DIABETIC KETOACIDOSIS

INTRODUCTION

Diabetic ketoacidosis (DKA) is a very serious complication of diabetes mellitus, a metabolic disorder that is characterized by hyperglycemia, metabolic acidosis, and increased body ketone concentrations. The most common causes of DKA are infection and poor compliance with medication regimens. Other causes include undiagnosed diabetes, alcohol abuse, and a multitude of medical conditions such as cerebrovascular accident (CVA), complicated pregnancy, myocardial infarction, pancreatitis, and stress.

Diabetic ketoacidosis is a complicated pathology. Early recognition of DKA, a good understanding of the pathological processes of DKA, and aggressive treatment are the keys to successful treatment. With good care, DKA can be managed and the patient will survive.

OBJECTIVES

When the student has finished studying this module, he/she will be able to:

1. Identify the correct definition of DKA.
2. Identify a basic function of insulin.
3. Identify the insulin derangements of types I and II diabetes.
4. Identify the basic cause of DKA.
5. Identify two specific causes of DKA.
6. Identify the two pathogenic mechanisms that produce the signs/symptoms of DKA.
7. Identify metabolic consequences of increased hormone concentrations in DKA.
8. Identify the criteria used to diagnose DKA.
9. Identify common signs and symptoms of DKA.
10. Identify laboratory abnormalities seen in DKA.
11. Identify complications of DKA.
12. Identify the three most important therapies for treating DKA.
13. Identify the correct roles of sodium bicarbonate and phosphate in treating DKA.
14. Identify an important rule for using potassium replacement in DKA.
15. Identify an important rule for switching from IV to subcutaneous insulin.

EPIDEMIOLOGY

Most cases of DKA are seen in patients with type I diabetes, but approximately 10%-30% of all cases of DKA occur in patients with type II diabetes. The incidence of DKA appears to be rising, and this may not be related to the well publicized increase in the incidence of diabetes that has become a serious public health problem. Diabetic ketoacidosis accounts for 50% of all diabetes-related admissions in young people with the disease, and DKA is the most common cause of diabetes-related death in children and adolescents with type I diabetes. Diabetic ketoacidosis is much more common in children than in adults, it is more common in women than in men, and it is more common in Caucasians. The exact incidence of death from DKA is not known, but it has been
estimated to be between 1%-10%.\textsuperscript{5} Survival depends on the severity of the case, the age of the patient, the presence/absence of certain medical conditions, and how quickly DKA is recognized and how effectively it is treated. If the condition is promptly diagnosed and properly treated, the mortality rate can be <1%.\textsuperscript{6}

**GLUCOSE, INSULIN, AND DIABETES: A SHORT REVIEW**

The body needs energy to function, and a great deal of this energy is provided by glucose. Glucose is derived from the breakdown of foods we eat (particularly carbohydrates) and glucose is converted into adenosine triphosphate (ATP) by the glycolytic pathway. Adenosine triphosphate provides energy for basic body functions when the high energy bonds of the ATP molecule are broken.

Glucose is an essential source of energy. In order for glucose to be used for energy it must be transported into the cells, but the glucose molecule is too large to passively move through the cell membrane. Glucose must be actively carried into the cell and that is the function of insulin: it is a transport molecule. The process by which insulin promotes glucose entry into the cells is called facilitated diffusion. This process has not been completely outlined and is not completely understood, but it may be that when insulin binds to an insulin receptor on a cell membrane, it increases the membrane concentration of a glucose transporter, Glut4.

In the normal person, blood glucose is maintained within a narrow range of 70-125 mg/dL, and fasting glucose for adults should be 70-99 mg/dL. Close control of blood glucose is important, as glucose is the only nutrient that can be used by important organs such as the brain, retina, etc. When blood glucose rises (e.g., after a meal), the secretion of insulin rises dramatically, both in amount and the speed in which this rise occurs, as glucose enters the pancreatic \(\beta\) cells and stimulates insulin release.

