Hypoglycemia and Diabetes
Self-Assessment Program

This program is intended to measure baseline knowledge; therefore, there is not a mandatory prerequisite for participating in this program.

Target Audience
All health care professionals involved in treating individuals with diabetes, including physicians, physician assistants, nurses, nurse practitioners, dietitians, pharmacists, and other health care professionals.

Learning Objectives
At the end of this activity, the participant should be able to:

- Define hypoglycemia and its various classifications.
- Discuss the implications of hypoglycemia on both short- and long-term outcomes for individuals with diabetes.
- Elaborate on the implications of hypoglycemia on treatment targets for patients with diabetes.
- Discuss how to provide assistance or guidance to individuals in the management of blood glucose levels in relation to hypoglycemia.
- List clinical recommendations for those at risk for hypoglycemia.
- Discuss strategies known to prevent hypoglycemia and incorporate these strategies into clinical practice.
CASE STUDY #1

Questions 1-11

KL, an 11-year old female, was diagnosed with type 1 diabetes 6 years ago and is currently controlled on insulin glargine 10 units once daily and insulin aspart 5 units before meals and 3 units at bedtime. She is late for her regular follow-up visit because gymnastics class was running late and traffic was bad; her mother apologizes.

You assess KL’s most recent A1C (measured last month: 6.8%), how many times a day she tests her plasma glucose, and her risk for hypoglycemia. She tests her blood glucose twice a day, before breakfast and at bedtime, and when symptoms occur, at which point her plasma glucose level is 65-70 mg/dL; is currently experiencing 1–2 episodes per week, typically after gymnastics class. She self-treats herself as soon as symptoms develop with three to four glucose tablets and then she feels fine. Symptoms include feeling jittery, starts to tremble, with a “pounding heart”, perspires, and sometimes she gets irritable.

She demonstrates the use of her glucose meter. Result reveals a plasma glucose level of 58 mg/dL. You inquire about symptoms, asking if she is feeling dizzy, lightheaded, or irritable. The patient is surprised the level is so low, since she was not aware or feeling any symptoms that she has had in the past.

1. How would you classify KL’s most recent hypoglycemic event in your progress notes?
   A. Severe hypoglycemia
   B. Documented symptomatic hypoglycemia
   C. Asymptomatic hypoglycemia
   D. Probable symptomatic hypoglycemia
   E. Pseudo-hypoglycemia

Answer: C

Rationale
Hypoglycemia is defined in patients with diabetes as all episodes of an abnormally low plasma glucose concentration that expose the individual to potential harm. Although usually termed “mild”, “moderate”, or “severe”, it is now recommended that hypoglycemia be classified according to symptoms and as they relate to the level of plasma glucose, that is, asymptomatic, pseudo-hypoglycemia, probable symptomatic, documented symptomatic, or severe.

Pseudo-hypoglycemia is defined as a patient having hypoglycemic symptoms with a blood glucose reading above 70 mg/dL (>3.9 mmol/L). Probable symptomatic hypoglycemia is when patients report definite symptoms typical of hypoglycemia and are assumed to be ≤70 mg/dL (≤3.9 mmol/L).
Documented symptomatic hypoglycemia is an event during which typical symptoms of hypoglycemia are accompanied by a measured plasma glucose concentration $\leq 70$ mg/dL ($\leq 3.9$ mmol/L). Severe hypoglycemia is an event requiring assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions.

Asymptomatic hypoglycemia is an event not accompanied by typical symptoms of hypoglycemia but with a measured plasma glucose concentration of $\leq 70$ mg/dL ($\leq 3.9$ mmol/L). With a plasma glucose level of 55 mg/dL, one would expect KL to be experiencing at least symptoms of a sympato-adrenal response, which would alert her to ingest carbohydrates to raise her plasma glucose levels. However, based on the HCP assessment, KL is unaware of her hypoglycemia based upon her lack of symptoms.

**Reference:**


2. According to the 2013 American Diabetes Association/The Endocrine Society Report on Hypoglycemia, which of the following statements is CORRECT regarding a plasma glucose threshold value that defines hypoglycemia?

A. A single threshold value for plasma glucose concentration of $\leq 70$ mg/dL only applies to individuals with diabetes.

B. A single threshold value for a plasma glucose concentration of $\leq 70$ mg/dL is lower than the glycemic threshold for symptoms in both non-diabetic individuals and those with well-controlled diabetes.

C. A single threshold value for plasma glucose concentration that defines hypoglycemia cannot be assigned, but rather assign an alert level that draws attention of the potential for harm to the person with diabetes as well as their caregiver(s).

D. Thresholds for symptoms of hypoglycemia shift to higher plasma glucose concentrations after a recent hypoglycemic event and to lower plasma glucose concentrations in persons with *poorly-controlled* diabetes and frequent hypoglycemia.

E. Thresholds for symptoms of hypoglycemia shift to higher plasma glucose concentrations after a recent hypoglycemic event and to higher plasma glucose concentrations in persons with *poorly-controlled* diabetes and infrequent hypoglycemia.

**Answer:** C

**Rationale:**

Hypoglycemia puts patients at risk for injury and death, and as such, is defined as all episodes of an abnormally low plasma glucose concentration that draws the attention of both patients and caregivers to the potential harm associated with hypoglycemia. A single threshold value for
plasma glucose concentration that defines hypoglycemia in diabetes cannot be assigned because glycemic thresholds for symptoms of hypoglycemia (among other responses) shift to lower plasma glucose concentrations after recent antecedent hypoglycemia and to higher plasma glucose concentrations in patients with poorly controlled diabetes and infrequent hypoglycemia. However, a plasma glucose concentration of \( < 70 \text{ mg/dL} \) has been assigned as an alert value because it is higher than the glycemic threshold for symptoms in both non-diabetic individuals and those with well-controlled diabetes. Although this alert value has been debated, it is recommended in the 2013 Report of a Workgroup of the American Diabetes Association and The Endocrine Society as a cut-off value when classifying hypoglycemia in diabetes.

**Reference:**


3. **Glycemic control is critical for managing diabetes and preventing diabetes-related complications.** You review KL’s monitoring log because she measures her plasma glucose only before breakfast and at bedtime. How often should KL do self-management of blood glucose (SMBG)?

   A. Only before meals  
   B. Only before bedtime and never during the early morning hours  
   C. Only before breakfast and at bedtime  
   D. Before meals, at bedtime, and during suggestive symptoms  
   E. Only during suggestive symptoms

**Answer: D**

**Rationale:**

The American Diabetes Association recommends self-monitoring of blood glucose (SMBG) as an integral part of diabetes management for patients who are treated with insulin. SMBG allows patients to adjust food intake, physical activity, or pharmacologic therapy in response to their blood-glucose readings and to assess whether their blood-glucose levels are under control. The frequency and timing of SMBG should be dictated by the particular needs and goals of the patient. SMBG is especially important for patients treated with insulin to monitor for and prevent asymptomatic hypoglycemia and hyperglycemia. It is recommended that most persons with type 1 diabetes and others (with type 2 diabetes) on intensive insulin regimens (MDI or insulin pump therapy) should do SMBG at least prior to meals and snacks, occasionally postprandially, at bedtime, prior to exercise, when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving. For many patients, this will require testing 6–8 times daily, although individual needs may be greater.
Reference:

4. Which of the following is INCORRECT regarding treatment of a plasma glucose concentration of ≤70 mg/dL in a person with diabetes?

A. Does not always need to treat with carbohydrates.
B. Repeat the test in the short term to determine if the original reading was correct.
C. Change their current behavior until the glucose level is elevated.
D. Should always be treated with carbohydrates.
E. If immediately prior to eating, partake in a planned meal.

Answer: D

Rationale:
As noted, a plasma glucose concentration of ≤70 mg/dL has been assigned as an alert value because it is higher than the glycemic threshold for symptoms. Therefore, a person with diabetes need not always self-treat at an estimated glucose concentration of ≤70 mg/dL (≤3.9 mmol/L). Options other than carbohydrate ingestion include repeating the test in the short term, changing behavior, such as avoiding driving or elective exercise until the glucose level is higher, and adjusting the treatment regimen. In addition, if the plasma glucose level is ≤70 mg/dL immediately prior to eating, no action is needed other than to eat the planned meal.

Reference:

5. What would be the preferred source(s) of carbohydrate for the INITIAL treatment of KL’s hypoglycemic episode?

A. Diet soda
B. Glucagon 1 mg subcutaneous injection
C. A glucose drink or glucose tablets
D. Chocolate
E. A glass of whole milk

Answer: C

Rationale:
Treatment of an acute hypoglycemia glycemic response correlates better with glucose content than with carbohydrate content of food. However, although pure glucose is the preferred
treatment (a glucose drink or glucose tablets), any form of carbohydrate that contains glucose will raise blood glucose. Therefore, glucose (15–20 grams) taken orally is the preferred treatment for the conscious individual with hypoglycemia.

But the type of carbohydrate can be important: 40 grams of carbohydrate in the form of juice gave approximately the same increase as 20 grams of carbohydrate in the form of glucose tablets, and a greater amount of sucrose is required to provide the same increase in plasma glucose. And added fat may retard and then prolong the acute glycemic response. For example, whole milk containing 20 grams of carbohydrate gave only a rise of approximately 20 mg/dL (1 mmol/L) due to the delayed emptying from the stomach because of the fat content. Therefore, milk, chocolate, and other foods that contain fats will cause the sugar to be absorbed more slowly and should be avoided if at all possible as the initial treatment of hypoglycemia.

References:


6. What plasma glucose level would be the goal of KL’s treatment of hypoglycemia?

A. 70 mg/dL  
B. 80 mg/dL  
C. 100 mg/dL  
D. A 20% increase from the current level  
E. A 30% increase from the current level

Answer: C

Rationale:
Treatment of a conscious individual with hypoglycemia should provide immediate oral, rapidly absorbed, simple carbohydrate calculated to restore the plasma glucose level to euglycemia, or at least 100 mg/dL (5.6 mmol/L).

References:


7. When should KL retest her plasma glucose?

A. Immediately after treatment  
B. After 10-15 minutes  
C. After 20-30 minute  
D. After 60 minutes  
E. After 2 hours

Answer: B

Rationale:
After treatment, the guidelines recommend to wait 10–15 minutes and then retest the plasma glucose. If there is no response or an inadequate response, repeat oral intake as above until the
target plasma glucose level has been achieved. Then, retest the plasma glucose in another 20–30 minutes to confirm the target plasma glucose level has been maintained.

