to non-insulin medications

B. Insulin is less expensive compared to non-insulin medications

C. Insulin has a faster onset of action compared to non-insulin medications

D. Insulin is easier to dose compared to non-insulin medications

4. For most patients, when initiating SC insulin therapy in the inpatient setting, a reasonable initial total daily dose (TDD) is _____units/kg/day?

A. 0.005

B. 0.05

C. 0.5

D. 5

5. Which of the following types of subcutaneous insulin components will most patients with acute hyperglycemia in the inpatient setting require to effectively attain ADA and ACE glycemic goals while minimizing the risk of hypoglycemia?

A. Basal only

B. Prandial and sliding scale only

C. Basal, prandial, and correctional scale

D. Sliding scale only

6. Acute hyperglycemia in the intensive care unit setting, with or without the diagnosis of diabetes, is correlated with:

A. Increased length of stay

B. Increased risk of myocardial infarction

C. Increase risk of bleeding

D. Increased risk of venous thromboembolism

7. Which of the following is true about correctional insulin?

A. It can be used without basal and nutritional insulin

B. It is recommended to be used at the same time as nutritional insulin

C. It is recommended to manage diabetic ketoacidosis

D. It should not be adjusted for insulin sensitivity

8. Which of the following statements most accurately describes point-of-care glucose testing?

A. Slow results

B. Variable accuracy

C. Samples need to be sent to the lab

D. Should only be used with capillary blood

9. Per the 2009 Hyperglycemic Crises in Adult Patients with Diabetes ADA guideline, the initial dosing of insulin for patients in a hyperglycemic emergency is:

   A. 10 units IV bolus followed by 1 unit/kg/hr

   B. No bolus followed by 0.01 units/kg/hr

   C. No bolus followed by 0.14 units/kg/hr

   D. 0.1 units/kg IV bolus followed by 0.14 units/kg/hr

10. The inpatient glucose clinical management team is typically tasked with all the following **except**:

    A. Manage complex patients

    B. Educate staff

    C. Develop the glucose goal for the health system

    D. Provide consultation services for clinical teams

11. Acute hyperglycemia in the outpatient setting is often caused by all the following **except**:

    A. Exercise

    B. Acute illness

    C. Infection

    D. Inadequate anti-diabetes medication

12. Which of the following is the goal blood glucose for most patients in the intensive care unit on an insulin infusion, according to the American Diabetes Association Standards of Medical Care?

    A. 110-140 mg/dL (6.1 - 7.8 mmol/L)

    B. 140-180 mg/dL (7.8 - 10.0 mmol/L)

    C. 80-110 mg/dL (4.4 - 6.1 mmol/L)

    D. 80-180 mg/dL (4.4 - 10.0 mmol/L)

13. Which of the following blood glucose values should serve as the threshold for initiation of intravenous insulin therapy in the ICU setting?

    A. ≥80 mg/dL (4.4 mmol/L)

    B. ≥110 mg/dL (6.1 mmol/L)

    C. ≥180 mg/dL (10.0 mmol/L)

    D. ≥220 mg/dL (12.2 mmmol/L)

14. A 51-year-old female with no history of diabetes mellitus is being admitted to the hospital for community acquitted pneumonia. Her blood glucose is 246 mg/dL (13.7 mmol/L) on admission and 242 mg/dL (13.4 mmol/L) when the test is immediately repeated. Should an A1C be measured now?

    A. No, an A1C does not need to be measured in the hospital, but it should be measured at his next ambulatory care visit.

    B. Yes, to detect hyperglycemia in the hospital.

C. No, because he does not have a past medical history of diabetes.

D. Yes, to help with his inpatient insulin needs and discharge planning.

15. Which of the following is true about the management of diabetic ketoacidosis (DKA)?

A. An intravenous bolus of insulin is required for severe DKA

B. Subcutaneous insulin may be appropriate for mild DKA

C. Insulin should be started regardless of serum potassium level

D. Rapid reduction in blood glucose is the primary goal of therapy

SELF-ASSESSMENT QUESTION-ANSWERS

1. **D.** Corticosteroids are known to cause acute hyperglycemia in the inpatient setting and beyond. Other causes include high carbohydrate meal/tube feeds, inflammation, and increased gluconeogenesis. NPO status would be a risk for hypoglycemia. See the Acute Hyperglycemia section.

2. **B.** Electronic protocols are becoming more frequently utilized by institutions to attempt to mitigate this manual calculation as a source of human error. There is no identified "gold standard" protocol now. Paper protocols typically require manual calculations and are not preferred to electronic protocols. The initial dosing of insulin should generally be based on the most recent blood glucose value. See the Intravenous Insulin Infusions section.