Diabetes is a disease that affects glucose metabolism. There are two types of diabetes: Type I (also called juvenile-onset diabetes) and type II (also called adult onset or non-insulin-dependent diabetes). Type I diabetes is caused by destruction of the pancreatic \(\beta\) cells that produce insulin. The destruction of the \(\beta\) cells is thought to be an autoimmune process that occurs in genetically susceptible people and is triggered by an infection or an environmental factor. People with type I diabetes essentially do not produce insulin. Type II diabetes is characterized for the most part by insulin resistance. Due to age, genetics, lifestyle factors, and possibly environmental triggers, the body is unable to use insulin to transport glucose into the cells. In both type I and type II diabetes, medications and lifestyle modifications are needed so that blood glucose remains within a specified range.

**PATHOPHYSIOLOGY OF DKA**

The underlying cause of DKA is insulin deficiency. This can be absolute (when no insulin is produced or no insulin is administered) or it can be relative (when the amount of insulin available is not sufficient to the needs).\textsuperscript{7} In either case, the lack of insulin causes hyperglycemia, and hyperglycemia initiates several pathogenic mechanisms that produce the signs, symptoms, and metabolic derangements of DKA. These mechanisms are:
• Increased hormone release: Hyperglycemia in DKA stimulates the body to increase production of the hormones cortisol, epinephrine, glucagon, and growth hormone in an attempt to produce energy. These hormones break down fats (to provide the body with energy), and stimulate the liver to increase fatty acid oxidation. They also increase blood glucose by initiating gluconeogenesis and glycogenolysis, and by decreasing the ability of peripheral tissues to use glucose.

• Metabolic shift: The increased release of hormones and the lack of insulin cause a shift in metabolism. The body now depends on fats for energy instead of carbohydrates. One of the byproducts of fat metabolism are ketones, and these (acetone, acetoacetate and beta-hydroxybutyrate) are acidic and have a low pH.

Because of the increased hormone production and the shift in metabolism, the serum glucose is elevated and there is high acid load and these derangements are the source of the signs and symptoms of DKA.

CAUSES OF DKA

The most common causes of DKA are infection and poor compliance by the patient with diabetic treatment regimens. The infections that are that most commonly cause DKA are pneumonias and urinary tract infections. Other causes of DKA such as CVA, myocardial infarction, and drugs such as atypical antipsychotics, diuretics, and steroids cause DKA by increasing the production of stress hormones, elevating the serum glucose, or blunting the normal physiological warning signs of hyperglycemia and acidosis.

DEFINING DIABETIC KETOACIDOSIS

When assessing a patient for DKA, perform a health history, check for the presence or absence of the typical signs and symptoms of DKA, and look for the characteristic laboratory abnormalities that are caused by DKA.

When performing the health history, be sure to ask these questions: Does the patient have diabetes and if so, what type? Has the patient been eating properly and drinking sufficient amounts? If the patient uses oral hypoglycemic agents or insulin, has the patient been taking the medications? Has the patient recently had a new medication added to his/her medication regimen? Has the patient recently lost weight or had a fever or infection?

There are signs and symptoms that are commonly noted in patients with DKA, but they are not specific to DKA. Patients suffering from DKA often have abdominal pain, dehydration, dry mucous membranes, electrolyte abnormalities, hypotension, hypothermia, malaise, mental status changes, nausea, polydipsia, polyuria, tachycardia, and vomiting, etc. – but these can be caused by many pathological processes and diseases.

However, many of these signs and symptoms (and some others that are specific to DKA) can be easily recalled and easily explained if you remember that they are directly
or indirectly caused by the two pathogenic mechanisms of DKA – increased hormone concentrations and a metabolic shift.

For example, dehydration (and some of the signs and symptoms that accompany it in DKA such as hypotension, nausea, polydipsia, polyuria, and tachycardia) is due to poor intake and vomiting but also due to diuresis caused by hyperglycemia and other factors. An elevated serum glucose (caused by increased hormone concentrations) acts as an osmotic diuretic. Dehydration can also result from the elevated serum potassium/low total body potassium (caused by the metabolic acidosis) and the high serum ketone levels induced by the metabolic shift. Both of these can cause nausea and vomiting. Kussmaul respirations (deep and rapid breathing) is a response to metabolic acidosis (an attempt to eliminate CO$_2$) which may be seen, and occasionally the patient’s breath will have an odor that is sweet or fruity because a certain amount of the high ketone load is excreted through the lungs.