**References:**

8. KL says she was not aware of her low plasma glucose level. Which statement about hypoglycemia unawareness is CORRECT?

A. Hypoglycemia unawareness is defined as failure to appreciate the onset of autonomic symptoms before those of neuroglycopenia activation.
B. Awareness of hypoglycemia is largely the result of the perception of neuroglycopenic symptoms.
C. Patients with hypoglycemia unawareness have an impaired response to cortisol as a result of very low plasma glucose levels.
D. The risk of severe hypoglycemia is increased three- to six-fold in patients with hypoglycemia unawareness.
E. Hypoglycemia unawareness only occurs while an individual with diabetes is awake and resting.

**Answer: A**

**Rationale:**
A coordinated group of endocrine and behavioral events comprise the counterregulatory responses to hypoglycemia. Primary responses consist of a reduction in plasma insulin concentrations, and increases in plasma epinephrine (and nor-epinephrine) and glucagon. These events are essentially reactive, and will rapidly increase plasma glucose by decreasing glucose uptake into cells and increasing hepatic glucose production. Secondary responses include rapid increases in plasma glucocorticoid, and growth hormone concentrations. The downstream effect of glucocorticoid and growth hormone are more adaptive than reactive responses because they provide the animal with the ability to modify metabolic processes over longer periods of time.

**References:**
9. Which of the following strategies MAY NOT decrease the risk of hypoglycemia in a person with hypoglycemia unawareness?

A. Patient education.
B. Maintain a target glycemic level of less than 7%.
C. Dietary intervention.
D. Exercise management.
E. Medication adjustment.

Answer: B

Rationale:
Although lower glycemic targets reduce the incidence of microvascular complications, the risk of hypoglycemia is increased. In the DCCT, intensification of glycemic control was associated with a 300% increase in the rate of hypoglycemia.

As part of the educational plan, the individual with diabetes and his or her caregivers need to recognize the symptoms of hypoglycemia and be able to treat a hypoglycemic episode properly with oral carbohydrates or glucagon. Hypoglycemia, including its risk factors and remediation, should be discussed routinely with patients receiving treatment with insulin or sulfonylurea/glinide drugs, especially those with a history of recurrent hypoglycemia or impaired awareness of hypoglycemia.

Patients with diabetes need to recognize which foods contain carbohydrates and understand how the carbohydrates in their diet affect plasma glucose. To avoid hypoglycemia, patients on long-acting secretagogues and fixed insulin regimens must be encouraged to follow a predictable meal plan. Patients on more flexible insulin regimens must know that prandial insulin injections should be coupled to meal times.

Physical activity increases glucose utilization, which increases the risk of hypoglycemia. The risk factors for exertional hypoglycemia include prolonged exercise duration, unaccustomed exercise intensity, and inadequate energy supply in relation to ambient insulinemia. Post-exertional hypoglycemia can be prevented or minimized by careful glucose monitoring before and after exercise and taking appropriate preemptive actions. Pre-exercise snacks should be ingested if plasma glucose values indicate falling glucose levels.
Patients who develop hypoglycemia unawareness do so because of frequent and recurrent hypoglycemia. To avoid such frequent hypoglycemia, adjustments in the treatment regimen that scrupulously avoid hypoglycemia are necessary.

**References:**


10. Which age group is the most vulnerable to the adverse effects of hypoglycemia?

   A. Children with type 1 diabetes.
   B. Adults with type 1 diabetes.
   C. Adolescents with type 2 diabetes.
   D. Middle-aged adults with type 2 diabetes.
   E. Elderly with type 2 diabetes.

**Answer:** A

**Rationale:**

All individuals who experience hypoglycemia are at long-term risk. Patients in the older age-groups are especially vulnerable to hypoglycemia, which is the most frequent metabolic complication experienced by older adults in the U.S. However, those most vulnerable to the adverse consequences of hypoglycemia are the youngest patients with type 1 diabetes, as ongoing maturation of the central nervous system puts these children at greater risk for cognitive deficits as a consequence of this adverse effect.

**References:**


11. To minimize both short- and long-term complications for their daughter, KL’s parents want her to maintain tight glycemic control. Which of the following statements is CORRECT regarding the effect of treatment on A1C levels and severe hypoglycemia in patients with type 1 diabetes in the Diabetes Control Complications Trial (DCCT)?

A. Intensive treatment in the DCCT was associated with a slight increase in the risk of severe hypoglycemia and was directly inversely correlated with the A1c level.
B. Standard treatment in the DCCT was associated with a threefold increase in the risk of severe hypoglycemia and was inversely correlated with the A1c level.
C. Both standard and intensive treatment in the DCCT was associated with a threefold increase in the risk of severe hypoglycemia and was directly correlated with the A1c level.
D. Intensive treatment in the DCCT was associated with a threefold increase in the risk of severe hypoglycemia and was inversely correlated with the A1c level.
E. Intensive treatment in the DCCT was associated with a threefold increase in the risk of severe hypoglycemia and was directly correlated with the A1c level.

Answer: D

Rationale:
The Diabetes Control and Complications Trial (DCCT) demonstrated that maintaining near-normal plasma glucose values with a regimen of intensive therapy markedly reduced the risks of development or progression of microvascular complications in patients with type 1 diabetes when compared with a conventional treatment regimen.

For those individuals randomized to the intensive treatment arm, there was a threefold increase in the risk of severe hypoglycemia, including episodes accompanied by coma and/or seizure. This risk persisted over the duration of the study and was inversely correlated with the A1C level. Among all of the factors most strongly associated with the risk of severe hypoglycemia, the dominant predictor was a history of prior episodes of hypoglycemia.

Reference:
CASE STUDY #2

Questions 12-19

BB is an overweight (BMI=29 kg/m²) 37-year old male with a 20-year history of type 1 diabetes. He is well-controlled on once daily basal insulin as well as prandial insulin injections, with an A1C of 6.9% and 1-hour postprandial glucose readings ranging from 150 to 165 mg/dL. On a recent bicycle vacation trip, he planned to ride his bicycle every day for 7 days. Riding the first two days was relatively easy, spending only an hour on the bike after breakfast. The route was flat and BB experienced no difficulties. On the third day, however, anticipating a strenuous day riding because of two steep climbs, BB reduced his basal insulin dose by 10%. While riding up the second hill, he started to feel dizzy and disorientated, had palpitations, paresthesias, and had a sour taste in his mouth. Although he did not test his plasma glucose, BB recognized the symptoms of hypoglycemia. He stopped riding, drank some apple juice, and waited for the symptoms to resolve.

12. How would you classify BB’s hypoglycemia in your progress notes?

A. Severe hypoglycemia  
B. Documented symptomatic hypoglycemia  
C. Asymptomatic hypoglycemia  
D. Probable symptomatic hypoglycemia  
E. Pseudo-hypoglycemia

Answer: D

Rationale

Because BB was able to recognize his symptoms of hypoglycemia and take action despite not knowing a plasma glucose reading, his hypoglycemia would be classified as probable symptomatic. Probable symptomatic hypoglycemia is when patients report definite symptoms of the complication, but plasma glucose readings, although not measured, are assumed to be <70 mg/dL.

Reference:


13. What might BB do in order to MOST EFFECTIVELY prevent hypoglycemia associated with physical activity?

A. Consume sufficient carbohydrates and reduce insulin during and following the activity.  
B. Consume sufficient carbohydrates during and following the activity, and do not overtreat post-exercise hyperglycemia.
C. Begin at a predetermined target plasma glucose level, reduce pre-exercise insulin, and eat plenty of carbohydrates following the activity.

D. Begin at a predetermined target plasma glucose level, consume sufficient carbohydrates, possibly reduce insulin, and do not over-treat post-exercise hyperglycemia.

E. Reduce insulin during and following the activity, and eat a full meal after completing it.

Answer: D

Rationale

Results from the Diabetes Research in Children Network Study revealed lower starting plasma glucose levels increase the incidence of hypoglycemia during physical activities. Hypoglycemia occurred in 86% of youth doing a 75-minute physical activity session with starting plasma glucose values less than 120 mg/dL, in 13% starting glucose between 120 to 180 mg/dL, and in 6% starting at 180 mg/dL or higher; a 15-gram carbohydrate snack was frequently insufficient to successfully treat a hypoglycemic event. This study reinforces the necessity of beginning at a target plasma glucose level and consuming a sufficient amount of carbohydrate to decrease the risk of experiencing a hypoglycemic episode during (and following) physical activity. In addition, insulin reductions may be necessary to prevent hypoglycemia during longer duration exercise.

Education is also important, especially for parents of young children with diabetes not to overreact to post-exercise hyperglycemia, which is usually only transient and may need reduced or no insulin to treat effectively for several hours afterwards. BB will need to plan ahead when riding his bicycle, especially for prolonged or strenuous rides. He also needs to be educated to lower his rapid-acting insulin doses to compensate and also be particularly vigilant about moderating his post-exercise meal insulin boluses and overnight basal rates, along with consuming an appropriate (balanced) bedtime snack to prevent nocturnal hypoglycemia and provide extra calories. One study showed a significant relationship (p < .001) between snack composition and the frequency of nocturnal hypoglycemia, whereby 71% of episodes (10 of 14) occurred with no snack and four episodes were associated with a cornstarch snack (one slide of white bread, one ounce of cheddar cheese, plus 14 grams of raw cornstarch dissolved in a placebo drink). However, no hypoglycemic episodes were associated with the standard or protein snacks irrespective of bedtime glucose levels.

Planned exercise should be preceded by carbohydrate ingestion, reduced insulin doses, or both. Unplanned exercise requires careful self-monitoring of plasma glucose at a minimum; that will often prompt carbohydrate ingestion. During his rides, BB should always have a rapid-acting carbohydrate source, like glucose tablets or gels, readily available to treat low plasma glucose levels, as well as additional snacks that can provide extra carbohydrates (like granola bars). A fellow cyclist, who is a pharmacist, recommended BB ask his health care provider to prescribe a glucagon pen that he could keep with him as a treatment for severe hypoglycemia.
### References:


### 14. Case Continuation:

After his symptoms resolved, BB continued riding his bicycle, but became cautious during the rest of the day, and seriously considered discontinuing the rest of his biking vacation.

Encouraging adults with diabetes to become physically active involves addressing barriers to participation and devising strategies to overcome them. Which of the following is the MOST COMMON exercise barrier for individuals with diabetes?