3. **C.** Insulin has a more rapid glucose-lowering effect when compared to non-insulin therapies. Insulin therapy can be just as expensive if not more expensive. Despite being the preferred agent for acute hyperglycemia, the dosing of insulin can be complex and is prone to hypoglycemia. See the Non-insulin Medications section and Table e95-1.

4. **C.** A reasonable starting TDD is 0.5 units/kg/day. Therefore, for a 70-kg patient, 35 units of insulin would be an appropriate starting dose based on the current guidelines. 0.005 and 0.05 units/kg/day would generally be too low of a dose. 5 mg/kg/day would typically be an excessively high dose. See the Subcutaneous Basal/Nutritional Insulin section and Table e95-3.

5. **C.** The guidelines support an inpatient insulin regimen generally consisting of the following three components: basal insulin to manage glucose between meals, nutritional (also known as prandial) insulin for meal-related nutritional BG spikes, and correctional insulin given in addition to the nutritional insulin dose in the event the patient might have premeal hyperglycemia. These guidelines emphasize the importance of not using a sliding scale insulin regimen as the only approach. See the Subcutaneous Basal/Nutritional Insulin section and Tables e95-3 to e95-5.

6. **A.** Hyperglycemia in the ICU setting is associated with increased length of stay. Myocardial infarction, bleeding, and venous thromboembolism are not correlated with acute hyperglycemia. See the Society of Thoracic Surgeons section.

7. **B.** Correctional insulin should be given in addition to the nutritional insulin dose in the event the patient might have premeal hyperglycemia. Guidelines discourage the use of correctional insulin only or sliding scale insulin only therapy. DKA should be treated with either an insulin infusion or standing doses of basal insulin, not correctional insulin. Correctional insulin should be adjusted for insulin sensitivity. See the Subcutaneous Basal/Nutritional Insulin section and Tables e95-3 to e95-5.

8. **B.** Point of care testing (POCT) is a bedside test of blood from capillary, venous, or arterial blood with fast results; however, these devices have variable accuracy. See the Glucose Monitoring section.

9. **C.** Debate exists regarding the need for intravenous bolus and the 2009 ADA guideline allows for either a bolus of 0.1 units/kg followed by 0.1 units/kg/hr, or no bolus with an insulin infusion rate starting at 0.14 units/kg/hr; therefore, either regimen can be used at the proper dosing. See the Electrolytes and Insulin sections and Table e95-7.

10. **C.** The clinical management team may be involved in helping the multidisciplinary steering committee create the glucose goals for the health system, but the multidisciplinary steering committee would be tasked with this getting input from many stakeholders. The clinical team can manage

complex patients and be available for consolations. See the Clinical Management Team section and Table e95-8.

11. **A.** Exercise generally lowers blood glucose, whereas acute illness, infection, or inadequate insulin therapy are primary reasons for acute hyperglycemia at home. See the Acute Hyperglycemia and Sick-Day Management in the Outpatient Setting section.

12. **B.** The 2021 ADA Standards of Medical Care in Diabetes support using a goal blood glucose of 140 to 180 mg/dL (7.8 to 10.0 mmol/L) for patients on insulin therapy. See the American Diabetes Association section and Table e95-5.

13. **A.** Most guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients suggest for ICU patients a blood glucose value of 180 mg/dL (10.0 mmol/L) or higher should trigger the initiation of insulin therapy. Both 80 mg/dL (4.4 mmol/L) and 110 mg/dL (6.1 mmol/L) are generally considered lower than the trigger and 220 mg/dL (12.2 mmol/L) would generally too high for a trigger. See the American College of Critical Care Medicine/Society of Critical Care Medicine section.

14. **D.** The ADA Standards of Medical Care recommend that an A1C should be measured in all patients with diabetes or hyperglycemia (blood glucose higher than 140 mg/dL [10.0 mmol/L]) admitted to the hospital if not performed within the prior 3 months. The A1C can help predict inpatient insulin needs and can aid in the diagnosis of previously unrecognized diabetes and discharge planning. This patient has no history of diabetes mellitus, but he has hyperglycemia in the hospital, so an A1C should be measured now. See the Epidemiology section.

15. **B.** In mild DKA, subcutaneous insulin therapy may be an appropriate option if the proper dosing regimen is initiated. Bolus intravenous insulin may not always be necessary. Insulin therapy should be delayed if the serum potassium is less than 3.3 mEq/L (mmol/L). Rapid reduction in blood glucose may be harmful and lead to cerebral edema. See the Electrolytes and Insulin sections and Table e95-7.