Learning Break: The classical clinical presentation of DKA is a patient with dehydration, mental status changes, polydipsia, polyuria, vomiting, weakness, and weight loss.$^{10}$

The laboratory abnormalities seen in DKA that are commonly considered to be the definitive criteria for a diagnosis of DKA are hyperglycemia (blood glucose > 250 mg/dL) metabolic acidosis (blood pH = 7.30) and an elevated level of serum ketones (> 5 mEq/L) and/or ketones in the urine.$^{11}$ Patients will also have an anion gap (Na$^+$ - Cl$^-$ + HCO$_3^-$), an elevated blood urea nitrogen (BUN), hyponatremia, hyperkalemia, and the serum amylase may be elevated. The total body phosphate level may be low but the serum level may be normal or elevated. At this time, there is no universally agreed upon consensus for the diagnostic criteria of DKA, and some sources feel that an anion gap > 10-12 mEq/L and serum bicarbonate (HCO$_3^-$) = 18 mEq/L should be part of the criteria.

Learning Break: Some authors feel that most important test for diagnosing DKA is total blood ketone concentration.$^{12,13}$

The acidosis and hyperglycemia of DKA and the electrolyte changes that are so commonly seen in DKA are closely related. The shift in metabolism and the high concentration of acidic ketones seen in cases of DKA produces a metabolic acidosis. Acidosis and insulin deficiency causes potassium to shift from the intracellular space to the extracellular space and serum hyperkalemia is common. However, the osmotic diuresis that is characteristic of DKA causes potassium to be excreted in the urine; although the serum potassium level may be high, the patient may be profoundly depleted. Sodium and phosphate are also excreted by the osmotic diuresis, and hyponatremia is common. However, the serum phosphate level is often falsely normal or falsely elevated because phosphate, like potassium, is excreted in the urine but acidosis induces phosphate to move from the intracellular space to the extracellular space. The serum level might be normal, but the actual total body load is low.
Learning Break: The serum glucose can be very elevated in severe cases of DKA. However, serum glucose can be close to normal, and approximately 10% of patients with DKA will be euglycemic with a serum glucose = 250 mg/dL.14

COMPLICATIONS OF DIABETIC KETOACIDOSIS

Patients who have diabetic ketoacidosis that is promptly recognized and promptly and correctly treated should survive. The complications of DKA are complications of treatment and cerebral edema.

Treatment complications are hypoglycemia, hyperkalemia, and occasionally pulmonary edema. These can be avoided by using low-dose insulin therapy, monitoring blood glucose very closely, and by carefully managing fluid replacement.

Cerebral edema is a very serious complication of DKA. It occurs in approximately 1% of all children with DKA, but the mortality rate and the rate of neurological sequelae for these children have both been reported to be 21%, and the mortality rate and rate of sequelae can be as high as 24% and 26% respectively15,16. Adults with DKA rarely develop cerebral edema.17 Signs and symptoms include mental status changes, bradycardia, seizures, abnormal response to pain, and decorticate and decerebrate posturing.

TREATMENT FOR DIABETIC KETOACIDOSIS

The most important treatments for DKA are fluid replacement, insulin therapy, and correcting electrolyte balances. Obtain baseline serum electrolytes, BUN, creatinine, serum glucose, an arterial or venous blood gas (either one is appropriate), a complete blood count, an ECG, and a CXR. Consider other laboratory studies if DKA is thought to be caused by an underlying disease.

- Fluid replacement: Fluid replacement will replace the fluid deficit, help decrease the blood glucose level, and maintain renal function. If the patient is severely hypovolemic, give 1 liter of 0.9% sodium chloride over 30 minutes. If the patient is mildly dehydrated, check the serum sodium. If it is normal or high, give 0.45% sodium chloride IV at a rate of 250-500 mL/h. If the serum sodium is low, give 0.9% sodium chloride IV at a rate of 15-20 mL/kg per hour. Once the blood glucose is approximately 200 mg/dL, a solution of % dextrose with 0.45% sodium chloride can be used.18

Learning Break: In the first hour of treating a patient with DKA, fluid replacement is more important than insulin therapy and should take precedent.19,20