A. Lack of motivation  
B. Being self-conscious  
C. Fear of hypoglycemia  
D. Altered perception of physical activity status
E. Lack of exercise clothing or proper footwear

Answer: C

Rationale:
Failure by patients to recognize and be aware of symptoms of hypoglycemia in an early phase of the complication, known as hypoglycemia unawareness, can increase the risk of both prolonging the duration and increasing the frequency of hypoglycemia. These events perpetrate a deleterious vicious circle leading to an increase in severe hypoglycemia with brain dysfunction. Because of these negative consequences, patients may develop psychological fear of hypoglycemia. While the symptoms of hypoglycemia alert individuals to an impending episode, these warning signs can diminish quality of life and reduce glycemic control. For individuals with diabetes, especially for who use insulin, fear of hypoglycemia associated with physical activity has been reported to be the strongest barrier to regular physical activity participation; therefore, they must be informed and supported in hypoglycemia management so they can overcome this barrier. Lack of motivation and being self-conscious may actually be as a consequence from fear.

If a family member or spouse observes a hypoglycemic event, that experience could elicit even greater fear than from the patient. As a result, hypoglycemic episodes may provoke marital conflict regarding diabetes management. In an effort to prevent future hypoglycemic episodes, an individual may resort to behaviors (e.g., reducing or eliminating insulin dose and/or consuming high–glycemic index food) that increase glucose levels.

References:
15. Each of the following is a pathophysiologic mechanism that could cause hypoglycemia in conjunction with exercise for those who use insulin EXCEPT?

A. Absorption and release of injected insulin from its subcutaneous depot during physical activity.
B. Replenishment of triglycerides in adipose tissue following a low-intensity, long-duration physical activity.
C. Additive effects of blood glucose uptake via muscle contractions and insulin action during exercise.
D. Impaired or defective release of counterregulatory hormones during hypoglycemia following a prior episode of hypoglycemia or a bout of exercise.
E. Replenishment of muscle glycogen stores during the 24−48 hour period following an acute bout of exercise.

Answer: B

Rationale:
Hypoglycemia can result from a number of factors, including defective counterregulatory hormonal mechanisms, acutely increased insulin mobilization and sensitivity, increased glucose utilization, and replenishment of glycogen stores. Any of these factors, alone or in combination, can result in hypoglycemia, with or without symptoms. Physical activity itself can cause hypoglycemia both during and following sessions, and its risk is affected by a number of factors, including exercise type, duration, and intensity, insulin and other medication doses, and food intake. However, replenishment of triglycerides into adipose tissue following a low-intensity, long-duration activity does not increase the risk of hypoglycemia.

References:


16. You recommend BB check his plasma glucose several times a day, either by self-monitoring of blood glucose (SMBG) or continuous glucose monitoring (CGM). Frequent glucose monitoring will enable him to do all of the following EXCEPT:

A. Detect glycemic excursions.
B. Identify current or impending hypoglycemia.
C. Monitor resolution of hypoglycemia.
D. Identify recurring patterns of hypoglycemia.
E. Significantly improve glycemic control.

Answer: E

Rationale:
SMBG allows patients to adjust food intake, physical activity, or pharmacologic therapy in response to their blood-glucose readings and to assess whether their blood-glucose levels are under control. It also provides a means of identifying daily hypoglycemic events, allowing immediate treatment and modification of therapeutic regimens to allow tighter glycemic control while minimizing future hypoglycemic risk. Effective SMBG requires that patients recognize when action needs to be taken; however, unless steps are taken by the patient/caregiver(s) to act on the results, SMBG may not significantly improve glycemic control.

References:

17. Each of the following statements regarding SMBG is correct EXCEPT:

A. Patients need to understand when testing should be done
B. Patients need to understand what the results of SMBG mean
C. SMBG are easy to use and do not require prior knowledge of their use
D. Measure glucose at one point in time
E. Date and time must be set correctly on the meter to enable proper interpretation of results

Answer: C

Rationale:
Effective SMBG requires that patients be trained in how to use their blood glucose meters, understand when testing should be done and what the test results mean, and recognize when
action needs to be taken. Unlike HbA1c measurements, SMBG is episodic: it measures glucose at 1 point in time. Accordingly, SMBG timing is important, and the date and time must be set correctly on the meter to enable proper interpretation of the results.

**Reference:**

18. The main difference between SMBG and continuous glucose monitoring (CGM) device is:

A. Real-time CGM devices measure interstitial glucose, which correlates reasonably well with plasma glucose.
B. Results from CGM devices can be used to make treatment decisions without verification with SMBG.
C. Real-time CGM can be used to make acute treatment decisions.
D. Only CGM devices allow the patient to detect either hypo- and/or hyperglycemic excursions.
E. CGM provides no benefits for individuals with type 1 diabetes who have achieved glycemic control.

**Answer:** A

**Rationale:**
SMBG provides patients with instant feedback about the effects of food choices, exercise, stress, and medications on their glycemic levels. Real-time CGM measures interstitial glucose, which correlates well with plasma glucose; however, CGM sensors require calibration with SMBG, which is still recommended for making acute treatment decisions. CGM devices have alarms for hypo- and hyperglycemic excursions. A 26-week randomized trial of individuals with type 1 diabetes (N=322) showed that adults aged ≥25 years using intensive insulin therapy and CGM experienced a 0.5% reduction in A1C (from ∼7.6 to 7.1%) compared with usual intensive insulin therapy with SMBG. Sensor use in children, teens, and adults to age 24 years did not result in significant A1C lowering, and there was no significant difference in hypoglycemia in any group. Importantly, the greatest predictor of A1C lowering in this study for all age-groups was frequency of sensor use, which was lower in younger age-groups. In a smaller RCT of 129 adults and children with type 1 diabetes and a baseline A1C <7.0%, outcomes combining A1C and hypoglycemia favored the group utilizing CGM, suggesting that CGM is also beneficial for individuals with type 1 diabetes who have already achieved excellent control.

**References:**


19. Which of the following is CORRECT regarding the accuracy of technologies available for individuals to measure their plasma glucose?

A. The International Organization for Standardization (ISO) and FDA standards require the analytical accuracy of point-of-care (POC) meters be within 15% of the actual value in 95% of samples with glucose levels ≥75 mg/dL and ±20 mg/dL for samples with glucose <75 mg/dL.

B. The International Organization for Standardization (ISO) and FDA standards the analytical accuracy of point-of-care (POC) meters be within 20% of the actual value in 95% of samples with glucose levels ≥75 mg/dL and ±15 mg/dL for samples with glucose <75 mg/dL.

C. In a study by Freckmann, none of the POC meters tested were capable of measuring a plasma glucose concentration of ±10 mg/dL.

D. The need for accurate POC meters in the <75 mg/dL range is essential in for all persons with diabetes, especially for those outpatients who are on medications that rarely cause hypoglycemia.

E. Because of being highly accurate, continuous glucose monitors (CGMs) meters are recommended for glycemic management of hospitalized patients.

**Answer: B**

**Rationale:**

At the present time, capillary measurements of plasma glucose with point-of-care (POC) glucose meters (self-monitored blood glucose [SMBG]) and interstitial measurement with continuous glucose monitors (CGMs) are available to outpatients. The International Organization for Standardization (ISO) and FDA standards require that POC meters’ analytical accuracy be within 20% of the actual value in 95% of samples with glucose levels ≥75 mg/dL and ±15 mg/dL for samples with glucose <75 mg/dL. However, an investigation by Freckmann et al found that only 15 of 27 meters on the market in Europe several years ago met the current analytical standards of ±15 mg/dL in the hypoglycemia range, 2 of 27 met ±10 mg/dL, and none were capable of measuring ±5 mg/dL.
It is essential for meters to be accurate in the <75 mg/dL range, especially for persons being treated with insulin (whether they are outpatients or inpatients), although it is less important for those in an outpatient setting who are on medications that rarely cause hypoglycemia. In critical care units, where the accuracy of POC meters is particularly crucial, their performance may be compromised by medications (vasopressors, acetaminophen), treatments (oxygen), and clinical states (hypotension, anemia).

With regard to existing real-time CGMs, accuracy can be achieved in only 60–73% of samples in the range of 40–80 mg/dL. Because the accuracy of CGMs, like POC meters, is negatively affected by multiple factors in hospitalized patients and they are calibrated with POC meters affected by those same factors, CGMs are not recommended for glycemic management in hospitalized patients at this time.

According to the American Diabetes Association Standards of Care, CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes.

(E)

References:


CASE STUDY #3
Questions 20-25

PAT, an 85-year-old woman with 3-year history of type 2 diabetes, is brought to the emergency room, unconscious; a plasma glucose reading reveals level of 43 mg/dL. Her daughter says her mother could not remember if she took her drugs over the past few days, so this morning she took a few extra doses of each.

Despite intravenous (IV) push of 50% dextrose, IV dextrose infusions, and glucagon 1 mg IV, she remains unconscious.

Past medical history: 3-year history of type 2 diabetes mellitus; 35-year history of hypertension, peripheral artery disease; depression since the death of her husband last year.

Physical exam: height, 5’1” (155 cm); weight, 157 pounds (71.3 kg); BMI, 29.7 kg/m².

Social history: denies smoking, alcohol consumption, or substance abuse.

Family history: Father died at age 75 of a heart attack; mother died at 82 of no specific reason; both had a history of type 2 diabetes, peripheral artery disease, and hypertension.

Lab results: A1C reading: 7.2%; creatinine, 2.7 mg/dL; plasma glucose, 43 mg/dL.

Medications: metformin 500 mg twice a day, glyburide 5 mg twice a day; lisinopril, 10 mg once daily; simvastatin 20 mg once daily in the evening; aspirin 81 mg once daily.

20. What immediate recommendation should be made for this patient based upon her lack of response to dextrose infusions?

A. Discontinue only the glyburide
B. Discontinue only the metformin
C. Discontinue both glyburide and metformin
D. Start octreotide 50 mcg subcutaneously
E. Initiate basal insulin therapy

Answer: D

Rationale:

Hypoglycemia is a common presentation to the Emergency Department. Management involves administration of intravenous (IV) dextrose 50% in water and dextrose-containing solutions administered via IV infusion, in addition to oral carbohydrates. For patients taking a sulfonylurea overdose, hospital admission is generally recommended with signs and symptoms...
of hypoglycemia due to the long duration of effect and delayed clearance of the drug and their metabolites, as well as subsequent high likelihood of recurrent hypoglycemic episodes. These recurrent hypoglycemic events take place despite adequate infusions of dextrose.

