DIABETIC KETOACIDOSIS

DANA BARTLETT, RN, BSN, MSN, MA

Dana Bartlett is a professional nurse and author. His clinical experience includes 16 years of ICU and ER experience and over 20 years of as a poison control center information specialist. Dana has published numerous CE and journal articles, written NCLEX material, written textbook chapters, and done editing and reviewing for publishers such as Elsevire, Lippincott, and Thieme. He has written widely on the subject of toxicology and was recently named a contributing editor, toxicology section, for Critical Care Nurse journal. He is currently employed at the Connecticut Poison Control Center and is actively involved in lecturing and mentoring nurses, emergency medical residents and pharmacy students.

ABSTRACT

Diabetic ketoacidosis (DKA) is an acute complication of diabetes mellitus, which requires prompt, aggressive, treatment. Complications of DKA throughout the age spectrum and during pregnancy require a close evaluation of symptoms, testing, treatment and outcomes to treatment. Anyone with diabetes, regardless of age or gender, can develop DKA. Guidelines exist that guide diabetes health teams and nursing care of the diabetic patient. Appropriate and timely treatment can reduce DKA complications and patients can recover to full health.
Continuing Nursing Education Course Planners
William A. Cook, PhD, Director, Douglas Lawrence, MA, Webmaster, Susan DePasquale, MSN, FPMHNP-BC, Lead Nurse Planner

Policy Statement
This activity has been planned and implemented in accordance with the policies of NurseCe4Less.com and the continuing nursing education requirements of the American Nurses Credentialing Center's Commission on Accreditation for registered nurses. It is the policy of NurseCe4Less.com to ensure objectivity, transparency, and best practice in clinical education for all continuing nursing education (CNE) activities.

Continuing Education Credit Designation
This educational activity is credited for 2 hours. Nurses may only claim credit commensurate with the credit awarded for completion of this course activity.

Statement of Learning Need
Diabetes mellitus is one of the leading chronic diseases in the country and DKA is one of the most serious complications. When patients in DKA crisis receive the right treatment they are able to recover to improved health. Nurses need to be able to identify prevalence and treatment of diabetes ketoacidosis (DKA) in all age groups and for special conditions, such as pregnancy.
Course Purpose
This course will help nurses identify signs and symptoms of diabetic ketacidosis and its recommended treatment.

Target Audience
Advanced Practice Registered Nurses and Registered Nurses
(Interdisciplinary Health Team Members, including Vocational Nurses and Medical Assistants may obtain a Certificate of Completion)

Course Author & Planning Team Conflict of Interest Disclosures
Dana Bartlett, RN, BSN, MSN, MA, William S. Cook, PhD,
Douglas Lawrence, MA, Susan DePasquale, MSN, FPMHNP-BC - all have no disclosures.

Acknowledgement of Commercial Support
There is no commercial support for this course.

Activity Review Information
Reviewed by Susan DePasquale, MSN, FPMHNP-BC

Release Date: 1/1/2016 Termination Date: 3/31/2017

Please take time to complete a self-assessment of knowledge, on page 4, sample questions before reading the article.

Opportunity to complete a self-assessment of knowledge learned will be provided at the end of the course.
1) Which of the following is the correct definition of DKA?
   a. Metabolic disorder with hyperglycemia, metabolic acidosis, elevated ketones.
   b. Metabolic disorder with normal glucose, metabolic alkalosis, elevated ketones.
   c. Endocrine disorder caused by inappropriate insulin secretion.
   d. Endocrine disorder caused by abnormal carbohydrate metabolism.

2) The two most common causes of DKA are:
   a. Atypical antipsychotics and gestational diabetes.
   b. Infection and poor compliance with medication regimens.
   c. CVA and pregnancy.
   d. Glucagon-producing tumors, sepsis.

3) The diagnostic criteria of DKA include:
   a. A serum pH > 7.5, a serum glucose > 250 mg/dL.
   b. A serum pH < 7.30, a serum glucose < 250 mg/dL.
   c. A serum pH > 7.2, a serum glucose < 125 mg/dL.
   d. A serum pH < 7.3, a serum glucose > 250 mg/dL.

4) The serum potassium in DKA is:
   a. Typically very low.
   b. Deceptively high: there is actually profound hypokalemia.
   c. Typically normal.
   d. Deceptively low: the total body content is normal.

5) Pregnant women who have DKA:
   a. Always have elevated serum glucose.
   b. Are rarely acidic.
   c. May be euglycemic.
   d. Have a high mortality rate.
Introduction

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

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.

Epidemiology

Most cases of DKA are seen in patients with type 1 diabetes, but approximately 10%-30% of all cases of DKA occur in patients with type 2 diabetes.¹ The incidence of DKA in the United States is increasing,²⁻³ and the incidence of DKA in people who have type 2 diabetes appears to be increasing, as well.⁴ There is also a variation of type 2 diabetes, ketosis-prone diabetes, and this subgroup of diabetics accounts for 20-50% of all persons with DKA.⁵ The incidence of DKA is approximately two episodes per 100 patient years of diabetes.⁶ Diabetic ketoacidosis is more common in Caucasians than in other racial groups, and the incidence of DKA is higher in women than in men.⁶ The mortality rate for DKA is approximately ≤ 2%.⁶
The danger of DKA also affects children and adolescents, and there is evidence that these age groups are increasingly at risk for DKA. Approximately one-third of children and adolescents with type 1 diabetes have DKA at the time of diagnosis, and one researcher found the incidence of DKA in these populations at the time of diagnosis to be 77.1%.