- Insulin therapy: Insulin is a critical part – perhaps the critical part – of the treatment of DKA. It can be given as an IV infusion or frequent subcutaneous injections: they are equally effective. Most clinicians prefer the IV route as the onset of action is quicker and the half-life is shorter with the IV route than the onset of action of and half-life of insulin given subcutaneously: because of that, therapy can be closely monitored. The American Diabetes Association
recommends giving an initial IV bolus of regular insulin, 0.1 U/kg. (Note: If the serum potassium is < 3.3 mEq/L insulin should not be given). Following the bolus dose, start a continuous IV infusion of regular insulin at a rate of 0.1 U/kg/h. An alternative is to omit the bolus dose and start a continuous IV infusion of regular insulin at a rate of 0.14 U/kg/h. If the serum glucose does not decrease by 10% within an hour of starting the insulin, give 0.14 U/kg as a bolus dose, then continue the IV infusion. Once the serum glucose is < 200 mg/dL, reduce the insulin dose to 0.02-0.05 U/kg/h or give subcutaneous doses of rapid-acting insulin, 0.1 U/kg every two hours. The goal at this point is to keep the serum glucose between 150-200 mg/dL. \(^{21}\)

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0.1 \text{ U/kg IV bolus} \\
0.1 \text{ U/kg/hr} *
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\text{When serum glucose} < 200 \text{ mg/dL, decrease infusion to 0.02-0.05 U/kg/h}
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\text{Keep serum glucose between 150-200 mg/dL until DKA resolves}
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* If serum glucose doesn’t ? by at least 10% in the 1st hour of insulin therapy, give an IV bolus of 0.14 U/kg and adjust the infusion.

- **Correcting electrolyte imbalances:** *If the serum potassium is < 3.3 mEq/L, do not start insulin therapy and give 20-30 mEq of potassium per hour until the serum level is >3.3 mEq/L.* Fluid replacement and insulin therapy lower blood sugar and correct acidosis and they also move potassium into the cells. If the serum potassium is < 3.3 mEq/L, serious arrhythmias could result. Once the hypokalemia has been corrected, insulin therapy can be started, and 20-30 mEq of potassium can be added to each liter of IV solution in order to maintain a serum potassium level between 4.0-5.0 mEq/L.

**Learning Break:** Serum glucose and serum potassium should be checked every hour until the patient is stable.

Two other considerations for treatment are administering sodium bicarbonate to help correct the acidosis and replacing phosphate losses. Using sodium bicarbonate is controversial. Severe acidosis can decrease myocardial contractility, can cause and prolong coma, shifts the oxyhemoglobin dissociation curve to the right, etc., so correcting an acidosis would seem important. However, there are risks involved (e.g., making body hypokalemia worse, cerebral edema), there are many clinical studies that indicate sodium bicarbonate therapy is not effective for patients with DKA, and for many patients the acidosis will correct with fluids and insulin and because they have adequate stores of bicarbonate. \(^{22}\) The use of sodium bicarbonate should not be standard care for DKA. However, the American Diabetes Association does recommend that if a patient has a
severe acidosis with a pH < 6.9, the patient should receive 100 mEq of NaHCO$_3$ in 400 mL IV fluid along with 20 mEq of potassium chloride; this should be infused at 200 mL/h. Repeat this every two hours until the pH is = 7.0.\textsuperscript{23}

Low phosphate levels will usually correct as the hyperglycemia and acidosis are corrected, and phosphate replacement is not standard care for DKA. However, if the phosphate is very low – < 1.0 mg/dL – or the patient has anemia, cardiac disease, or hypoxia, 20-30 mEq of phosphate can be given.\textsuperscript{24,25}

**SWITCHING TO SUBCUTANEOUS INSULIN**

Diabetic ketoacidosis is considered to be resolved when the blood glucose is < 200 mg/dL and at least two of these laboratory values are present: a venous pH > 7.3, an anion gap < 12 mEq/L, and a serum bicarbonate level > 15.0 mEq/L.\textsuperscript{26} If these laboratory values are present and the patient can eat, it is safe to start subcutaneous insulin. *Intravenous insulin should be continued for one to two hours after the first dose of subcutaneous insulin has been given.* If this is not done, hyperglycemia and ketosis may recur.

**NURSING CARE, PREVENTION AND EDUCATION**

When providing care for a patient in the acute phase of DKA, the nurse should focus on hydration status/fluid replacement, monitoring of acid-base status, serum glucose, and serum electrolytes, close observation of the patient’s neurological status, and vital signs.

Once a case of DKA has resolved it is important to know why it happened. Infections, medical conditions, and drugs are common causes of DKA. However, one of the most important causes of DKA is patient non-compliance with diabetic treatment regimens: patients do not take their medication or do not take them properly, they fail to follow their prescribed diet and lifestyle plans, and they do not or cannot understand the basics of self-care and prevention as they relate to diabetes.

If non-compliance was the cause of a particular case of DKA, it is very important to determine why the non-compliance occurred, and there many possible reasons. Some of the more common ones are:

- Poor access to medical care: The patient may not have access to health care information, may not have easy access to a physician, clinic, etc., may not have or not know how to use community or public access health care resources. The patient may not have money for medications.

- Lack of information: The patient may have a poor understanding of diabetes, and the patient may not understand the treatment regimens that have been prescribed. Lack of information can be damaging in many ways. If the patient doesn’t understand the disease of diabetes, he/she might be less willing to comply with lifestyle and diet restrictions and less willing to take medications. The patient would not recognize possible warning signals of DKA.
• Emotional issues: For many people, diabetes requires lifestyle changes that they may not be willing to emotionally accept.

**Learning Break:** Although it may be said that non-compliance happens when the patient fails to provide good self-care, the word fail typically has a negative connotation. Also, when many people hear the term non-compliance, they think of a person willfully failing to do what he/she knows is best. However, there are many cases of non-compliance that happen because the patient has not been properly educated, or doesn’t have or doesn’t know how to get the resources he/she needs.

So when it has been determined that non-compliance was the cause of a particular case of DKA, interview the patient and find out a) the emotional impact of diabetes on the patient’s life, b) how much he/she knows about the disease and the treatments, and c) what financial, medical, personal, and social resources the patient has available for self-treatment.

Some of these issues must be addressed by social workers, psychologists, or the patient’s physician. However, nurses have a primary role in supporting and educating patients who have had an incident of DKA related to non-compliance. The nurse will often be the first person to find out that the patient did not seek medical attention for an infection because of financial concerns, or due to inability to each a physician, or because of a lack of understanding of the implications of infection in diabetes. The nurse must then discuss making the appropriate referrals and then set up a teaching plan. Some of the nursing diagnoses that might apply in theses situations would be imbalanced nutrition, noncompliance, knowledge deficient, and risk for injury.
SUMMARY

- Diabetic ketoacidosis is a metabolic disorder characterized by hyperglycemia, metabolic acidosis, and elevated body ketone concentrations.

- The basic cause of DKA is insulin deficiency, absolute or relative. The insulin deficiency most often occurs because of infection or non-compliance with diabetic treatment regimens.

- Excess hormone concentration and a metabolic shift are the pathogenic mechanisms that cause the signs and symptoms of DKA.

- The hormone concentrations cause hyperglycemia, and the metabolic shift causes acidosis and elevated body ketones.

- The basic diagnostic criteria for DKA are a blood glucose > 250 mg/dL, a serum pH < 7.3, and elevated serum and/or urine ketone concentrations.

- Other important criteria are an anion gap > 10-12 mEq/L and serum bicarbonate (HCO$_3^-$) = 18 mEq/L.

- Hyperkalemia and hyponatremia are common in DKA. Hypophosphatemia can be seen. However, the total body load of potassium and phosphate is often low.

- Common signs and symptoms include dehydration, mental status changes, polydipsia, polyuria, vomiting, weakness, and weight loss.

- Complications of DKA include complications caused by treatment and cerebral edema.

- Treatment for DKA should focus on fluid replacement, insulin therapy, and correcting electrolyte abnormalities. Sodium bicarbonate is not standard care.

- If DKA if promptly recognized and properly an aggressively treated, patients should survive.
REFERENCES