Discontinuing the use of both the metformin and glyburide in this patient is warranted, especially with the patient’s elevated serum creatinine level. However, based upon the immediacy of need, that action would be part of the long-term treatment plan. Administration of insulin at this time will only compound the immediate problem of recurrent hypoglycemia.

Octreotide is a somatostatin analog that is known to suppress numerous hormones including insulin. In a small study of 9 patients, the risk of hypoglycemia before and after octreotide administration was evaluated. Results showed the number of ampules of 50% dextrose administered per patient before octreotide was greater than the number of ampules administered per patient after octreotide (mean of 2.9 versus 0.2; \( p = .004 \)). And the risk of recurrent hypoglycemia before octreotide treatment was significantly decreased after octreotide treatment \( (p < .001) \), with stabilization of plasma glucose and cessation of rebound hypoglycemia occurring immediately after octreotide administration in all 9 patients. In another study of 40 patients (18 placebo; 22 octreotide), mean serum glucose values for those receiving octreotide patients were consistently higher during the first 8 hours compared with placebo, but showed no difference in subsequent hours. Although not indicated for treatment of recurrent hypoglycemia, octreotide appears to provide an alternate to preventing rebound hypoglycemia after sulfonylurea ingestion.

References:


21. What would be an appropriate target A1C for this patient to minimize episodes of hypoglycemia?
   A. Less than 6.5%
   B. Less than 7.0%
   C. Less than 8.0%
   D. Between 7.5% and 8.5%
   E. No need to set a target A1c
Answer: C

Rationale:

Older adults with diabetes have a disproportionately high number of clinical complications and comorbidities, all of which can be exacerbated by and sometimes contribute to episodes of hypoglycemia. Older adults with diabetes are at much higher risk for the geriatric syndrome, which includes falls, incontinence, frailty, cognitive impairment, and depressive symptoms. Low and high mean A1C values were associated with increased all-cause mortality and cardiac events.

Data from a 5-year longitudinal, observational study of Italian patients with type 2 diabetes suggested patients with high levels of comorbidity may not receive cardiovascular benefit from intensive plasma glucose control. And results of a study from the U.K. General Practice Research Database showed that for patients with type 2 diabetes over 50 years of age (mean age 64 years) whose treatment was intensified from oral monotherapy to addition of other oral agents or insulin, a U-shaped association between A1C and mortality was observed, with the lowest risk of mortality with an A1C of about 7.5%.

A retrospective cohort study of 71,092 patients with type 2 diabetes aged >60 years evaluated the relationships between baseline A1C and subsequent outcomes (acute nonfatal metabolic, microvascular, and cardiovascular events and mortality). Risk of any end point (complication or death) became significantly higher at A1C >8.0%.

According to the American Diabetes Association’s Standards of Care for patients with diabetes, less stringent A1C goals (such as <8%) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, and those with long-standing diabetes in whom the general goal is difficult to attain despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents including insulin. (Level of Evidence: B)

References:


**22. Which of the following factors does NOT put the patient at an increased risk for severe hypoglycemia?**

A. Short duration of diabetes  
B. History of severe hypoglycemia  
C. Advanced atherosclerosis  
D. Advanced age  
E. Tight glycemic control

**Answer:** A  
**Rationale:**

There has been uncertainty regarding whether intensive glycemic control can reduce the increased risk of cardiovascular disease in people with type 2 diabetes. In the past decade, several large long-term trials, ACCORD, ADVANCE, and VADT, compared the effects of intensive versus standard glycemic control on cardiovascular disease outcomes in relatively high-risk participants with established type 2 diabetes. Although overall results did not show a benefit, a subset analysis of these studies suggested the hypothesis that patients with shorter duration of type 2 diabetes and without established atherosclerosis might reap cardiovascular benefit from intensive glycemic control.

However, this patient has several co-morbidities, which include atherosclerosis. Therefore, it is possible for her that potential risks from intensive glycemic control may outweigh its benefits. An analysis of ACCORD, ADVANCE, and VADT revealed factors associated with intensive treatment of type 2 diabetes increased the risk for episodes of severe hypoglycemia without providing any cardiovascular benefits include: a very long duration of diabetes, known history of severe hypoglycemia, advanced atherosclerosis, and advanced age/frailty. Healthcare providers need to be vigilant in preventing severe hypoglycemia in patients with advanced disease and not aggressively attempt to achieve near-normal A1C levels in those in whom such a target cannot be reasonably easily and safely achieved.

**References:**


23. The ACCORD (Action to Control Cardiovascular Risk in Diabetes), ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation), and VADT (Veterans Affairs Diabetes Trial) examined the effect of glucose lowering on cardiovascular events in patients with type 2 diabetes. Which of the following statements is INCORRECT regarding results from these studies?

A. In each study, individuals randomized to the intensive arm experienced more episodes of hypoglycemia than did those who were randomly assigned to the standard treatment arm.

B. A relationship between mortality and randomization to intensive glucose control was observed in ACCORD but not in ADVANCE or VADT.

C. A relationship between mortality and randomization to intensive glucose control was observed in ADVANCE but not in ACCORD or VADT.

D. In VADT, the strongest independent predictor of mortality at 90 days was a recent severe hypoglycemic event.

E. Results from the three trials demonstrated an episode of severe hypoglycemia was associated with an increased risk of subsequent mortality.

Answer: C

Rationale

In ACCORD (Action to Control Cardiovascular Risk in Diabetes), ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation), and VADT (Veterans Affairs Diabetes Trial), a total of 24,000 patients with high cardiovascular risk were randomly assigned to either intensive glycemic control or standard therapy. Although severe hypoglycemia was not directly related to an increase in mortality, results from all three trials clearly demonstrated an associated between an episode of severe hypoglycemia and an increased risk of subsequent mortality.

In ACCORD, those who had one or more severe hypoglycemic episodes had higher rates of death than those without such episodes across both study arms (hazard ratio 1.41 [95% CI 1.03–1.93]). One-third of all deaths were due to cardiovascular disease, and hypoglycemia was associated with higher cardiovascular mortality.

In VADT, a recent severe hypoglycemic event was the strongest independent predictor of death at 90 days. And although the rates of hypoglycemia were low in ADVANCE, a similar pattern was observed.

References:


24. Which of the following statements is CORRECT with regard to the rate of severe hypoglycemia in the ACCORD study?

A. Rates of severe hypoglycemia were significantly increased in those individuals with a lower achieved A1C level.
B. For every 1% decline in A1C from baseline, there was a significant increase in the rate of severe hypoglycemia only in those randomized to standard treatment.
C. For every 1% decline in A1C from baseline, there was a significant increase in the rate of severe hypoglycemia only in those randomized to intensive treatment.
D. For every 1% decline in A1C from baseline, there was a significant decrease in the rate of severe hypoglycemia only in those randomized to standard treatment.
E. For every 1% decline in A1C from baseline, there was a significant decrease in the rate of severe hypoglycemia irrespective of treatment randomization.

Answer: E

Rationale:

In ACCORD, participants were asked at every visit if they had experienced episodes of low blood sugar. The circumstances surrounding episodes of symptomatic, severe hypoglycemia were investigated further by the research staff and information on precipitating events, symptoms, and consequences were recorded. All symptomatic, severe hypoglycemic events were reported to the coordinating center; those events requiring medical assistance were reported as serious adverse events. The primary outcome of ACCORD trial was time to the first episode of non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death. A subsequent epidemiological analysis of the study results sought to determine whether there is a link between hypoglycemia and mortality. Results of this analysis showed that for every 1% decline in A1C from baseline, there was a significant decrease in the rate of severe hypoglycemia irrespective of treatment randomization. While there was an increase in mortality in those randomized to intensive treatment, this outcome cannot be attributed to the increased rate of severe hypoglycemia.

References:


25. Case Continuation:

PAT is admitted to the hospital and an in-hospital endocrine consult is ordered. While in the hospital, PAT is at risk for further episodes of severe hypoglycemia.

The following is a complication of severe hypoglycemia that can occur as a result of a person with diabetes being hospitalized.

A. Reduction in the length of stay.
B. Reduction in the risk of in-patient mortality.
C. Death within 12 months of hospital discharge.
D. Less chance of having a myocardial infarction.
E. Less chance of having an ischemic stroke.

Answer: C

Rationale:

The true incidence and prevalence of hypoglycemia among hospitalized patients with diabetes are not exactly known, ranging from 10.5% of individuals admitted to the general wards of an academic medical center who experienced at least one episode of hypoglycemia (≤70 mg/dL) to 1.9% of individuals admitted to ICUs who had at least one episode of severe hypoglycemia (<40 mg/dL). With regard to impact, a retrospective analysis of 4,368 admissions involving 2,582 diabetic patients admitted to a general ward indicated that severe hypoglycemia, defined as a plasma glucose level of ≤50 mg/dL, was associated with increased length of stay, greater odds of in-patient mortality, and death within 1 year of hospital discharge.

References:


CASE STUDY #4
Questions 26-32

KK, a 76 years old Caucasian female with a 26-year history of type 2 diabetes, was brought to the clinic for complaints of decreased appetite within the last 2-3 months, having gotten worse in the last three weeks after she fell and hit her head on the coffee table. When the visiting nurse found her on the floor, disorientated, her plasma glucose was 52 mg/dL and she was given glucose tablets. She also complains of generalized weakness, unsteadiness, and has difficulty in hearing and seeing the television. Since her fall, she has had episodes of hypoglycemia (2-3 times a week), in which her blood glucose level would range from 50-60 mg/dL (measured by her daughter and a visiting nurse). Her sleep has also decreased markedly and she is very anxious due to this. She has loathing for life and said she was “not afraid of death”.

KK is cared for by her daughter, who comes in to see her once a day in the morning to draw up her insulin injections, and a visiting nurse who sees her in the afternoon. With concerns with her recent symptoms, loathing for life, and a visit to the emergency room because of being found unconscious by the visiting nurse, her family is going to place her in an assisted living setting in a long-term care facility, where she can still take care of herself but still be closely supervised. She currently takes metformin 500 mg twice a day, glyburide 10 mg once a day, NPH insulin 10 units in the morning, and 7 units of regular before meals and 4 units at bedtime. Results of her last lab test (last week) revealed an A1C of 7.3%, preprandial plasma glucose of 80 mg/dL, and 2-hour postprandial plasma glucose of 140 mg/dL.