In children and adolescents who have type 2 diabetes, approximately 25% will have DKA at the time of diagnosis, and children aged 0-4 had an incidence of DKA at the time of diagnosis of 37.3%. Diabetic ketoacidosis is the most common cause for hospitalization in the pediatric population, and DKA is the most common cause of diabetes-related death in children and adolescents with type I diabetes. Unlike adults, infection is an infrequent cause of DKA in children.

**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 (i.e., after a meal), the secretion of insulin rises dramatically, both in the amount and the speed in which this rise occurs, as glucose enters the pancreatic β cells and stimulates insulin release.

Diabetes is a disease that affects glucose metabolism. There are essentially two types of diabetes: Type 1 (also called juvenile-onset diabetes) and type 2 (also called adult onset or non-insulin-dependent diabetes). Type 2 diabetes is caused by destruction of the pancreatic β cells that produce insulin. The destruction of the β 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 2 diabetes is characterized for the most part by insulin resistance and inadequate insulin secretion. 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 1 and type 2 diabetes, medications and lifestyle modifications are needed so that blood glucose remains within a specified range.
Type 1 and type 2 Diabetes Classification System: Out of Date?

Diabetes mellitus has traditionally been classified as type 1 or type 2; however, there is growing recognition that not everyone with diabetes mellitus can be described by one of those two categories. Many researchers now feel that the age of onset, the presence or absence of auto-antibodies, and the functioning of the β cells should be considered when classifying diabetes as these factors may have important clinical considerations. For example, Vacante, et al., (2011) proposed three classifications of diabetes for older adults and the elderly: maturity onset diabetes, maturity onset diabetes in the elderly, and senile diabetes. Adolescents and children with diabetes could be considered to have one of four types of diabetes, as listed below:

- Autoimmune plus insulin-sensitive (IS)
- Autoimmune plus insulin-resistant (IR)
- Non-autoimmune plus IS, and
- Non-autoimmune plus IR

Also, some people who have type 2 diabetes are much more susceptible to developing DKA, a sub-group of diabetics that are said to have ketosis-prone diabetes.

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). 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 outlined below:18-19

- **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 is ketones, and the ketones (acetone, acetoacetate and beta-hydroxybutyrate) dissociate to produce hydrogen ions, thus causing the metabolic acidosis. Acetoacetate and beta-hydroxybutyrate are the two ketones that are primarily responsible for this metabolic effect.

Because of the increased hormone production and the shift in metabolism, the serum glucose is elevated and there is high acid load. The high serum glucose causes an osmotic diuresis, which leads to dehydration. The intense production of ketones overwhelms the body’s buffering mechanisms. This causes a metabolic acidosis which in turn causes: 1) nausea and vomiting; 2) Kussmaul respirations, and; 3) a
shift of potassium from the intracellular space to the extracellular space. These pathologic mechanisms lead to profound dehydration, hyperkalemia, and loss of electrolytes.

**Causes Of DKA**

Diabetic ketoacidosis is caused by: 1) new-onset diabetes; 2) poor compliance with prescribed insulin regimen; 3) increased insulin need because of infection or stress, or; 4) prescription or illicit drug use. The majority of cases of DKA are caused by non-compliance with the prescribed insulin regimen or by an infection.

Gastroenteritis, pneumonias, sepsis, and urinary tract infections are common infections that may precipitate DKA. Acromegaly, CVA, Cushing disease, glucagon-producing tumors, heat-related illness, hemochromatosis, hemorrhage, hyperthyroidism, major trauma, myocardial infarction or ischemia, pancreatitis, pregnancy, pulmonary embolism, or major surgery can all cause DKA; and, these stressors, along with infections, account for approximately 40% of all cases of DKA. These medical conditions and pathologies can cause or contribute to DKA by increasing the production of stress hormones, elevating the serum glucose, or blunting the normal physiological warning signs of hyperglycemia and acidosis. Pregnancy can also be a cause of DKA, and this will be discussed in a separate section of this learning module.

Drugs that may cause or contribute to DKA, or have been temporally associated with DKA include cocaine, corticosteroids or glucocorticoids, diuretics, glucagon, interferon, and sympathomimetics. The atypical antipsychotics are known to cause
weight gain, adversely affect glucose regulation, and can cause DKA.\textsuperscript{34} The topic of DKA and the atypical antipsychotics will also be discussed in a separate section of this learning module.

**Defining DKA**

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. In 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, decreased skin turgor, dehydration, dry mucous membranes, electrolyte abnormalities, fever, hypotension, hypothermia, malaise, mental status changes, such as drowsiness, or in profound cases there may be coma, nausea, polydipsia, polyuria, tachycardia, tachypnea, and vomiting.\textsuperscript{2,18,20} These signs and symptoms are certainly not exclusive to DKA, but if the pathological processes of DKA are examined, the genesis of the clinical picture of DKA becomes clear. Several examples are raised below:
**Example #1:**

*Hypotension* in the patient who has DKA is caused by dehydration. Poor oral intake, nausea and vomiting, polyuria, and the osmotic diuresis caused by hyperglycemia lead to the complication of dehydration in individuals with DKA.

**Example #2:**

*Abdominal pain, nausea and vomiting* are very common in patients who have DKA. Acidosis, elevated serum potassium, and high serum ketone levels cause these gastrointestinal complaints.

**Example #3:**

*Kussmaul respirations* are caused by metabolic acidosis and are a way of excreting carbon dioxide (CO₂). This breathing pattern can also contribute to dehydration. 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. Diabetic ketoacidosis can develop very quickly, for example, over several hours, in patients who have type 1 diabetes, or it can develop very slowly over a period of weeks in patients who have type 2 diabetes. The presentation can be mild with the patient complaining of abdominal pain, fatigue, malaise, and nausea or the presentation can be profound. In a serious case of DKA the patient may be comatose and have severe metabolic abnormalities.

**Laboratory Tests And DKA**

The laboratory abnormalities seen in DKA that are commonly considered to be the definitive criteria for a diagnosis of DKA are listed below:²,²⁰
1. hyperglycemia with a blood glucose > 250 mg/dL;
2. metabolic acidosis with a blood pH < 7.30 and a serum bicarbonate of < 18 mEq/L;
3. an elevated serum ketone level and ketones in the urine, and;
4. an elevated anion gap.

Other laboratory test results that may be abnormal in a patient who has DKA are identified and explained below:

- **Hyperkalemia:**
  Acidosis, release of potassium from the cells caused by glycogenolysis, insulin deficiency, and several other mechanisms all cause potassium to shift from the intracellular space to the extracellular space, and serum hyperkalemia is common. However, the osmotic diuresis and vomiting that are commonly part of DKA cause potassium to be excreted in the urine and lost in the vomit. The serum potassium level may be high, but the patient may be profoundly depleted of potassium.

- **Hyponatremia:**
  Hyperglycemia causes an osmotic shift of fluid into the vascular space and hyponatremia. Sodium is also lost renally because of the osmotic diuresis. Some sources report that each 100 mg/dL of glucose above the top normal will lower the serum sodium by 1.6-2.4 mEq/L. So if the patient’s serum glucose is 420 mg/dL and the serum sodium is 118 mEq/L, the corrected serum sodium would be 123-125 mEq/L.

- **Other electrolytes:**
  Serum calcium, magnesium, and phosphate are lost through diuresis. Initially the serum phosphate may be normal or even
high because an insulin deficiency will drive phosphate out of the cells, but the typical phosphate deficit may be up quite high.

- **Amylase and lipase:**
  Serum amylase and lipase levels can be elevated by DKA. It is important to remember that pancreatitis can be a cause of DKA.

- **Hepatic transaminases:**
  The level of hepatic transaminases can be elevated. This can be from DKA or a combination of DKA and fatty liver disease.

- **Leukocytosis:**
  An elevated white blood cell count is common and is caused by hemoconcentration and by stress.

- **Serum osmolality:**
  This may be elevated.

- **Renal function studies:**
  The blood urea nitrogen (BUN) and serum creatinine are often elevated in patients who have DKA. These results can be explained by volume depletion, pre-renal azotemia, or by a laboratory error caused by interference by ketones.

- **Troponin levels:**
  Elevated serum tropinin levels associated with DKA have been reported. $^{35,36}$

It is important to remember that laboratory values in a patient who has DKA can be misleading as the length and severity of the DKA, the clinical signs and symptoms, and the stage of treatment affect these
values. For example, serum sodium, phosphate, and potassium may be low, normal, or high, but the measurements must always be interpreted with caution and with the knowledge that they often may not reflect the “true” levels. Additionally, several of the diagnostic criteria of DKA must be interpreted carefully; for example, normal serum glucose has been reported in pregnant women who have DKA.

Serum and urine ketones are positive in DKA, but in DKA there are three ketone bodies, acetone, acetoacetate, and β-hydroxybutyrate. The primary ketone produced in DKA is β-hydroxybutyrate, but commonly used urine dipsticks that are used to check urine for ketones have a poor specificity for β-hydroxybutyrate so there is the possibility of false negatives.

**Learning Break:**

Euglycemic diabetic ketoacidosis in pregnancy is well described and will be discussed later in this learning module. However, can someone who is not pregnant have euglycemic DKA? This phenomenon has been reported sporadically in the literature. It is important to remember that _euglycemia means normal serum glucose_. In the cases of euglycemic diabetic ketoacidosis that have been reported, all of the patients had elevated serum glucoses that were above the upper limit of normal.

It is true that some patients diagnosed as having euglycemic diabetic ketoacidosis had serum glucoses that were < 250 mg/dL, some as low as 171 mg/dL; however, serum glucose levels below 180mg/dL in patients with diabetic ketoacidosis is rare. It is not clear how this phenomenon happens. Possible causes include a pre-existing fasting state, decreased hepatic stores of glucose, decreased hepatic glucose production, and greater than normal urinary losses of glucose.
Some authors have divided DKA into three categories, mild, moderate, and severe, based on the initial laboratory test results. These categories are described below.

- **Mild DKA:**
  The anion gap is > 10; the arterial pH is 7.24-7.30; the serum bicarbonate level is 15-18 mEq/L, and; the patient is awake and alert.

- **Moderate DKA:**
  The anion gap is > 12; the arterial pH is 7.00-7.24; the serum bicarbonate level is 10-15 mEq/L, and; the patient is alert or drowsy.

- **Severe DKA:**
  The anion gap is > 12; the arterial pH is < 7.00; the serum sodium bicarbonate is < 10 mEq/L, and; the patient is stuporous or comatose.

### Complications Of DKA

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 complications associated with or caused by the DKA itself.

Treatment complications are hypoglycemia, hyperkalemia, and occasionally pulmonary edema. These can be avoided by careful insulin therapy, monitoring blood glucose very closely, and by carefully
managing fluid replacement. The complications of treatment will be discussed in more detail later on in this learning module.

Complications associated with or caused by DKA itself include: Cerebral edema, electrolyte disorders, prolonged QT interval, renal failure, rhabdomyolysis, thrombosis and stroke.\textsuperscript{20,46-52} Cerebral edema and electrolyte disorders are the most common of these complications. Cerebral edema is a very serious consequence of DKA, and it will be discussed in more detail later in the module.

**Pregnancy And DKA**

Diabetic ketoacidosis occurring during pregnancy deserves special consideration, and it is considered to be a serious complication of pregnancy.\textsuperscript{53} Diabetic ketoacidosis during pregnancy is quite uncommon, with an incidence rate of 1-3%.\textsuperscript{53-55} If DKA in the pregnant woman is recognized early and treated properly, the outcome for the mother should be good, and the maternal mortality rates have been reported to be < 1.0%.\textsuperscript{55} However, serious maternal morbidities such as acute renal failure, adult respiratory distress syndrome, cerebral edema, and myocardial ischemia are possible, and the fetal mortality rate associated with maternal DKA can be quite high; the incidence of fetal death caused by DKA has been reported to be 9-36%.\textsuperscript{55}

Diabetic ketoacidosis occurring during pregnancy tends to happen more quickly than DKA will in women who are not pregnant; it affects women with type 1 diabetes and women with type 2 diabetes, and it usually develops in the second or third trimester.\textsuperscript{56} Diabetic ketoacidosis in pregnant women who have type 2 diabetes is more common if glucocorticoids or \( \beta_2 \) agonists are used during the
pregnancy. Diabetic ketoacidosis is considered to be a rare complication of gestational diabetes.

Pregnant women have a higher risk for developing DKA than do women who have diabetes who are not pregnant. Factors that can predispose a pregnant woman to developing DKA include those listed below:  
- Starvation
- Dehydration
- Decreased calorie intake
- Decreased buffering capacity (caused by the compensated respiratory alkalosis of pregnancy)
- Increased production of insulin antagonistic hormones cortisol, human placental lactogen, and prolactin.

Pregnant women of course are also susceptible to infections that may cause DKA, and they may be non-compliant with their medication regimens.

One of the most important issues regarding DKA during pregnancy is euglycemic DKA. Euglycemic DKA is a well-known phenomenon, and serum glucose levels as low as 87 mg/dL have been reported in pregnant woman with DKA. Increased glucose uptake by the fetus and the placenta could in part explain euglycemic DKA. In addition, glomerular filtration rate and renal blood flow are increased during pregnancy, but tubular reabsorption of glucose is not increased so excess glucose of DKA may be lost in the urine.
Other factors that can explain euglycemic DKA during pregnancy are increased glucose utilization during pregnancy, water retention that can cause hemodilution, and the high risk for ketosis that accompanies pregnancy, causing DKA to occur at lower glucose levels.59

**Atypical Antipsychotics And DKA**

The atypical antipsychotics can cause many metabolic disorders such as hyperlipidemia, hyperglycemia, hyperprolactinemia, insulin resistance, intra-abdominal obesity, metabolic syndrome, type 2 diabetes and weight gain.63-64 These drugs have also been noted to cause DKA. The mechanism or mechanisms by which the atypical antipsychotics cause DKA are not known. These drugs, as mentioned previously, can cause weight gain, and that is a risk factor for developing type 2 diabetes and DKA. However, many patients who have been taking an atypical antipsychotic who developed DKA had not gained weight and were not obese.65,66 It may be that it is not weight gain, but a relative increase in the amount of adipose tissue that is partly to blame, or glucose dysregulation caused by the binding of these drugs to certain neuroreceptors that in turn affects insulin sensitivity.65

Fortunately, DKA caused by the use of atypical antipsychotics appears to be rare. A 2013 review of the literature indentified only 69 cases 65 and given the widespread popularity of these drugs and their increasing use, this is a very small number. Routine monitoring of patient’s weight and BMI (body mass index) is recommended as part of the treatment plan when FGA’s (1st generation antipsychotics) and SGA’s (2nd generation antipsychotics) are prescribed that have the risk to cause weight gain and increase the potential to develop diabetes.
Adults should have waist circumference measured and, especially, children and adolescents should have routine height and weight, as well as BMI, trends on follow up exams. Consistent monitoring of weight gain and BMI when a patient is prescribed antipsychotic medication can help to avoid health problems later on.

**Children, DKA And Cerebral Edema**

Cerebral edema is perhaps the most feared complication of DKA in children. It is fortunately rare, occurring in < 1% of all pediatric cases of DKA, but the mortality rate has been estimated to be 20-60%, and 10-25% of these children will suffer permanent long-lasting or permanent cognitive or motor deficits and in the worst case, a permanent vegetative state. This complication of DKA affects children almost exclusively and it is rarely seen in adults over the age of 20.

Cerebral edema caused by DKA usually occurs in the first 4 to 12 hours of treatment, but the onset can be seen earlier or delayed for 24-48 hours, and it can occur before therapy has been started. Children who have DKA and are likely to develop cerebral edema typically have some of these risk factors:

- New onset of diabetes
- Prolonged duration of symptoms
- A $P_{CO_2}$ that is < 20 mm Hg
- Treatment with NaHCO$_3$
- A high BUN
- High volume of fluid resuscitation in the first four hours of treatment, e.g., > 50 mL/kg
- Serum pH < 7.1
• Insulin administration in the first hour of treatment
• Young age: Cerebral edema caused by DKA is more common in children < 5 years.
• Failure of serum sodium to increase as expected after insulin therapy and fluid resuscitation.

Learning Break:
There are many reasons why young children are more likely to develop DKA-related cerebral edema: 1) The early signs and symptoms can be non-specific and attributed to a viral illness; 2) young children cannot communicate how they feel and this can make diagnosing DKA difficult; 3) young children have a higher basal metabolic rate and surface area relative to body weight, therefore, during treatment for DKA they are more likely to suffer from fluid and electrolytes disorders, and; 4) for several physiological reasons young children are more vulnerable to cerebral edema. Adolescents are more likely than adults to be non-compliant with their insulin regimen.

The signs and symptoms of cerebral edema caused by DKA include age-inappropriate incontinence, agitation, bradycardia, central nervous system (CNS) decorticate or decerebrate posturing, depression, fluctuations in mental status, headache, hypertension, irregular respirations, papillary edema, and persistent vomiting. Coma and seizures may be seen, as well. However, not all children with cerebral edema will have dramatic or obvious signs of neurological impairment, and premonitory symptoms may be absent in many children. The exact incidence is not known, but sub-clinical cerebral edema caused by DKA appears to be relatively common, and it is likely that all children with severe DKA have some degree of cerebral edema. Children with sub-clinical cerebral edema may be asymptomatic or have only subtle signs of cerebral edema, and approximately 40%
of children who have cerebral edema caused by DKA will have a normal brain imaging scan.\textsuperscript{37} Whether or not subclinical cerebral edema is predictive of progression to significant cerebral edema is not known.

The cause, or causes of DKA-related cerebral edema are not clearly understood.\textsuperscript{76} Decreased cerebral perfusion, reperfusion injury, vasogenic edema that is caused by disruption of the blood-brain barrier, and excessive fluid resuscitation have all been identified as possible causes.\textsuperscript{7,37,77} The close temporal association between excessive fluid resuscitation and the development of cerebral edema in children who have DKA has long been a subject of interest. However, many children with DKA will develop cerebral edema before treatment begins, and the current literature does not support excessive fluid resuscitation as a primary cause of cerebral edema.\textsuperscript{7,12,37,71,77} The diagnosis of cerebral edema is a clinical diagnosis. The diagnostic criteria for cerebral edema are:\textsuperscript{77}

- Abnormal motor or verbal response to pain
- Decoricate or decerebrate posturing
- Cranial nerve palsy, especially III, IV, and VI
- Neurogenic respiratory patterns, such as apneusis, Cheyne-Stokes respiration, grunting, or tachypnea

In addition, cerebral edema is likely to be present if any of the following two major criteria or one of the major criteria and two of the minor criteria is present.\textsuperscript{77} The \textit{major} criteria are:

1) altered or fluctuating level of consciousness;
2) a sustained decrease in heart beat of more than 20 beats a minute, and;
3) age-inappropriate incontinence.
The *minor* criteria are:

1) vomiting;
2) headache;
3) lethargy;
4) difficulty rousing from sleep; and,
5) diastolic blood pressure > 90 mm Hg, and 6) age < 5 years.

**Treatment For Diabetic Ketoacidosis**

Treatment of a patient who has or is suspected of having DKA begins with an assessment and a physical exam. The diagnostic and laboratory tests that should be done are listed below:

- A1c level
- Serum glucose
- Serum ketones
- Urine ketones
- Arterial or venous blood gas
- Serum electrolytes
- Bun and creatinine
- Serum lactate level
- Serum osmolality
- Serum calcium, magnesium, and phosphate
- 12-lead ECG
- CT scan of the head
- Depending on the patient’s clinical presentation, serum amylase and lipase, hepatic transaminases, and troponin should be measured. If an infection is suspected, the appropriate diagnostic tests should be done.
Treatment of DKA is focused on the following five areas:

1) fluid replacement;
2) insulin therapy;
3) monitoring for and correcting electrolyte imbalances;
4) monitoring for and correcting acid-base disturbances; and,
5) monitoring for and treating complications.

**Fluid Replacement**

Fluid replacement will replace the fluid deficit, help decrease the blood glucose level, and maintain renal function. Because patients who have DKA often have very significant fluid losses of 3 to 10 liters, in the initial treatment of a patient who has DKA fluid replacement is more important than insulin therapy and should take precedence.\(^2,6,20,21,78\) There are several different approaches/formulas available that can help guide fluid replacement.\(^6,20,21\) These are highlighted below.

---

**Give 1000 mL of 0.9% normal saline solution (NSS) over 30 minutes.**

Some authorities recommend this initial bolus for all patients, some recommend the bolus only if the patient is severely dehydrated.

↓

**After the initial bolus, give 15-20 mL/kg/hour of NSS. This should be continued until the patient is euvoletic.**

↓

**Once the patient is euvoletic, the rate of fluid infusion should be decreased to 4-14 mL/kg/hour.** Depending on the corrected serum sodium level, the fluid should be either 0.95 NSS or 0.45% NSS.

↓

**When the serum glucose is 200-250 mg/dL, the IV fluid should be changed to 5% dextrose/0.45% NSS at a rate of 150-250 mL/hour.**
Insulin Therapy

Insulin therapy is a critical part of the treatment of DKA. There is agreement on the general guidelines of insulin therapy. The two areas in which there is some disagreement and/or treatment guidelines differ are: 1) the use of an initial bolus of insulin, and; 2) the use of IV versus subcutaneous insulin. These issues will be discussed at the end of this section.

The following are the guidelines for insulin therapy.\(^2,6,20,21\) Insulin therapy should not be started immediately. It should be started one to two hours after fluid resuscitation has been started. This is highlighted in the table below.

<table>
<thead>
<tr>
<th>Event</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Give a bolus of regular insulin, 0.1 units/kg. A bolus dose is not recommended in children and is optional for adults.</td>
<td></td>
</tr>
<tr>
<td>After the bolus dose, start a continuous infusion of regular insulin, 0.1 units/kg/hour. The continuous infusion should be delayed if the serum potassium is &lt; 3.3 mEq/L because of the risk of hypokalemia.</td>
<td></td>
</tr>
<tr>
<td>The insulin infusion should be continued until: 1) the serum pH is greater than 7.3; 2) the bicarbonate is ≥ 18 mEq/L; 3) the ketonemia has resolved; 4) the anion gap is normal, and; 5) the serum glucose is &lt; 200 mg/dL.</td>
<td></td>
</tr>
<tr>
<td>Once the serum glucose is 250mg/dL, the insulin infusion should be decreased to maintain the serum glucose between 150-200 mg/dL.</td>
<td></td>
</tr>
</tbody>
</table>
The serum glucose level will usually decrease by 50-70 mg/dL an hour. If the serum glucose does not decrease as expected it is likely that an infection is the cause of the DKA. If the serum glucose does not decrease by 50-70 mg/dl in the first hour, the patient can be given a bolus of 0.2-0.4 units/kg or the infusion rate can be doubled.\textsuperscript{21}

When the insulin infusion has been stopped the patient should be transitioned to subcutaneous insulin. There are no universally accepted protocols for this transition,\textsuperscript{21} but most sources agree on the following points:

1) the insulin infusion can be stopped once the patient tolerates oral fluids, the serum glucose is < 200 mg/dL, and the other criteria mentioned above have been met;

2) the IV infusion of insulin should be continued for one to two hours after the subcutaneous insulin regimen has been started. If this is not done there is a risk for a recurrence of hyperglycemia and/or ketoacidosis;

3) the patient should be given both a short-acting insulin and along-acting insulin.

It is prudent to consult with an endocrinologist during the transition, especially if the patient has new-onset diabetes.

The use of an insulin bolus has been recommended, but there is no evidence that a bolus dose, when compared to simply initiating the continuous infusion, is helpful.\textsuperscript{79-81} A bolus of insulin should not be given to a child who has DKA; it is not needed, and, may increase the risk of developing hypoglycemia and cerebral edema.\textsuperscript{37,82-85}
Patients who have what would be considered uncomplicated DKA may be able to be managed with rapid acting insulin analogs given subcutaneously rather than a continuous insulin infusion by a pump. This has been shown to be safe, cost-effective, and equally as effective as an IV infusion of insulin.\textsuperscript{21,86-88} Several different regimens have been recommended; such as, an initial injection of 0.2 unit/kg followed by 0.1 unit/kg every hour or an initial dose of 0.3 unit/kg followed by 0.2 unit/kg every 2 hours until the serum glucose is < 250 mg/dL. When that point is reached, decrease the insulin dose by half to 0.05 or 0.1 unit/kg, respectively, and administer it every 1 or 2 hours until DKA has been resolved.\textsuperscript{21}

**Electrolyte Imbalances**

The total body loss of potassium caused by DKA can be profound, up to 5 mEq/kg; however, as mentioned earlier, the measured serum potassium will often be normal or elevated. When fluids are given and insulin is administered, serum potassium will drop because of correction of acidosis, hemodilution, movement into the cells, and renal excretion - at that point the true level of potassium will be revealed.

The following guidelines can be used to manage serum potassium in cases of DKA.\textsuperscript{21}

1. If the initial serum potassium is < 3.3 mEq/L, insulin therapy should not be started and the patient should be given 10-15 mEq/hour until the serum potassium is > 3.3 mEq/L.
2. If the initial serum potassium is > 3.3 mEq/L but < 5.3 mEq/L, the initial IV fluid resuscitation should provide 10 mEq of potassium per hour for at least four hours.

3. If the initial serum potassium is > 5.3 mEq/L, do not give supplemental potassium, check the level every two hours.

4. The goal is to maintain the serum potassium between 4-5 mEq/L.

The treatment recommendations for DKA may differ from source to source, and there are certainly other treatment protocols that are used for monitoring and replacing serum potassium in cases of DKA. However, despite differences in recommendations as to when to give supplemental potassium and how much to give, all of these protocols have similarities, which are outlined below:

1) if the initial serum potassium is very low, insulin therapy should be delayed until this has been corrected;

2) if the serum potassium is above the top normal, no supplementation is needed, and;

2) if the serum potassium is somewhere in between, potassium supplementation is indicated.

Serum magnesium and serum phosphate should also be closely monitored in cases of DKA. Replacement of serum phosphate is not recommended unless the serum level is < 1.0 mg/dL, and magnesium supplementation is not recommended unless the serum level is < 1.2 mg/dL. In either case, magnesium and/or phosphate
supplementation should be considered if the patient has signs of a deficit of either of these electrolytes.

**Acid-Base Disturbances and Bicarbonate**

Patients who have DKA can be severely acidotic, and there can be a temptation to administer bicarbonate. Acidosis can cause decreased cardiac contractility, peripheral vasodilation, hypotension, shifting of the oxyhemoglobin dissociation curve to the right, and worsening of CNS depression. However, the routine use of bicarbonate to treat DKA is not recommended as there is no proof that it improves clinical outcomes, and there is evidence that suggests that the use of bicarbonate can have many harmful effects, such as, severe hypokalemia, oxyhemoglobin dissociation, cerebral edema, and central nervous system.\(^6,20,21,89,90\)

The potential for harmful effects may be especially true for children who have DKA. Bicarbonate therapy should only be used if the serum pH is < 6.9 or if the acidosis is causing severe systemic effects, such as, coma, hypotension, or hyperkalemia that is life threatening.\(^20,21\) If bicarbonate therapy is needed, the American Diabetes Association (ADA) does recommend, for 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 \(\geq 7.0.\)^{1,20}

**Monitoring For Complications**

Common complications of DKA and the treatment of DKA include hypoglycemia, hypokalemia, hyperkalemia, pulmonary edema, and
renal failure. These can be prevented by close monitoring of BUN and creatinine, serum electrolytes, serum glucose, and intake and output.

**Treatment Of Cerebral Edema**

Treatment of cerebral edema caused by DKA should be focused on reducing intracranial pressure. Initiate the following therapies before confirmation from imaging studies.\(^6,12,37,91\)

1. Elevate the head of the bed.
2. Reduce the IV fluid rate by 30%.
3. Administer mannitol: the dose is 0.25-1.0 grams/kg IV, infused over 20 minutes. Repeat the dose if there is no response or an inadequate response. Monitor the patient’s urine output because mannitol can cause diuresis, hypotension and thus reduced cerebral blood flow.
4. If the patient needs elective intubation and mechanical ventilation make sure that the \(P_{\text{CO}_2}\) does not fall below 22 mm Hg; this could decrease cerebral blood flow and cause cerebral ischemia.

Some sources recommend the use of 3% hyper tonic saline 5-10 mL/kg IV, infused over 30 minutes, if the response to mannitol is not ideal, given along with mannitol, or as an alternative to mannitol.\(^7,12,37\) However, the clinical experience with 3% hypertonic saline for this purpose is limited,\(^67,76,92,93\) and there is evidence suggesting that when compared to mannitol, 3% hypertonic saline was associated with an increased risk of mortality.\(^67\)
Nursing Care, Prevention And Education

When providing care for a patient in the acute phase of DKA, the nurse should focus on hydration status and 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 related 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 are many possible reasons. Some of the more common reasons are listed below:

- **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., and, 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.

When it has been determined that non-compliance was the cause of a particular case of DKA, the patient should be interviewed to find out the following:

  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.
Social workers, psychologists, or the patient’s provider must address some of the issues listed above. 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 reach 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 these 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. However, there are multiple medical conditions that can cause DKA and many medications that can do so as well.

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 serum ketones and ketones in the urine. The basic diagnostic criteria for DKA are a blood glucose > 250 mg/dL, a serum pH < 7.3, a serum bicarbonate < 18 mEq/L, an elevated serum ketone level and ketones in the urine, and an elevated anion gap. 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 of DKA include abdominal pain, decreased skin turgor, dehydration, dry mucous membranes, electrolyte abnormalities, fever, hypotension, hypothermia, malaise, mental status changes such drowsiness or in profound cases coma, nausea, polydipsia, polyuria, tachycardia, tachypnea, and vomiting. Complications of DKA include cerebral edema, electrolyte disorders, prolonged QT interval, renal failure, rhabdomyolysis, thrombosis and stroke. Cerebral edema a rare complication of DKA in children, but the mortality and morbidity rates of this complication are high. Cerebral edema caused by DKA is rare in adults. Euglycemic DKA is possible in pregnant women. Fetal mortality is a common complication of DKA, but maternal death is unusual.

Treatment for DKA should focus on fluid replacement, insulin therapy, and correcting electrolyte abnormalities, correcting acid-base disturbances, and monitoring for complications. The complications of treatment of DKA include hypoglycemia, hyperkalemia, and pulmonary edema. However, if DKA if promptly recognized, properly and aggressively treated, and treatment outcomes appropriately evaluated and followed, patients should survive.

Please take time to help NurseCe4Less.com course planners evaluate the nursing knowledge needs met by completing the self-assessment of Knowledge Questions after reading the article, and providing feedback in the online course evaluation.

Completing the study questions is optional and is NOT a course requirement.
1) **Which of the following is the correct definition of DKA?**
   a. Metabolic disorder with hyperglycemia, metabolic acidosis, elevated ketones.
   b. Metabolic disorder with normal glucose, metabolic alkalosis, elevated ketones.
   c. Endocrine disorder caused by inappropriate insulin secretion.
   d. Endocrine disorder caused by abnormal carbohydrate metabolism.

2) **The two most common causes of DKA are:**
   a. Atypical antipsychotics and gestational diabetes.
   b. Infection and poor compliance with medication regimens.
   c. CVA and pregnancy.
   d. Glucagon-producing tumors, sepsis.

3) **The diagnostic criteria of DKA include:**
   a. A serum pH > 7.5, a serum glucose > 250 mg/dL.
   b. A serum pH < 7.30, a serum glucose < 250 mg/dL.
   c. A serum pH > 7.2, a serum glucose < 125 mg/dL.
   d. A serum pH < 7.3, a serum glucose > 250 mg/dL.

4) **The serum potassium in DKA is:**
   a. Typically very low.
   b. Deceptively high: there is actually profound hypokalemia.
   c. Typically normal.
   d. Deceptively low: the total body content is normal.

5) **Pregnant women who have DKA:**
   a. Always have elevated serum glucose.
   b. Are rarely acidotic.
   c. May be euglycemic.
   d. Have a high mortality rate.
6) DKA complications almost exclusively affecting children are:
   a. Cerebral edema.
   b. Hypokalemia.
   c. Renal failure.
   d. Cardiac arrhythmias.

7) The first step in treating DKA is:
   a. Administration of insulin.
   b. Fluid resuscitation.
   c. Administration of bicarbonate.
   d. Potassium supplementation.

8) DKA can be treated by using:
   a. IV insulin.
   b. Subcutaneous insulin.
   c. IV or subcutaneous insulin.
   d. IM insulin.

9) The use of bicarbonate when treating DKA
   a. Is reserved for children who have DKA.
   b. Is only indicated if the serum pH is < 7.30.
   c. Is reserved for pregnant women who have DKA.
   d. Is only indicated if the serum pH is < 6.9.

10) When switching from continuous IV to SUBQ Insulin:
    a. The IV infusion should be continued for 1-2 hours after starting SC insulin.
    b. The IV infusion should be stopped 1-2 hours before starting SC insulin.
    c. The IV infusion should be increased for 1-2 hours before starting SC insulin.
    d. The IV insulin should be continued for 10-12 hours after starting SC insulin.
Correct Answers:

1) Which of the following is the correct definition of DKA?
   a. Metabolic disorder with hyperglycemia, metabolic acidosis, elevated ketones.

2) The two most common causes of DKA are:
   b. Infection and poor compliance with medication regimens.

3) The diagnostic criteria of DKA include:
   d. A serum pH < 7.3, a serum glucose > 250 mg/dL.

4) The serum potassium in DKA is:
   b. Deceptively high: there is actually profound hypokalemia.

5) Pregnant women who have DKA:
   c. May be euglycemic.

6) DKA complications almost exclusively affecting children are:
   a. Cerebral edema.

7) The first step in treating DKA is:
   b. Fluid resuscitation.

8) DKA can be treated by using
   c. IV or subcutaneous insulin.

9) The use of bicarbonate when treating DKA
   d. Is only indicated if the serum pH is < 6.9.

10) When switching from continuous IV to SUBQ Insulin:
    a. The IV infusion should be continued for 1-2 hours after starting SC insulin.
The reference section of in-text citations include published works intended as helpful material for further reading. Unpublished works and personal communications are not included in this section, although may appear within the study text.


The information presented in this course is intended solely for the use of healthcare professionals taking this course, for credit, from NurseCe4Less.com. The information is designed to assist healthcare professionals, including nurses, in addressing issues associated with healthcare.

The information provided in this course is general in nature, and is not designed to address any specific situation. This publication in no way absolves facilities of their responsibility for the appropriate orientation of healthcare professionals. Hospitals or other organizations using this publication as a part of their own orientation processes should review the contents of this publication to ensure accuracy and compliance before using this publication.

Hospitals and facilities that use this publication agree to defend and indemnify, and shall hold NurseCe4Less.com, including its parent(s), subsidiaries, affiliates, officers/directors, and employees from liability resulting from the use of this publication.

The contents of this publication may not be reproduced without written permission from NurseCe4Less.com.