26. **KK’s hypoglycemia would be classified as:**
   - A. Severe hypoglycemia
   - B. Documented symptomatic hypoglycemia
   - C. Asymptomatic hypoglycemia
   - D. Probable symptomatic hypoglycemia
   - E. Pseudo-hypoglycemia

**Answer: A**

**Rationale**
Pseudo-hypoglycemia is defined as a patient having hypoglycemic symptoms with a blood sugar reading above 70 mg/dL. Documented symptomatic hypoglycemia is an event during which typical symptoms of hypoglycemia are accompanied by a measured plasma glucose concentration \( \leq 70 \text{ mg/dL (} \leq 3.9 \text{ mmol/L)} \). Probable symptomatic hypoglycemia is when patients report definite symptoms of the complication, but plasma glucose readings, although not measured, are assumed to be \( \leq 70 \text{ mg/dL} \).
Since KK was found unconscious with an episode of hypoglycemia and required assistance for treatment, it would be classified as severe (an event requiring assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions).

Reference:

27. Which of the following would the preferred initial treatment of an unconscious person experiencing severe hypoglycemia?
   A. Glucagon 1 mg IM
   B. Glucose tablets
   C. Glucose gel
   D. Glass of milk
   E. IV Dextrose 5% in Water IV

Answer: A

Rationale:
Parenteral treatment of hypoglycemia is necessary when an individual is unwilling or unable to take carbohydrates by mouth. Glucagon 1 mg, either by subcutaneous, intramuscular, or intravenous administration is recommended; however, a transient increase in blood glucose can ensue, causing nausea and/or vomiting. In addition, intravenous administration of dextrose in water is also warranted, but not as the first step of initial treatment.

References:


28. Conventional risk factors for hypoglycemia include excessive or ill-timed dosing of, wrong type of, insulin or insulin secretagogue and conditions where:
   A. Exogenous glucose delivery is decreased.
   B. Endogenous glucose production is increased.
   C. Glucose utilization is decreased.
   D. Sensitivity to insulin is decreased.
   E. Insulin clearance is increased.
Answer: A

Rationale:
Guidelines on Hypoglycemia strongly recommend that both the conventional risk factors and those indicative of compromised defenses against hypoglycemia be considered in a patient with recurrent treatment-induced hypoglycemia. Conventional risk factors are excessive or ill-timed dosing of, or wrong type of, insulin or insulin secretagogue and conditions under which:

- Exogenous glucose delivery decreased or endogenous glucose production is decreased.
- Glucose utilization is increased.
- Sensitivity to insulin is increased.
- Insulin clearance is decreased.

References:

29. Which of the following increases the risk of severe hypoglycemia in an elderly person with diabetes?

A. Use of a DDP-4 antagonist as monotherapy
B. Antecedent hypoglycemia
C. Hospital discharge within the prior year
D. Caucasian race
E. Use of up to three concomitant medications

Answer: B

Rationale:
Assessment of risk factors for hypoglycemia is an important part of the clinical care of older adults with hypoglycemia. Education of both patient and caregiver on the prevention, detection, and treatment of hypoglycemia is paramount. Although the prevalence of any hypoglycemia (plasma glucose ≤70 mg/dL) or severe hypoglycemia (requiring third-party assistance) in older populations is not known, older participants in both glycemic intervention arms in the ACCORD study had an approximately 50% higher rates of severe hypoglycemia than participants under age 65 years. In a population analysis of Medicaid enrollees treated with insulin or sulfonylureas, the incidence of serious hypoglycemia, defined as that leading to emergency department visit, hospitalization, or death, was approximately 2 per 100 person-years. In this study, independent risk factors included hospital discharge within the prior 30 days, advanced age, black race, and use of five or more concomitant medications. Other studies have shown antecedent hypoglycemia increases the risk for severe hypoglycemia.
References:


30. Each of the following is a long-term complication that KK may experience as a result of her hypoglycemic episodes EXCEPT:

A. Cognitive dysfunction.
B. Functional impairment.
C. Improvement in health-related quality of life.
D. Depression.
E. Increased risk of falling.

Answer: C

Rationale:
Assessment of risk factors for hypoglycemia is an important part of the clinical care of older adults with hypoglycemia, which is linked to various co-morbidities, including cognitive dysfunction, functional impairment, depression, an increase in falling. Cognitive dysfunction in a bidirectional fashion: cognitive impairment increases the subsequent risk of hypoglycemia, and a history of severe hypoglycemia is linked to the incidence of dementia. And cognitive dysfunction makes it difficult for patients to perform complex self-care tasks such as glucose monitoring, changing insulin doses, or appropriately maintaining timing and content of diet. In older patients with cognitive dysfunction, regimens should be simplified, caregivers involved, and the occurrence of hypoglycemia carefully assessed.

The etiology of functional impairment in diabetes may include interaction between coexisting medical conditions, as well as gait and balance problems, which can increase the risk of falls. Avoidance of severe hypoglycemia can decrease this risk.

Both dementia and cognitive impairment are independently associated with a greater risk of hypoglycemia. In a study of military veterans, the frequency of hypoglycemia was comparable across age groups, but increased incrementally with greater cognitive impairment and the complexity of the treatment regimen: oral anti-glycemic regimens (oral) versus insulin alone versus oral plus insulin. The lowest frequency of hypoglycemia was in those cognitively-
impaired not taking anti-glycemic medications (4%), whereas the highest frequency of hypoglycemia was in those with dementia aged 65-74 years taking insulin alone (27%) and in those greater than 75 years of age using a combined oral anti-glycemic plus insulin regimen who had dementia (27%).

References:

31. You are reconciling KK’s medications. What change, if any, to her medication regimen would you recommend?

A. Lower the dose of glyburide.
B. Discontinue the glyburide.
C. Increase the dose of regular insulin.
D. Increase the dose of metformin.
E. Discontinue the glyburide and decrease the insulin doses.

Answer: E

Rationale:
Older patients are at increased risk for adverse drug events from most medications due to age-related changes in pharmacokinetics, in particular those that are renally elimination. For the person with diabetes, this may translate into increased risk for hypoglycemia, the potential need for reduced doses of certain medications, and attention to renal function to minimize side effects. Hypoglycemia unawareness or an episode of severe hypoglycemia should trigger a re-evaluation of the patient’s treatment regimen. Sulfonylureas are also a low-cost class of medications, but the risk of hypoglycemia with these agents may be problematic for older patients. Glyburide has the highest hypoglycemia risk and should not be prescribed for older adults. Although the risk of
hypoglycemia with metformin is low, that risk is increased with the metformin is given in combination with a sulfonylurea and/or insulin. Changing from regular insulin to short-acting insulin analog and from NPH to long-acting insulin analogs (insulin glargine or insulin detemir) has been shown to reduce the incidence of hypoglycemia, especially while sleeping.

References:

32. Case Continuation:

KK is transferred to a long-term care facility.

Which of the following would NOT minimize KK’s risk of experiencing hypoglycemia while in the long-term care facility?

A. Careful education regarding symptoms and treatment to both patient and caregiver(s).
B. Assess the elderly patient with diabetes for functional status as part of their overall clinical assessment.
C. Incorporate short-acting insulin sliding scales.
D. Avoid the use of glyburide in favor of shorter-acting insulin secretagogues.
E. Simplify complex treatment regimens.

Answer: C

Rationale
To minimize the risk of hypoglycemia in the elderly, education of the patient, caregivers, and staff within long-term care facilities on the causes and risks of hypoglycemia and the proper surveillance and treatment of this condition regarding the symptoms and treatment of hypoglycemia is essential. Regular reinforcement, is extremely important because of the recognized gaps in the knowledge base of these individuals. It is also important that the functional status of elderly patients be assessed as part of an overall clinical assessment, so as to properly apply individualized glycemic control goals. Medications that do not cause
hypoglycemia should be prescribed and avoid glyburide in favor of shorter-acting insulin secretagogues. If the patient is in a long-term care facility, arbitrary short-acting insulin sliding scales should also be avoided. And complex regimens requiring multiple decision points should be simplified, especially for patients with decreased functional status.

References


CASE STUDY #5
Questions 33-39

GRL, a 68-year-old obese male (32 kg/m²), was diagnosed with type 2 diabetes 19 years ago. Initial treatment strategy included lifestyle modification (nutrition and exercise) along with metformin 500 mg BID and glyburide 5 mg once daily. He initially enjoyed good glycemic control, but that slowly deteriorated over time. Nine months ago he complained of a burning and painful sensation in his feet, which caused him to stop exercising. He became depressed, feeling worthless, and his nutrition suffered, with a subsequent loss of glycemic control: A1C: 9.4%; fasting plasma glucose (FPG): 198 mg/dL; and PPBG 365 mg/dL.

At that time, his medications were changed to metformin 500 mg TID, glyburide 15 mg once daily, saxagliptin 10 mg once daily, and NPH insulin 24 units once daily in the morning. His A1C is now 8.1%, his FPG ranges anywhere from 75 to 180 mg/dL. Lately he has noticed being more irritable, increase in sweating, and a fast heartbeat, which occurs 2-3 times a week. When this happens, usually between 10-11 am, his plasma glucose is 70-80 mg/dL. He wonders what is happening since his plasma glucose level is in his target zone.

During his most recent office visit, the patient’s wife told the doctor that several times last week her husband was “acting confused and irrational”, plus he has been “slipping” a lot lately. Each time the episode resolved after he drank some apple juice.

33. Which symptom alerts you that GRL is likely experiencing an episode of severe hypoglycemia?
   A. Tachycardia
   B. Irritability
   C. Sweating
   D. Confusion
   E. Trembling

   Answer: D

   Rationale:
   Symptoms of hypoglycemia can be divided into adrenergic (rapidly falling and changing glucose levels) and neuroglycopenic (low central nervous system [CNS] glucose). Adrenergic symptoms are most pronounced with acute onsets and when present, precede neurobehavioral features, thus functioning as an early warning system. These symptoms include anxiety, irritability, dizziness, diaphoresis, pallor, tachycardia, headache, shakiness, and hunger. However, patients with frequent hypoglycemia may not experience these symptoms until the plasma glucose reach very low levels.

   If the warning signs are ignored and the plasma glucose levels continue to decline, more severe hypoglycemia may lead to alteration of mental function. The first sign of hypoglycemia in these
patients is confusion, and they often must rely on the assistance of others to recognize and treat low blood glucose. If untreated, symptoms proceed to headache, malaise, impaired concentration, disorientation, irritability, lethargy, slurred speech, and irrational or uncontrolled behavior, which may be confused with dementia. The medullary phase of hypoglycemia, characterized by deep coma, pupillary dilatation, shallow breathing, bradycardia, and hypotonicity, occurs at very low plasma glucose levels, approximately 10 mg/dL.

**References:**


34. A decrease in plasma glucose (PG) concentration produces a characteristic hierarchy of responses to avoid the development of hypoglycemia. For each physiologic response, match the respective role in prevention or correction of hypoglycemia. Note: there is only one correct answer for each physiologic response.

A. Decrease in insulin
B. Increase in glucagon
C. Increase in epinephrine
D. Increase in cortisol and growth hormone
E. Symptoms
F. Decrease in cognition

___ Compromises behavior defense
Answer: _F_

___ Not critical to the immediate correction of hypoglycemia
Answer: _D_

___ Prompts behavior defense (food/carbohydrate ingestion)
Answer: _E_

___ Third defense against hypoglycemia; critical when glucagon is deficient
Answer: _C_
First defense against hypoglycemia; primary glucose regulatory factor
Answer: A

Second defense against hypoglycemia; primary glucose counterregulatory factor
Answer: B

Overall Rationale
A decrease in plasma glucose (PG) concentration usually produces a characteristic hierarchy of responses to avoid hypoglycemia development. At approximately 70 mg/dL (4 mmol), there is increased secretion of counter regulatory hormones (glucagon, epinephrine, growth hormone, and cortisol [ACTH]) and an increase in the discharge of autonomic nervous system neurotransmitters (norepinephrine and acetylcholine).

The first physiological defense against hypoglycemia is a decrease in pancreatic islet β-cell insulin secretion, which occurs when plasma glucose concentrations decline within the physiological range of 80-85 mg/dL.

The second physiological defense is an increase in pancreatic islet α-cell secretion of glucagon. This response occurs as plasma glucose concentrations fall just below the physiological range of 60-65 mg/dL.

The third physiological defense is an increase in epinephrine secretion, which becomes critical when glucagon secretion is deficient. This increase in epinephrine secretion also occurs as plasma glucose concentrations fall just below the physiological range similar to glucagon.

An intense sympatho-adrenal response will produce neurogenic symptoms that cause the person to become aware of hypoglycemia and prompts a behavioral defense: the ingestion of carbohydrates.

If ingestion of carbohydrates does not take place and blood glucose levels continue to decline, a decrease in cognition will take place. This decrease in cognition can impair the behavioral defense of carbohydrate ingestion. Confusion is the first sign of hypoglycemic unawareness and if continued to be left untreated, severe hypoglycemia can ensue. The patient can then progress into seizures, coma, and even death if the hypoglycemia is not reversed.

Reference(s):

35. Which of the following is CORRECT regarding hypoglycemia-associated autonomic failure in an individual with diabetes?

A. The pathophysiology of glucose counterregulation is the same in both type 1 and type 2 diabetes, and both develop at the same rate.
B. The pathophysiology of glucose counterregulation is the same in both type 1 and type 2 diabetes, but develops slowly in type 1 diabetes and rapidly in type 2 diabetes.

C. The pathophysiology of glucose counterregulation is the same in both type 1 and type 2 diabetes, but develops rapidly in type 1 diabetes and slowly in type 2 diabetes.

D. The pathophysiology of glucose counterregulation is different between type 1 and type 2 diabetes, as it develops rapidly in type 1 diabetes and slowly in type 2 diabetes.

E. The pathophysiology of glucose counterregulation is different between type 1 and type 2 diabetes, but develops slowly in type 1 diabetes and rapidly in type 2 diabetes.

Answer: C

Rationale:
The concept of hypoglycemia-associated autonomic failure (HAAF) in patients with diabetes was first documented in those with type 1 diabetes, as it stems fundamentally from beta-cell failure. More recently, this concept has been extended to patients with long-standing type 2 diabetes and absolute insulin deficiency. Differences in the time course of the evolution of HAAF plausibly explain, at least in part, the relatively low frequency of treatment-induced hypoglycemia early in the course of T2DM and the higher frequency of treatment-induced hypoglycemia, approaching that in T1DM, later in T2DM. Although the pathophysiology of glucose counterregulation is the same in T1DM and T2DM, it develops rapidly in T1DM (as absolute insulin deficiency develops rapidly) but slowly in T2DM (as absolute insulin deficiency develops slowly).

References:


36. The goal is to minimize microvascular and cardiovascular complications for GRL. Which large outcome study revealed long-term benefits of achieving a glycemic target with an A1C of <7% for individuals with type 2 diabetes?

A. ACCORD  
B. ADVANCE  
C. VADT  
D. UKPDS  
E. DCCT

Answer: D

Rationale:
The benefits of achieving glycemic control with intensive therapy are well documented. A 10-year follow-up to the United Kingdom Prospective Diabetes Study (UKPDS) revealed prolonged benefits of achieving a glycemic target of a A1C of less than 7%.

Patients in the sulfonylurea plus insulin group had a significantly lower risk for many outcomes, including any diabetes-related end point, diabetes-related death, death from any cause, and myocardial infarction, and microvascular disease. However, there are risks associated with glycemic control, namely hypoglycemia.

An analysis of ACCORD, ADVANCE, and VADT revealed factors associated with intensive treatment of type 2 diabetes increased the risk for episodes of severe hypoglycemia without providing any cardiovascular benefits include: a very long duration of diabetes, known history of severe hypoglycemia, advanced atherosclerosis, and advanced age/frailty.

References:

37. The concept of hypoglycemia-associated autonomic failure (HAAF) in diabetes:

A. Doubles the risk of recurrent severe hypoglycemia.  
B. Suggest that recurrent antecedent hypoglycemia causes only defective glucose counterregulation.
C. Suggests that recurrent antecedent hypoglycemia causes both defective glucose counterregulation and hypoglycemia unawareness.
D. Leads to a vicious cycle of recurrent hypoglycemia without impairment of glucose counterregulation.
E. Involves the lack of an increase in insulin and decrease in glucagon.

Answer: C

Rationale:
Impaired awareness of hypoglycemia, or hypoglycemia unawareness, increases the risk of recurrent severe hypoglycemia by a factor of 6 or more. Pivotal findings show that hypoglycemia attenuates defenses (including increased epinephrine secretion and symptomatic defenses) against subsequent hypoglycemia in persons without diabetes and those with type 1 diabetes. Those findings led to the concept of hypoglycemia-associated autonomic failure (HAAF) in diabetes, which suggest recent hypoglycemia causes both defective glucose counterregulation (by attenuating the adrenomedullary epinephrine response, in the context of an insulin concentration that is not reduced and glucagon secretion that is not increased) and hypoglycemia unawareness (largely by attenuating the sympathetic neural response). This leads to a vicious cycle of recurrent hypoglycemia with impairment of glucose counterregulation. The mechanism of HAAF involves a lack of a decrease in insulin and of an increase in glucagon.

References:

38. Which of the following statements is INCORRECT regarding the impact of hypoglycemia?

A. Causes recurrent physical and psychological morbidity and some mortality.
B. Impairs defenses against subsequent hypoglycemia.
C. Precludes maintenance of euglycemia over a lifetime of diabetes.
D. Causes brain fuel deprivation that results in irreversible functional brain failure.
E. Can impair judgment, behavior, and performance of physical tasks.

Answer: D

Rationale:
Hypoglycemia, including iatrogenic hypoglycemia in people with diabetes, can cause recurrent physical and psychological morbidity and some mortality. Hypoglycemia can also cause brain fuel deprivation that initially triggers a series of physiological and behavioral defenses but if unchecked results in functional brain failure that is typically corrected after the plasma glucose concentration is raised. As a result of the interplay of relative or absolute therapeutic insulin excess and compromised physiological and behavioral defenses against falling plasma glucose concentrations, hypoglycemia is the limiting factor in the glycemic management of diabetes. If left untreated, hypoglycemia can impair judgment, behavior, and the performance of physical tasks, although permanent neurological damage is rare. The psychological morbidity includes fear of hypoglycemia, which can also be a barrier to glycemic control.

References:

39. Which of the following may increase the risk of hypoglycemia in adults with diabetes (Answer Yes or No).

___ Sulfonylurea monotherapy
Answer: _Y_ Sulfonylurea monotherapy

___ Metformin monotherapy
Answer: _N_ Metformin monotherapy

___ GLP-1 receptor agonist monotherapy
Answer: _N_ GLP-1 receptor agonists monotherapy

___ GLP-1 receptor agonist in combination a sulfonylurea
Answer: _Y_ GLP-1 receptor agonist in combination with a sulfonylurea

___ Renal failure (in critically-ill patients)
Answer: _Y_ Renal failure (in critically-ill patients)

___ NPH Insulin
Answer: _Y_ NPH Insulin

___ Alpha glucosidase inhibitor monotherapy
Answer: _N_ Alpha glucosidase inhibitor monotherapy
___ Non-sulfonylurea insulin secretagogue (glinide)
Answer: _Y_ Non-sulfonylurea insulin secretagogue (glinide)

___ DDP-4 antagonist monotherapy
Answer: _N_ DDP-4 antagonist monotherapy

___ Alcohol
Answer: _Y_ Alcohol

___ Sepsis (in a critically-ill individual)
Answer: _Y_ Sepsis (in a critically-ill individual)

___ Thiazolidinedione monotherapy
Answer: _N_ Thiazolidinedione monotherapy

Rationale:
Drugs include insulin or insulin secretagogues, such as a sulfonylurea or a non-sulfonylurea insulin secretagogue. Early in its course, T2DM may respond to drugs that do not raise insulin levels at normal or low plasma glucose concentrations and, therefore, should not cause hypoglycemia. Those include a metformin, thiazolidinediones; alpha-glucosidase inhibitors; glucagon-like peptide-1 receptor agonists; and dipeptidyl peptidase-IV inhibitors.

Even when GLP-1 receptor agonists are given in supra-physiological doses, hypoglycemia is not provoked in fasting healthy subjects. However, in clinical studies including those individuals with type 2 diabetes receiving both a GLP-1 mimetic and sulfonylurea medication, hypoglycemia occurred in up to 36% of patients.

However, the risk of hypoglycemia is increased when these drugs are administered in combination insulin or an insulin secretagogue. Individuals at risk for hypoglycemia should be cautious when drinking alcohol, as it can suppresses gluconeogenesis, thereby possibly inducing hypoglycemia unawareness. Also, alcohol ingestion acutely improves insulin sensitivity, and in combination with exercise, drinking can lead to severe hypoglycemia, which may occur 10–12 h after the exercise or alcohol ingestion.

References:


CASE STUDY #6
Questions 40-43

EPL, a 66-year old male with a history of hypertension and uncontrolled type 2 diabetes, is brought to the emergency room by EMTs with complaints of chest pain that has lasted for the past 6 hours. After evaluating his EKG and assessing enzyme levels, EPL is diagnosed with having an acute myocardial infarction and undergoes a percutaneous coronary intervention (PCI). Afterward, he is admitted to the intensive care unit and placed on a ventilator to maintain oxygenation.

Past Medical History: diagnosed with type 2 diabetes 15 years ago, but has had difficulty in controlling his blood sugar; 16-year history of hypertension; hypercholesterolemia.

Social history: Father died of a myocardial infarction at age 72; mother, age 85, is alive with a history of hypertension and type 2 diabetes mellitus; he drinks 1 glass a wine a day; smoked 2 packs of cigarettes per day for 50 years, quit smoking 4 years ago.

Vital signs: height, 5'10"; weight, 220 pounds (100 kg); BMI, 31.6 kg/m²; blood pressure, 146/92 mm Hg; heart rate, 62 beats/minute (irregular rhythm).

Laboratory results in the intensive care: serum creatinine, 1.2 mg/dL (eGFR, ~63 mL/minute); A1C, 8.7%; fasting plasma glucose, 213 mg/dL; total cholesterol, 194 mg/dL; LDL-C: 140 mg/dL; HDL-C, 31 mg/dL; triglycerides, 210 mg/dL.

Medications at home: sitagliptin 50 mg (extended release)/metformin 1000 mg: 2 tablets daily; pravastatin 10 mg once daily; telmisartan 80 mg once daily, aspirin 81 mg once daily.

In the ICU, he is started on metoprolol 5 mg IV, ticagrelor, NPH insulin, parenteral nutrition (which includes regular insulin), and with an order for sliding scale regular insulin. On the second day of hospitalization, EPL has several premature ventricular contractions. He acts confused and diaphoretic. A plasma glucose reading with a point-of-care glucose monitor reveals a plasma glucose level of 58 mg/dL.

40. Which of the following is NOT a risk factor for hypoglycemia in EPL?

A. Older age  
B. Tight glycemic control  
C. Normal renal function  
D. Long duration of diabetes  
E. Mechanical ventilation

Answer: C

Rationale:
The risk factors for hypoglycemia in diabetes in general are older age, use of insulin or insulin secretagogues, duration of diabetes, antecedent hypoglycemia, erratic meals, exercise, renal insufficiency (clearance less than 60 mL/minute). For EPL, his creatinine clearance is greater than 60 mL/minute, so this would not be a risk factor for him. For critically-ill patients in the hospital, mechanical ventilation has also been shown to increase the risk of hypoglycemia. Another potential risk for hypoglycemia is the use of β-blocker medication in cardiac and hypertensive patients. Pharmacologic blockade of β-receptors may shift the glycemic threshold for some adrenergic symptoms, but it does not reduce neuroglycopenic symptoms.

Reference(s):


41. Common source(s) of errors that threaten the safety of a hospitalized patient with diabetes include all EXCEPT:

   A. Lack of coordination between feedings and administration of medications that could cause a mistiming of the onset of action of different medications, especially insulin.
   B. Insufficient frequency of plasma glucose monitoring.
   C. Orders not clearly or uniformly written.
   D. Need for changes in insulin requirement due to a variety of patient factors.
   E. The use of electronic medical records

Answer: E

Rationale:

Inpatient management of hyperglycemia and avoidance of hypoglycemia have become important measures of the quality of health care afforded to hospitalized patients. To minimize the risk of hypoglycemia, errors by hospital personnel must be eliminated. Some of the common sources of errors that threaten the safety of hospitalized patients with diabetes include a lack of coordination between feeding and administration of medications, which can lead to mistiming of insulin action; insufficient frequency of blood glucose monitoring; orders not clearly or uniformly written; failure to recognize the need for changes in insulin requirements as a result of advanced age, liver disease, renal failure, change in clinical status, use of corticosteroids, or interruption or changes in feeding.
Personnel need to consider the timing of procedures for individuals with diabetes. It is best to schedule patients first thing in the morning or after a meal to avoid potential hypoglycemia. Sometimes, patients are taken off the nursing unit for procedures during scheduled meal times. For example, a patient may be given regular subcutaneous insulin at breakfast, be taken for a laboratory study, and have a significant delay in lunch and, as such, because of the prolonged action of regular insulin, there is an increased risk of hypoglycemia. Because fast analog insulin effect has dissipated 3 to 4 hours after injection, a significant delay in lunch has a markedly reduced risk of hypoglycemia versus patients treated with regular insulin in the same circumstances. Thus, plasma glucose monitoring should be performed before the patient leaves the unit, and precautions for treating the patient in the event that hypoglycemia symptoms occur must be considered. Ideally, a hospital staff member or the patient will be able to monitor capillary blood glucose while the patient is off the unit to ensure safety. If the patient is able to eat but is to be taken off the unit just before mealtime, then supplemental carbohydrate can be given to patient. Conversely, a strategy to minimize medical errors that can lead to safety issues include the use electronic medical records.

References:


42. Which of the following mechanism may increase the risk of sudden death as a result of prolonged, profound hypoglycemia in this patient?

A. An increase in QTc interval.
B. Inhibition of proinflammatory molecules.
C. Blocking the activation of platelets.
D. Increased systemic fibrinolytic balance by decreases in PAI-1 levels.
E. No change in ventricular repolarization.

Answer: A

Rationale:

Although profound and prolonged hypoglycemia can cause brain death, most episodes of fatal hypoglycemia are probably the result of other mechanisms. These include:

- Ventricular arrhythmias secondary to increases in the QTc interval.
- Activation of proinflammatory molecules, such as intracellular adhesion molecules-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), E-selectin, VEGF, interleukin-6 (IL-6). These proinflammatory molecules are important in the development of atherosclerosis and other inflammatory diseases.
- Increases platelet activation.
- **Decreases** systemic fibrinolytic balance by **increasing** levels of plasminogen activator inhibitor-1 (PAI-1), which regulates thrombus formation.

In response to hypoglycemia, a release of catecholamines provoke a fall in plasma potassium and causes electrocardiographic (ECG) changes, including prolongation of the QT interval and cardiac repolarization, which in some susceptible individuals with diabetes may provoke a cardiac arrhythmia. A prolonged corrected QT interval has been found to be associated with episodes of nocturnal hypoglycemia in patients with type 1 diabetes. In a study by Murphy et al, prolonged QTc occurred frequently with spontaneous overnight hypoglycemia in young patients with type 1 diabetic, which may be related to insulin-induced hypokalemia. Prolonged QTc (>440 ms) occurred on 27% of nights (20 out of 74) and was more prevalent on nights with hypoglycemia (13/29, 44%) than on nights without (7/45, 15%; p = .0008).

A study by Gogitidze-Joy et al showed significant increases (p < .05) in plasminogen activator inhibitor (PAI-1), vascular cell adhesion molecule (VCAM), intercellular adhesion molecule (ICAM), E-selectin, P-selectin, interleukin-6 (IL-6), vascular endothelial growth factor (VEGF), and adiponectin responses during the 2 hours of hyperinsulinemic hypoglycemia when compared with euglycemia in healthy control subjects.

**References:**


Gogitidze-Joy N, Hedrington MS, Briscoe VJ, Tate DB, Ertl AC, Davis SN. Effects of acute hypoglycemia on inflammatory and pro-atherothrombotic biomarkers in individuals with type 1 diabetes and healthy individuals, *Diabetes Care.* 2010;33:1529-1535.

**43. Case Continuation:**

EPL is stabilized in the intensive care unit and then transferred to a cardiac step-down unit. He is discharged home after 5 days, although his A1C is still not in control.

Which of the following has been shown to reduce the risk of rehospitalization for EPL?

A. Elderly  
B. Inpatient diabetes education  
C. Previous hospitalization
D. Shorter length of stay
E. An elevated A1C

Answer: B

Rationale:
Risk factors that influence hospital readmissions include previous hospitalization, extremes of age, and socioeconomic barriers. In a study of patients with diabetes, one group received inpatient diabetes education (IDE) by a certified diabetes educator (CDE) and one group did not. All-cause first readmissions were determined within 30 days and 180 days after discharge. Results revealed those who received IDE had a lower frequency of readmission within 30 days (11% vs. 16%; \( p = .0001 \)) and 180 days (37% vs. 45%; \( p = .002 \)) than did those who did not. The relationship between IDE and hospital readmission persisted after correction for socio-demographic factors, discharge diagnosis, and A1C. Although few patients in this study were actually admitted primarily for uncontrolled diabetes, IDE may have had more of an indirect effect, through promoting adherence to medical and dietary therapies and better self-care behaviors, in general.

Reference:
CASE STUDY #7
Questions 44-45

SK, a 24-year old office worker who just moved to the area, presents to your office for a first-time visit with complaints of dizziness, headache, and nausea and vomiting for the past week. During your exam, and following a urine pregnancy test, you determine her to be pregnant, based on last menstrual period estimate that she is in 9th gestational week. She reveals a 12-year history of type 1 diabetes, which she controls with short-acting insulin administered via an insulin pump. She is 5’4” and weighs 178 pounds. Last A1C (2 months ago) was 6.4%; yesterday’s plasma glucose (by meter) was 85mg/dL. A urinalysis is negative for glucose and ketones.

During the discussion about her diabetes treatment plan, she states her previous doctor set a target A1C of <6.5%, with a preprandial plasma glucose of <90 mg/dL. She acknowledges this tight control has resulted in several episodes of hypoglycemia in the past few months, each time requiring assistance from her husband. Now she is concerned with maintaining her treatment goals without any adverse effects on her or her baby.

44. Which of the following does NOT increase the risk for experiencing severe hypoglycemia during the first trimester of pregnancy?
   A. Longer duration of type 1 diabetes
   B. Low A1C levels (<6.5%) early in pregnancy
   C. Pregnancy-related nausea and vomiting
   D. A steady dosing regimen with insulin
   E. A history of severe hypoglycemia

Answer: C

Rationale:
For pregnant women with type 1 diabetes, achieving glycemic control is important to avoid complications for both the mother and the child; however, the risk for severe hypoglycemia (requiring assistance from others) is increased when trying to achieve/maintain a targeted glycemic level. Thus, preventing severe hypoglycemia during pregnancy is essential. Knowledge of these factors can provide direction for clinicians developing a treatment plan for their pregnant patients with type 1 diabetes.

In a study of 278 pregnant women with type 1 diabetes, investigators assessed risk indicators for severe hypoglycemia during the first trimester of pregnancy. Results showed the risk factors related to the occurrence of severe hypoglycemia during this timeframe were independently related to the duration of diabetes (greater than 10 years), a A1C of less than 6.5%, a history of severe hypoglycemia 4 months before gestation, and a total daily insulin dose.
Although pregnancy-related nausea and vomiting might be contributing factors for severe hypoglycemia during pregnancy, another study ruled out nausea and vomiting as major contributing factors for severe hypoglycemia in pregnancy.

**References:**


45. At the 35th gestational week, KAP delivers a 9 lb 8 oz baby boy, large for gestation age (LGA). Which of the following statements is INCORRECT regarding screening of high-risk infants for hypoglycemia in the first hour of life?

A. The risk of hypoglycemia in the first 24 hours occurs to a greater extent in infants born to insulin-dependent mothers.

B. Hypoglycemia occurs to a greater extent in newborns weighing <2000 grams or >4000 grams.

C. Hypoglycemia is less common in neonates born at less than 37 weeks' gestation.

D. Hypoglycemia is more common in neonates born at or after 40 weeks' gestation.

E. Newborns with symptoms suggestive of hypoglycemia, including jitteriness, tachypnea, temperature instability, and/or lethargy.

**Answer:** C

**Rationale:**

High-risk infants who need screening for hypoglycemia in the first hour of life include newborns who weigh <2000 grams and >4000 grams; large (>90th percentile) and small (<10th percentile) for gestational age; infants born to insulin-dependent mothers or mothers with gestational diabetes; gestational age <37 weeks; newborns suspected of sepsis or born to a mother suspected of having chorioamnionitis; and newborns with symptoms suggestive of hypoglycemia: jitteriness, tachypnea, hypotonia, poor feeding, apnea, temperature instability, seizures, and/or lethargy.

**References:**


CASE STUDY #8

Questions 46-48

A 23-year-old male with a 5-year history of type 1 diabetes presents to his endocrinologist for a routine visit. Being recently married, his wife has accompanied him to meet the doctor. The patient reports he is doing well overall and maintains adherence to his treatment plan. However, he occasionally has low blood glucose readings first thing in the morning, especially when he does not eat a late night snack the night before. He reports having nightmares that wake him up, which has been causing both he and his wife some distress. He has noticed this occurs usually on those nights after playing a tennis match.

Medications include: glargine insulin 24 units at bedtime, and aspart insulin 8 units before meals daily. His plasma glucose log is reviewed and reveals fasting plasma levels before breakfast: 47–235 mg/dL (mean 205); before lunch: 71–187 mg/dL (mean 159); before dinner: 63–184 mg/dL (mean 146); and at bedtime: 64–178 mg/dL (mean 134). One night, after awakening from a nightmare, he measured his glucose level at 3:30 AM, which was 54 mg/dL; his last A1C test (3 weeks ago) was 7.0%.

46. Iatrogenic hypoglycemia, including severe hypoglycemia, often occurs during sleep and is common in individuals with type 1 diabetes. Each of the following has been shown to reduce the risk and/or frequency of nocturnal hypoglycemia, EXCEPT:

A. Regular glucose monitoring.
B. Eat appropriate bedtime snacks.
C. Moderate their alcohol intake in the evening.
D. Intensive exercise in the evening.
E. Utilize both short- and long-acting insulin analogs.

Answer: D

Rationale:

Individuals with type 1 diabetes are at risk for nocturnal hypoglycemia; however, patient behavior can influence whether nocturnal hypoglycemia will occur. Providing education about risks and risk-reduction strategies is critical in preventing nocturnal hypoglycemia. Diabetes education can also provide patients with options that reduce fear and discourage choices that provide a rationale for poor glycemic control. Patients should be encouraged to plan meals and exercise, adhere to dosing guidelines for diabetes therapy, moderate their alcohol intake, carefully and consistently perform SMBG, and be made aware that a simple change in routine (eg, change in time zone, holidays, vacation) may increase their risk for nocturnal hypoglycemia. Most nocturnal hypoglycemia episodes occurred with no snacks compared to any snacks, thus eating a snack at bedtime is important, especially when one exercises in the evening or in the late
afternoon. Exercise can result in delayed hypoglycemic events. In addition, ingestion of alcohol in the evening may increase the risk for nocturnal hypoglycemia.

Rather than a bedtime snack of fast-acting carbohydrates, whose glycemic effects can wear off earlier than desired, food that is slowly absorbed and provides a steady supply of nighttime glycemic support may be more appropriate. However, there is no clear consensus as to which is the best bedtime snack to prevent overnight hypoglycemia in patients with type 1 diabetes. Therefore, the administration of bedtime snacks may need to be individualized and be part of a comprehensive strategy (balanced diet, patient education, optimized drug regimens, and physical activity counseling) for the prevention of nocturnal hypoglycemia.

Progress has also been made to minimize the risk for nocturnal hypoglycemia in insulin-using patients with the advent of continuous subcutaneous insulin infusion (CSII) pumps and the introduction of the long-acting [basal] analogs, insulin detemir and insulin glargine rather than the use of NPH insulin.

**References:**


47. Undetected nocturnal hypoglycemia may often contribute to each of the following **EXCEPT:**

A. Hypoglycemia unawareness.
B. Anxiety.
C. Poor quality of life.
D. No change in vitality.
E. Possibly neurocognitive deficits.
Answer: D

Rationale:
Nocturnal hypoglycemia occurs during sleep and is particularly dangerous because individuals with diabetes, especially type 1 diabetes, are unlikely to recognize symptoms or awaken during an episode. Undetected nocturnal hypoglycemia may often contribute to hypoglycemia unawareness, anxiety, loss of vitality, physical injury, poor quality of life, and possibly neurocognitive deficits. Major episodes require emergency care as they can lead to seizures and unconsciousness.

References:

48. Which of the following statements about nocturnal hypoglycemia is CORRECT?

A. During the Diabetes Control and Complications Trial (DCCT), only a minority of episodes of severe episodes reported occurred during sleep.
B. Ingestion of alcohol in the evening may decrease the risk for nocturnal hypoglycemia.
C. Patients with diabetes are easily awakened by a deep sleep by hypoglycemia because of increased plasma epinephrine levels.
D. Sympatho-adrenal responses to hypoglycemia, subjective symptoms that warn the individual and cognitive function are suppressed during sleep.
E. Insulin and counterregulatory responses are increased in individuals with diabetes, which can contribute to nocturnal hypoglycemia.

Answer: D

Rationale:
During the Diabetes Control and Complications Trial (DCCT), 43% of all hypoglycemic episodes and 55% of severe episodes reported occurred during sleep. As such, nocturnal hypoglycemia is more worrisome than daytime hypoglycemia because sympatho-adrenal responses to hypoglycemia, subjective symptoms that provide warn the individual, and cognitive function are suppressed during sleep. Stimuli for self-treatment are absent, thus, waking during an episode to ingest a snack is unlikely. Ingestion of alcohol in the evening may increase the risk for nocturnal hypoglycemia. Patients with diabetes may have a reduced tendency to be awakened by hypoglycemia, mediated by reduced plasma epinephrine, cortisol, and pancreatic polypeptide responses. Factors such as reduced insulin and counterregulatory responses in individuals with either type 1 or type 2 diabetes, diminished physiologic defenses during sleep,
behavioral factors, and limitations of therapy used for diabetes management contribute to nocturnal hypoglycemia.

**References:**


Questions 49-56

Effective approaches known to decrease the risk of iatrogenic hypoglycemia include patient education, dietary and exercise modification, adjustments to medication/treatment regimens, careful glucose monitoring by the patient, and conscientious surveillance by the clinician. Answer TRUE or FALSE to the following statements regarding these approaches:

49. ___ As part of the educational plan, the individual with diabetes and his or her domestic companions need to recognize the symptoms of hypoglycemia and be able to treat a hypoglycemic episode properly with oral carbohydrates or glucagon.

Answer: True

Reference:

50. ___ Patients do not need to understand how their medications work.

Answer: False

Rationale:
Patients must understand how their medications work so they can minimize the risk of hypoglycemia.

Reference:

51. ___ To avoid hypoglycemia, patients on long-acting secretagogues and fixed insulin regimens can eat whenever and whatever they desire.

Answer: False

Rationale:
To avoid hypoglycemia, patients on long-acting secretagogues and fixed insulin regimens must be encouraged to follow a predictable meal plan.

Reference:
52. ___Post-exertional hypoglycemia can be prevented or minimized by careful glucose monitoring before and after exercise and taking appropriate preemptive actions.

Answer: True

Reference:

53. ___When rapid-acting and intermediate-acting insulin are used to treat a person with well-controlled diabetes and a history of exercise-related hypoglycemia, there is no need to empirically adjust insulin doses on the days of planned exercise.

Answer: False

Rationale:
Because of the kinetics of rapid-acting and intermediate-acting insulin, it may be prudent to empirically adjust insulin doses on the days of planned exercise, especially in patients with well-controlled diabetes with a history of exercise-related hypoglycemia.

Reference:

54. ___To counteract iatrogenic hypoglycemia, continuous subcutaneous insulin infusion provides no benefit for adjusting the doses and administration pattern of insulin.

Answer: False

Rationale:
A continuous subcutaneous insulin infusion offers great flexibility for adjusting the doses and administration pattern of insulin to counteract iatrogenic hypoglycemia.

References:

55. Real-time continuous glucose monitoring (CGM), by virtue of its ability to display the direction and rate of change, provides helpful information to the wearer leading to proactive measures to avoid hypoglycemia, e.g., when to think about having a snack or suspending insulin delivery on a pump.

Answer: True

Reference:

56. Clinicians and educators must assess the risk of hypoglycemia at every visit with patients treated with insulin and insulin secretagogues. An efficient way to begin this assessment might be to have the patient complete a questionnaire that addresses circumstances that caused the hypoglycemia, as well as awareness, frequency, severity, and response to treatment of hypoglycemia.

Answer: True

Reference: