# DIABETIC KETOACIDOSIS MANAGEMENT PROTOCOL

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DIABETIC KETOACIDOSIS MANAGEMENT PROTOCOL

“The key to successful management of DKA is….CAREFUL ATTENTION TO DETAIL!”

I. INTRODUCTION/DEFINITION:

Diabetes Ketoacidosis is one of two serious, acute life-threatening complications of Type I, insulin deficient diabetes mellitus (IDDM), or Type II, insulin insufficient diabetes mellitus, the other being severe hypoglycemia. Diabetic ketoacidosis (DKA) may initiate the clinical onset of Type I diabetes or may occur at any time during its subsequent course. About one-quarter of persons with new onset IDDM will present in DKA. Rarely will patients with Type II diabetes mellitus develop DKA.

Diabetic ketoacidosis is always caused by a relative or absolute insulin deficiency. Biochemically, it is characterized by hyperglycemia of varying degree and:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pH</td>
<td>&lt; 7.30</td>
</tr>
<tr>
<td>Blood Glucose</td>
<td>&gt; 250 mg/dl</td>
</tr>
<tr>
<td>HCO₃</td>
<td>&lt; 15 mEq/L</td>
</tr>
<tr>
<td>Ketonemia</td>
<td>&gt; 1:2 dilution</td>
</tr>
</tbody>
</table>

Diabetic ketoacidosis in persons with established IDDM may occur as a consequence of the person’s failure to administer the prescribed insulin or from environmental factors that interfere with the action of insulin. Factors such as illnesses, infections and psychologic stress result in the increased production and release of “stress” hormones such as epinephrine, norepinephrine, cortisol, growth hormone and glucagon. These hormones not only interfere with the peripheral action of insulin but also stimulate the release of hepatic glucose (glycogenolysis) as well as the production of new glucose from endogenous precursors (gluconeogenesis). Free fatty acids released by the increased rate of lipolysis are metabolized in the liver into β-hydroxybutyrate, acetoacetate and acetone (collectively known as “ketones”). The resulting ketonemia raises plasma hydrogen ion concentration (i.e. lowers pH) thus leading to the development of ketoacidosis. Simply speaking, in the diabetic person already on insulin therapy, the stress-provoking environmental factors cause a significant imbalance between the insulin effect and the counter-regulatory hormones effects and results in a state of accelerated tissue catabolism that may progress to DKA.

Ketonemia per se does not always result in metabolic acidosis. It does, however, indicate that insufficient insulin is present and that the other metabolic changes associated with such insufficiency (e.g. hyperglycemia) will result in increased fluid losses due to osmotic diuresis. Under conditions of normal thirst sensation, the person will be able to keep up with the increased fluid losses by drinking. When this compensatory response is interrupted by nausea and vomiting, there can be a rapid progression to dehydration and metabolic ketoacidosis. Correction of this metabolic decompensation state requires re-establishing insulin balance and the proper replacement of fluid and electrolyte deficits.
Frequently, for any given episode of ketoacidosis the precipitating event remains unknown. Although a careful screen for infection is appropriate, one should be aware that leukocytosis, with counts as high as 30,000/mm³, is common with DKA as a result of the associated leukemoid response to stress. The clinical picture can also, on occasion, resemble appendicitis or an acute abdomen. However, abdominal pain, nausea and vomiting are often the consequence of an acidosis-related increased prostaglandin (PGI₂ and PGI₃) production from adipose tissue. Failure to self-administer insulin is much more common than generally appreciated and may be a manipulative event by the young patient with diabetes, especially in the adolescent. It is worth noting that there is no evidence that DKA will result SOLELY from dietary indiscretion. The amount of insulin required to suppress lipolysis is approximately one order of magnitude (10 fold) less than the amount required to adequately control plasma glucose levels.

Diabetic ketoacidosis is a serious complication and the mortality rate in pediatric hospitals is STILL between 0.5 % and 2 %, mostly secondary to intra-cerebral crises. Patients admitted with a diagnosis of DKA need to be monitored closely and aggressively until clinically and biochemically stable and the acidosis and hyperglycemia are fully corrected. The placement within the hospital of the child or adolescent with DKA is an important management consideration. Careful and timely monitoring is mandatory and should be done only by a trained professional observer at least every thirty minutes. If such monitoring can be accomplished without undue burden on the staff, then admission to a regular pediatric hospital floor is acceptable. If NOT, then the child with DKA MUST be admitted to an intensive care setting that will facilitate the needed, close observation and care.

II. GOALS:

A. Correct volume depletion

B. Replace electrolyte losses

C. Correct acidosis

D. Abolish ketosis

E. Treat precipitating factors:
   1. infection
   2. emotional stress
   3. trauma
III. GENERAL EVALUATION:

* Admit patients with diabetic ketoacidosis only to a unit in which vital signs and neurological status can be monitored frequently and glucose levels can be measured hourly. All patients with a pH < 7.15 and/or any of the following must be admitted ONLY to a pediatric Intensive Care Unit:

  a. depressed or deteriorating mental status
  b. blood glucose > 1000 mg/dl
  c. age < 3 years
  d. cardiovascular instability after 1st hour of fluid therapy (i.e. required > 40 ml/kg IV bolus fluids)
  e. respiratory insufficiency

* Maintain constant cardiac monitoring until ketoacidosis resolves and patient is clinically stable.

* Keep precise and timely notes about the patient and his or her clinical progress, including rationalization for therapeutic decisions.

* Maintain a thorough flow sheet record of all laboratory and treatment measures pertinent to the patient’s progress and therapeutic decisions.

A. Physical Signs:

At presentation, assess ABCS for stability of patient’s status (A = airway; B = breathing; C = circulation; S = sensorium/brain function)

1. Respiratory Status. If patient’s airway is compromised or if there are signs of an impending compromise (i.e. respiratory fatigue, elevated pCO₂), use bag-valve-mask ventilation and consider intubation and control of the airway.

2. Sensorium/Mental Status. Severe lethargy, drowsiness and somnolence are common accompaniments of DKA and are due to the combined effects of dehydration and acidosis. Semi-coma and coma may also occur and may either be present at onset or develop during the course of treatment. A thorough neurological evaluation must be performed on admission and at regular intervals during treatment for DKA. Throughout the first 48 hours the patient should be closely monitored for neurologic deterioration due to cerebral edema.
a. To assess the level of consciousness in children ≤ 3 years of age, use the Children’s Coma Scale:

<table>
<thead>
<tr>
<th>Eye Opening</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>4</td>
</tr>
<tr>
<td>Reaction to speech</td>
<td>3</td>
</tr>
<tr>
<td>Reaction to pain</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
</tbody>
</table>

**Best Motor Response**

<table>
<thead>
<tr>
<th>Best Motor Response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous (obeys verbal commands)</td>
<td>6</td>
</tr>
<tr>
<td>Localizes pain</td>
<td>5</td>
</tr>
<tr>
<td>Withdraws to pain</td>
<td>4</td>
</tr>
<tr>
<td>Abnormal flexion response to pain (decorticate posturing)</td>
<td>3</td>
</tr>
<tr>
<td>Abnormal extension response to pain (decerebrate posturing)</td>
<td>2</td>
</tr>
<tr>
<td>No response to pain</td>
<td>1</td>
</tr>
</tbody>
</table>

**Best Verbal Response**

<table>
<thead>
<tr>
<th>Best Verbal Response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smiles; oriented to sound; follows objects and interacts appropriately</td>
<td>5</td>
</tr>
<tr>
<td><strong>Crying</strong></td>
<td></td>
</tr>
<tr>
<td>consolable</td>
<td>4</td>
</tr>
<tr>
<td>inconsistently consolable</td>
<td>3</td>
</tr>
<tr>
<td>inconsistently consolable moaning</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
</tbody>
</table>

b. For children > 3 years of age:

<table>
<thead>
<tr>
<th>Eye Opening</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>5</td>
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<td>Reaction to pain</td>
<td>3</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
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**Best Motor Response**

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<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
</tbody>
</table>
Best Verbal Response

<table>
<thead>
<tr>
<th>Oriented and converses</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disoriented but converses</td>
<td>4</td>
</tr>
<tr>
<td>Inappropriate words</td>
<td>3</td>
</tr>
<tr>
<td>Incomprehensible sounds</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
</tbody>
</table>

Total Score Scale:

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>Normal, awake, conversive and oriented</td>
</tr>
<tr>
<td>12-13</td>
<td>Disoriented, localizes to pain, opens eyes to verbal commands (&lt;13 suggests the presence of cerebral edema)</td>
</tr>
<tr>
<td>8-10</td>
<td>Opens eyes only to painful stimuli, shows flexor or extensor response to pain (non-localized) (&lt;8 is considered a medical emergency)</td>
</tr>
<tr>
<td>3</td>
<td>Brain dead</td>
</tr>
</tbody>
</table>

3. Dehydration/Vascular Volume. Determine patient’s clinical hydration status by examining vital signs (heart rate, blood pressure, pulse pressure), the quality of the peripheral pulse quality and capillary refill time. Weigh patient carefully. Fluid administration may be the most important early treatment intervention.

4. Acidosis. Check for fruity-smelling breath and increased depth as well as rate of breathing. Classic “Kussmaul” respirations occur when the pH is ≤ 7.25. Shallow breathing may indicate a more severe degree of acidosis.

5. Infection. Screen for a source of infection. Severe leukocytosis may occur with DKA and NOT be indicative of an underlying infection.

6. Monitoring. Monitor vital signs, including assessment of mental status and overall state of hydration, at least hourly via a competent, professional observer. Record intake and output accurately. Weigh patient every 24 hours.

B. Assessment of Dehydration:

<table>
<thead>
<tr>
<th>% Dehydration</th>
<th>% Dehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>10-15%</td>
</tr>
<tr>
<td>Moderate</td>
<td>5-10%</td>
</tr>
<tr>
<td>Mild</td>
<td>&lt; 5%</td>
</tr>
</tbody>
</table>

The degree of dehydration observed in DKA is variable and, on occasion, may be profound. The magnitude of the water deficit may be deceiving and
the extent of dehydration underestimated due to the fact that in DKA there is a disproportionate loss of water from the intracellular fluid compartment (ICF) in distinction to the extracellular fluid space (ECF). In fact, it is unusual to see a patient in DKA who is initially shocky (hypotension, decreased peripheral perfusion, pallor, mottling, delayed capillary refill) since the high level of glucose in the extracellular fluid space usually protects against this. Shock, if it occurs, does so late in the untreated course or in response to the rapid movement of blood glucose into the intracellular compartment. The presence of shock is an ominous sign and should be treated vigorously and aggressively with isotonic fluid administration.

The person with acute DKA often has good color and may even appear flushed from the vasodilatory effects of increased circulating levels of prostaglandins. This situation is in marked contrast to the more common types of dehydration secondary to vomiting and diarrhea seen in pediatrics where the loss of fluid is predominantly from the extracellular compartment. Since most physicians use various clinical signs of dehydration that reflect extracellular fluid deficits, it is not surprising that the degree of dehydration in DKA, the classic example of intracellular dehydration, is often underestimated.

The degree of dehydration may be estimated by considering the solute:water ratio of the extracellular fluid (i.e. osmolality). This may be either measured or estimated from the following formula:

\[
\text{Serum osmolality} = [2 \times (\text{sodium concentration})] + \frac{\text{blood glucose (mg/dl)}}{18} + \frac{\text{BUN}}{2.8}
\]

C. Assessment of Acidosis:

<table>
<thead>
<tr>
<th></th>
<th>PH</th>
<th>HCO₃⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>&lt; 7.10</td>
<td>&lt; 5 mEq/L</td>
</tr>
<tr>
<td>Moderate</td>
<td>7.10-7.30</td>
<td>5-10 mEq/L</td>
</tr>
<tr>
<td>Mild</td>
<td>&gt; 7.30</td>
<td>&gt; 10 mEq/L</td>
</tr>
</tbody>
</table>

The metabolic acidosis in DKA is primarily related to the elaboration of hydrogen ions as a consequence of fatty acid breakdown from the exaggerated catabolic rate. The concomitant dehydration produces a decrease in renal perfusion limiting the body’s normal attempts at elimination of non-volatile, organic and ketoacids.

At presentation, arterial pH in DKA is commonly in the range of 7.00 to 7.10 with serum bicarbonate concentrations below 10 mM/L. Insulin is required to reverse the fatty acid breakdown and appropriate fluid replacement is essential to reestablish kidney’s normal excretory function. Without the latter, the kidney cannot excrete the acid end products of lipid and protein metabolism.
Excess acetone, however, is still excreted through the lungs and gives many patients a characteristic fruity odor to their breath.

D. Initial Laboratory Studies:

1. Blood Glucose. Bedside capillary blood sugar testing results should be confirmed intermittently with serum samples run by the laboratory to ensure technical competence by the nursing/medical staff doing the bedside monitoring. Caution: Initial blood glucose levels may exceed the limits of most capillary blood glucose monitors.

2. Venous or Arterial pH and pCO₂. Unless there is concern with the patient’s ventilatory status, initial arterial or arterialized venous blood samples may be used to assess pH. Subsequent determinations may be done from non-tourniquet venous blood since only the pO₂ will be markedly affected. At presentation, plasma pH values in the range of 7.00 to 7.10 are common with HCO₃⁻ concentrations below 10 mM/L.

3. Serum Acetone/β-hydroxybutyrate

4. Na/K/Cl/CO₂. The initial sodium concentration is usually low due to the movement of free water into the extracellular fluid compartment and the loss of sodium in the urine as well as from vomiting. Potassium is usually high-normal to high. CO₂ is characteristically low.

5. BUN/Creatinine. BUN in DKA is initially a better measure of renal function than creatinine since the presence of ketonemia, specifically acetoacetate, may interfere with the laboratory measurement of serum creatinine levels. Caution: Although an elevated BUN in DKA most frequently reflects a decrease in extracellular fluid volume and a decrease in glomerular filtration rate (GFR), the BUN may alternatively be increased secondary to excess protein breakdown.

6. Calculated Serum Osmolality

   Note: serum osmolality = 2(Na) + \( \frac{BUN}{2.8} \) + \( \frac{Glucose}{18} \)

   [Normal: 275-295]

7. Anion Gap

   Note: anion gap = Na – (Cl + HCO₃⁻)

   [Normal: 8-16 mEq/L]
8. Calcium/Phosphorus/Magnesium. If readily available, ionized calcium results are preferred while the patient is acidotic because of the known effect of acid-base imbalance on calcium binding (i.e. calcium binding increases thereby decreasing the ionized calcium concentration, as pH increases).

9. Complete Blood Count with differential. Leukocytosis is common in DKA but does not necessarily imply the presence of an underlying infection. The elevated white blood cell count may be secondary to a stress response. Alternatively, fever may be absent in patients whose DKA is triggered by infection.

10. If patient is a new onset IDDM, obtain the following lab before the administration of any insulin:
   a. insulin (2 cc’s blood in a red top or “tiger” tube)
   b. C-peptide (2 cc’s blood in a red top or “tiger” tube)
   c. Islet cell antibodies (1 cc blood in a red top or “tiger” tube)
   d. Anti-GAD antibodies (2 cc’s blood in a red top or “tiger” tube)
   e. Hemoglobin A1C (3 cc’s blood in a purple top tube)

E. Serial Laboratory Monitoring:

1. Glucose. Obtain hourly glucose determinations for as long as insulin is being given. These should be done at the bedside with intermittent confirmation (i.e. every 4 hours) of the accuracy of results by the hospital laboratory on concurrently obtained serum samples.

2. Electrolytes. Sodium, potassium, chloride and CO2 should be monitored every two hours during the initial phase of DKA therapy. Subsequent frequency of testing will depend on the patient’s clinical progress and state of recovery. Calculate osmolality and anion gap concurrently with each set of electrolyte results.

3. Venous pH and pCO2. Venous blood gases should be checked every two hours until pH ≥ 7.25. Subsequent monitoring of acid-base status can be effectively achieved via serum HCO3 levels found in most electrolyte panels.

4. Ketones. Urine ketones may be checked once every 8 to 12 hours until clear. Serum ketone determination should be done initially to confirm a diagnosis of ketoacidosis. Subsequently, serum ketones should be checked only when serum CO2 is > 20 to document the complete eradication of ketosis. Repetitive measurements of serum ketones (acetate and acetoacetate) are NOT helpful for monitoring the patient’s therapeutic progress unless β-hydroxybutyrate results can be rapidly measured. Under
normal circumstances, β-hydroxybutyrate is converted to acetate and acetoacetate. As a result, ketosis may seem to paradoxically worsen as the patient gets clinically better because of increased conversion when vascular circulation is reestablished and tissue oxygenation is restored. In the absence of readily available β-hydroxybutyrate results, the KEY parameters to follow are the serum pH, the calculated anion gap and the total HCO₃⁻ since these give a more accurate assessment of therapeutic progress.

5. BUN and Creatinine levels should be monitored every 8 to 12 hours.

6. Ca/Phos/Mg should be checked every 8 to 12 hours as indicated by prior results. If the patient is hypophosphatemic or hypocalcemic, calcium and phosphorous levels will need to be monitored more frequently.

7. EKGs should be performed only if hypo- or hyperkalemia is clinically indicated.

F. DKA Flow Sheet (see appendix)

IV. TREATMENT:

A. Fluid Therapy. The following guidelines for management of the DKA patient must be individualized to fit the clinical picture. Adequate support staff care is the **sine quo non** of successful DKA treatment. This requires the constant presence of a competent professional observer, especially in the early hours of therapy.

1. Successful management of DKA is dependent upon the proper selection and administration of sufficient intravenous fluids as determined by close, **serial** monitoring of:

   a. the patient’s clinical response (sensorium, blood pressure, pulse pressure, heart rate, respiratory rate, capillary filling time)

   b. plasma glucose, pH and electrolytes including CO₂

   c. strict recording of intake and output and serial body weight measurements on admission and every 24 hours. Unless the patient’s sensorium is significantly depressed, avoid bladder catheterization as the risk of secondary infection substantially outweighs the potential benefits.

Restoration of vascular perfusion will increase glucose utilization in peripheral tissues, increase urinary glucose and ketone excretion and reverse the progression of acidosis.
2. Intravenous fluids can be calculated on the basis of existing fluid deficits, clinical evidence of hypovolemia or shock, ongoing fluid losses and expected maintenance requirements. Ongoing losses may be marked and are due to the osmotic diuresis and the increased fluid demands of persistent tachypnea and hyperventilation.

   a. Initial loading dose of normal saline at 10-20 ml/kg body weight over 20-30 minutes. Additional boluses may be administered based on patient’s clinical hydration status such as blood pressure, pulse pressure, rate and quality of peripheral pulses and capillary filling time.

   b. Following initial fluid resuscitation, give the rest of the total calculated fluid requirements/replacement over the subsequent 48 hours.

* Maintenance fluids:

  1500 ml/m²/24 hrs.

  OR

  0 - 10 kg. = 100 ml/kg/24 hrs.
  10 - 20 kg. = 1000 ml + [(weight in kg. – 10) x 50]
  > 20 kg. = 1500 ml + [(weight in kg. – 20) x 20]

* Deficit fluids:

<table>
<thead>
<tr>
<th>Percent Dehydration</th>
<th>Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 %</td>
<td>50 ml/kg</td>
</tr>
<tr>
<td>10 %</td>
<td>100 ml/kg</td>
</tr>
<tr>
<td>15 %</td>
<td>150 ml/kg</td>
</tr>
</tbody>
</table>

   c. Calculate total fluids required for rehydration over 48 hours. Rate of fluid administration should be kept at < 4000 ml/m²/day or less than 250 % of maintenance unless patient’s clinical status dictates otherwise. A few studies have suggested that limiting total fluid administration to ≤ 4000 ml/m²/day may lessen the risk of developing cerebral edema.

* Calculate the required IV fluid rate for the first 24 hours of rehydration as follows:

\[
\text{Rate/hr} = \frac{\text{Daily Maintenance Fluids}}{24 \text{ hours}} + \frac{1}{2}(\text{Calculated Fluid Deficit})
\]
* calculate the required IV fluid rate for the second 24 hours of rehydration as follows:

\[
\text{Rate/hr} = \frac{\text{Daily Maintenance Fluids}}{24 \text{ hours}} + \frac{1}{2}(\text{Calculated Fluid Deficit}) \quad \frac{24 \text{ hours}}{24 \text{ hours}}
\]

When administering calculated fluid requirements, it is imperative that the patient’s clinical hydration status and intake/output be frequently assessed. Changes in the rate of fluid administration must be urgently instituted to compensate for persistent, symptomatic fluid deficits (tachycardia, hypotension, decreased pulse pressure) or iatrogenic fluid overload (eyelid, extremity or lumbar edema, pulmonary rales).

3. Crystalloid Solutions

   a. give the initial fluid bolus(es) as isotonic (0.9 %) Normal Saline or Lactated Ringer’s

   b. limit volume to 1 liter per bolus

   c. continue calculated fluid replacement (deficit plus maintenance) as 0.9 % Normal Saline until Dextrose added to IV solution. Then change to Ds $\frac{1}{2}$ (0.45 %) Normal Saline with potassium supplement as indicated by lab/clinical findings.

   d. If glucose falls $\leq 250 \text{ mg/dl}$ while on Ds $\frac{1}{2}$ (0.45 %) Normal Saline as a result of insulin administration and the resolution of the acidosis, change IV to D10 $\frac{1}{2}$ (0.45 %) Normal Saline with potassium supplement to maintain desired glucose:insulin ratio.

   e. A hypernatremic state at DKA presentation suggests the need for even slower and more careful correction of the patient’s fluid deficit.

B. Glucose

The blood glucose at the time of DKA presentation is quite variable and may range from the low 200’s to well over 1000 mg/dl. The degree of acidosis bears little relationship to the degree of hyperglycemia. DKA may occur with a serum glucose as low as $\leq 300 \text{ mg/dl}$ if the patient is having problems with recurrent emesis OR as a result of a decreased carbohydrate intake in the face of additional doses of subcutaneous insulin given at home. However, although the height of the blood glucose is NOT a good index of the severity of the patient’s illness, extremely high serum glucose concentrations tend to be often associated with a more severe degree of dehydration and, thereby, with an increased morbidity and mortality.
* No dextrose infusion if initial blood glucose is > 500 mg/dl

* Add 5% dextrose to the intravenous fluids when blood glucose is \( \leq 400 \text{ mg/dl} \) or decreasing at \( \geq 100 \text{ mg/dl/hour} \). Caution: The rate of decrease of serum glucose is sometimes greater in the first hour of rehydration as the intravascular volume expands and GFR (glucosuria) increases.

* Administered glucose to insulin ratio (grams of glucose per hour : units of insulin per hour) should be between 4:1 and 6:1. Increase glucose to insulin ratio when blood glucose is \( \leq 200 \text{ mg/dl} \) to maintain serum glucose in the 200-250 mg/dl range.

* Avoid blood glucose levels \( < 150 \text{ mg/dl} \). Signs and symptoms of hypoglycemia include somnolence, headache, confusion, fatigue, seizures, loss of consciousness, anxiety, tremors and diaphoresis. Maintain serum glucose in the 200 - 250 mg/dl range until plasma ketones are cleared and ketoacidosis resolves

* Plasma glucose invariably falls more rapidly than plasma ketones and correction of the acidosis. Insulin should not be stopped because plasma glucose concentrations approach the normal range; rather glucose infusion rates should be increased and insulin infusion continued until the ketosis has cleared. Maintain serum glucose in the 200 – 250 mg/dl range.

C. Bicarbonate

Indicated only when initial pH \( < 7.10 \), \( \text{pCO}_2 < 40 \text{ torr} \) and repeat pH fails to improve after initial fluid bolus(es) resuscitation (repeat pH still \( < 7.10 \) one hour after initial results). Give \( \frac{1}{2} \text{ mEq HCO}_3 \text{ per kilogram of body weight intravenously over 1-2 hours} \). Intravenous bolus bicarbonate is very rarely, if ever, indicated except under a full cardiorespiratory arrest situation.

* The fluid rate of the bicarbonate infusion should be determined by the patient’s calculated fluid requirements

* Give bicarbonate continuously either via separate venous access or piggybacked into the main IV line. Do NOT administer the bicarbonate in the same intravenous line containing calcium. Do not mix the bicarbonate directly into the insulin infusion IV bag.

* Do NOT give bicarbonate if the patient is hypokalemic.
* Overcorrection, or too rapid correction, of pH with bicarbonate may result in:

a. hypokalemia. Bicarbonate causes a shift of the serum potassium into the intracellular fluid compartment.

b. paradoxical CSF acidosis. Bicarbonate results in the production of CO₂. The produced CO₂ crosses the blood-brain barrier more readily than bicarbonate and can cause a paradoxical lowering of CSF pH.

c. impaired oxygen-hemoglobin dissociation. Bicarbonate shifts the oxygen-hemoglobin dissociation curve to the left leading to an impaired oxygen release to the tissues and an increased production of lactate.

d. deterioration of mental status

e. increased tonicity. The administration of bicarbonate concurrently infuses the patient with a high sodium load and may result in a hyperosmolar serum.

f. alkalosis. Alkalosis may result either from too much bicarbonate administration (overshoot alkalosis) or can occur as ketoacids and lactate are metabolized to bicarbonate during insulin therapy (rebound alkalosis).

Administration of bolus bicarbonate therapy has been related to worsening of the mental status/sensorium. Do NOT give bicarbonate if unable to adequately ventilate the patient since the administered bicarbonate can cause an increase in pCO₂ and an acutely rapid decrease in serum pH.

* Correction of acidosis. Often during the improving phase of DKA treatment, the pH rises and the anion gap narrows even though the plasma bicarbonate (HCO₃⁻) remains low. The persistently low bicarbonate is most likely a consequence of the hyperchloremia that develops during DKA treatment as a result of the rapid or excess infusion of sodium (NaCl) or potassium chloride (KCl) and the loss of bicarbonate from the blood either via the urine as ketones or through its exchange with intracellular buffers.

However, if the anion gap remains elevated and the pH remains persistently low by 4 to 6 hours after treatment was initiated, this indicates insulin resistance or a persistent insulin insufficiency and requires aggressive increases in the amounts of administered insulin and fluids.

Alternatively, some patients may demonstrate a persistent anion gap despite clinical improvement and a rising pH. In this situation, the unmeasured
anion is presumably derived from tissue buffers and the anion gap persistence does NOT indicate insulin resistance or insufficiency especially if present in the face of clinical improvement and a rising pH.

D. Sodium

The serum sodium (Na) concentration at onset is variable but total body sodium is almost always depressed by ≥ 10 mEq per kilogram of body weight. Serum Na may be as low as 120 mEq/L yet, this does NOT generally require specific management since the hyponatremia is predominantly dilutional. Such falsely depressed serum sodium concentrations are caused by the solute Na being diluted by free water drawn from the intracellular fluid compartment as a result of an elevated serum glucose concentration. The corrected serum sodium can be calculated as follows:

$$\text{Corrected Sodium} = (\text{Na in mEq/L}) + \left\{ (\text{[Glucose in mg/dl]} - 100) \times 1.6 \right\}$$

A quick method for calculating the corrected sodium is to add 1.6 mEq/L for every 100 mg/dl of serum glucose above 100 mg/dl. Put another way, for each 100 mg/dl increase in serum glucose above 100 mg/dl, the serum Na decreases by 1.6 mEq/L.

Note: Hyponatremia usually self-corrects as the blood glucose falls as a result of fluid replacement and insulin therapy. High or high-normal serum sodium levels at DKA presentation are worrisome and have been associated with the development of cerebral edema. A hypernatremic state suggests the need for even slower and more careful correction of the fluid deficit.

Note: In some laboratories, factitious hyponatremia may also be caused by hyperlipidemia.

E. Potassium

Serum potassium (K) will often be initially elevated due to the acidosis. Much of the increase in the extracellular hydrogen ion concentration is buffered within the cells by the intracellular proteins, phosphates and amino acids. To maintain the electrical neutrality of the cell, the major intracellular cation, K, moves out from the intracellular into the extracellular fluid compartment. As such, the usual and expected finding at DKA presentation is an elevated serum potassium concentration, the degree of elevation being principally dependent on the degree of acidosis. Plasma concentrations of potassium in the range of 5-7 mEq/L are therefore expected and require no specific treatment if renal function is normal and the EKG is unremarkable.
Despite the actual serum potassium concentration, the patient in DKA is usually total body potassium depleted upon initial presentation. Hypokalemia is thereby often a management problem if not anticipated and treated accordingly.

Serum potassium levels will decrease with each of the following:

a. administration of both glucose and insulin
b. correction of acidosis
c. rehydration which promotes an increased renal function with an increased renal potassium excretion

If, in the presence of severe acidosis (i.e. pH ≤ 7.20), the child presents with a low, or even low-normal potassium, prompt treatment must be immediately instituted to prevent severe hypokalemia from developing later. When initial K is ≤ 3.0 mEq/L, potassium should be given in the initial expansion fluids without waiting for demonstration of renal function and insulin therapy should be held until the initial treatment fluids have been infused. It is crucial to know the patient’s initial serum potassium status either by blood sample or EKG T-wave changes.

If there is EKG or clinical evidence of hypokalemia and the serum potassium concentration is NOT known, provide KCl as an infusion of 0.5 mEq. per kilogram of body weight over one hour (maximum dose: 10 mEq. per hour; maximum potassium concentration: 1 mEq. per 5 cc’s). Avoid rapid infusions of potassium since these can result in cardiac dysrhythmias.

* Supplemental potassium is NOT given until the patient’s functional renal status is known. If functional renal status is a concern, wait until urine output is adequate and the serum K (potassium) is NOT elevated (i.e. < 5.5 mEq/L). If the initial serum potassium is ≥ 5.5 mEq/L, follow serum potassium concentrations hourly until the level is ≤ 5.0 mEq/L.

* Do NOT add potassium to the IV fluids if any of the following conditions are present:
  a. oliguria or anuria
  b. acute renal failure
  c. cardiac arrest

* Once serum K ≤ 5.0 mEq/L and renal status acceptable (BUN/Creat. Ratio < 20), give 20–40 mEq/L of potassium intravenously. The lesser concentration should be used initially in the treatment regimen when the fluid rate is highest. Alternatively, in the face of hypokalemia, concentrations of IV potassium considerably in excess of the above range may be therapeutically necessary.
* Guidelines for potassium replacement.

<table>
<thead>
<tr>
<th>Serum Potassium (mEq/L)</th>
<th>Fluid Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3.0 without EKG changes</td>
<td>30 mEq/L KCl plus 30 mEq/L KPO₄</td>
</tr>
<tr>
<td>3.0 – 5.5</td>
<td>20 mEq/L KCl plus 20 mEq/L KPO₄</td>
</tr>
<tr>
<td>&gt; 5.5</td>
<td>Hold potassium</td>
</tr>
</tbody>
</table>

* Give potassium as a mixture of ½ potassium phosphate (K₂PO₄) and ½ potassium chloride (KCl). If patient is hypophosphatemic (i.e. serum phosphorous < 1.5 mg/dl) give all of the potassium replacement as K₂PO₄. Caution: if patient is hypocalcemic, consider giving the potassium replacement as ½ potassium citrate or acetate in place of the phosphate or all as KCl.

* Monitor the patient’s lead II EKG continuously for electrical evidence of hypo- or hyperkalemia.

<table>
<thead>
<tr>
<th>Serum K (mEq/L)</th>
<th>EKG Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2.5</td>
<td>Depressed ST segment</td>
</tr>
<tr>
<td></td>
<td>Diphasic T wave</td>
</tr>
<tr>
<td></td>
<td>Prominent U wave</td>
</tr>
<tr>
<td>&gt; 6.0</td>
<td>Peaked T wave</td>
</tr>
<tr>
<td>&gt; 7.5</td>
<td>Prolonged PR Interval</td>
</tr>
<tr>
<td></td>
<td>Wide QRS complex</td>
</tr>
<tr>
<td></td>
<td>Peaked T wave</td>
</tr>
<tr>
<td>&gt; 9.0</td>
<td>Absent P wave</td>
</tr>
<tr>
<td></td>
<td>Sinusoidal wave</td>
</tr>
<tr>
<td></td>
<td>Ventricular Fibrillation</td>
</tr>
<tr>
<td></td>
<td>Asystole</td>
</tr>
</tbody>
</table>

F. Phosphorous

Despite the initial serum phosphorous level, a patient in DKA is usually total body phosphorous depleted at presentation. Further, insulin therapy will drive phosphorous intracellularly, thereby decreasing its serum (extracellular fluid compartment) concentration.
Severe hypophosphatemia (< 1.0 mg/dl) can cause congestive heart failure, respiratory failure, hemolysis, decreased 2,3-DPG concentrations leading to tissue hypoxia from a leftward shift of the oxygen-hemoglobin dissociation curve, thrombocytopenia, rhabdomyolysis, muscle weakness, CNS depression, irritability and paresthesias. Moderate hypophosphatemia (< 1.5 mg/dl) can cause weakness, malaise, anorexia, nausea and vomiting.

Administer phosphorous as K$_2$PO$_4$. If serum phosphorous level is < 1.5 mg/dl, then give all of IV potassium replacement as K$_2$PO$_4$. Unless hyperphosphatemia or hypocalcemia develops, maintain fluid potassium replacement as K$_2$PO$_4$.

Adverse effects associated with phosphorous administration include hypocalcemia, metastatic calcifications and hypotension. During treatment for DKA, patients must be monitored for hypocalcemia as a complication of phosphorous replacement/administration. Do NOT give phosphorous if there is clinical evidence of hypocalcemia or if serum phosphorous is < 8.0 mEq/L.

G. Calcium

Hypocalcemia can result in muscle twitching, muscle spasms (including laryngospasm), seizures, Chvostek’s sign (spasm of the facial muscles elicited by tapping the facial nerve in the region overlying the parotid gland) and Trousseau’s sign (wrist flexion with fingers drawn together when blood pressure cuff is used to occlude brachial artery).

If patient is hypocalcemic at presentation or develops same as a complication of phosphorous treatment for DKA (Calcium ≤ 7.5), change IV KPO$_4$ to KCL. Give 100 mg of Calcium Gluconate per kilogram of body weight IV over 30-60 minutes. Monitor patient’s heart rate and rhythm during calcium administration for evidence of bradycardia or heart block.

H. Magnesium

The presence of hypomagnesemia can lead to tremors, tetany, seizures, apathy, delirium, coma and various cardiovascular effects including congestive heart failure, hypotension, ventricular dysrhythmias and EKG changes of a prolonged PR, QT and QRS intervals and t wave inversion.

If initial, or subsequent, magnesium concentration is ≤ 1.6 mg/dl (normal range: 1.8 - 2.9), supplement with MgSO$_4$ at 25-50 mg/kg/dose given IV every 4 to 6 hours. Magnesium supplementation may also be given by mouth as tolerated at 100-200 mg/kg/day divided q.i.d. (1 gram = 8 mEq.) Monitor patient closely for hypocalcemia, hypotension, loss of deep tendon reflexes, prolonged cardiac conduction time and respiratory paralysis.
I. Insulin Administration

Regular or Humalog human insulins are the ONLY insulin types that should be administered in the acute treatment of DKA. Except in situations where the peripheral circulation is compromised, insulin is almost as effective given IM or SQ as it is IV. Insulin is used to turn off ketone production through its inhibitory effects on lipolysis and proteolysis. Insulin will also stimulate glucose uptake and utilization into peripheral tissues. If the patient presenting with DKA is an established diabetic, note the usual home insulin dosages and whether they were given. If SQ insulin was administered at home a few hours prior to admission for DKA, it may not have been fully absorbed due to the associated dehydration. Knowledge and anticipation of this factual history may help avoid subsequent hypoglycemia from the delayed absorption of the home administered insulin as the patient’s vascular fluid status is restored.

1. Continuous Low Dose Intravenous Insulin Infusion:

Initiate insulin infusion therapy only when intensive medical/nursing supervision of the patient’s clinical status is available and the rapid determination of serial glucose levels is possible.

a. Rationale:

* maintains a steady state plasma insulin level thereby, avoiding marked variations in acid-base balance and serum glucose levels

* allows for easy, rapid regulation of the administered insulin dose

* requires less total insulin to correct the ketoacidosis

* may reduce the time necessary to clear serum ketones and correct ketoacidosis

* effectively inhibits ketosis and hepatic glucose production

* the short half-life of intravenous insulin (approximately 5 minutes) allows for better, more accurate “minute to minute” control of therapy as well as a more rapid treatment response time to changes in insulin dosage

b. Dose:

1. Administer initial IV bolus of 0.025-0.1 units per kilogram of body weight of fast-acting insulin (Regular or Humalog) to saturate the insulin receptors. The bolus dose is based on the level of initial
hyperglycemia and acidosis. This bolus may be omitted if the patient’s initial blood pH is > 7.15 OR initial serum glucose is ≤ 400 mg/dl.

2. Start continuous infusion of 0.1 units/kg/hour of fast-acting insulin (Regular or Humalog). The desired concentration of insulin is calculated and mixed in either ½ (0.45%) normal saline or 0.9% normal saline. The infusion rate per hour is varied to administer the needed insulin treatment regimen. The insulin infusion rate, however, should be maintained between 0.05 and 0.1 units per kilogram of body weight per hour unless there is evidence of intrinsic insulin resistance (i.e. Type II diabetes mellitus, obesity, therapeutic hypercortisolism or the presence of an underlying bacterial infection) OR the initial hyperglycemia fails to decrease by at least 50 mg/dl/hour.

The standard recommended insulin concentration/dilution for continuous intravenous infusion is:

<table>
<thead>
<tr>
<th>Insulin Concentration</th>
<th>Dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00 U/ml</td>
<td>Mix 100 units R/H in 100 mls. NS</td>
</tr>
</tbody>
</table>

For young children requiring lower insulin infusion dosages use:

<table>
<thead>
<tr>
<th>Insulin Concentration</th>
<th>Dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.10 U/ml</td>
<td>Mix 25 units R/H in 250 mls. NS</td>
</tr>
<tr>
<td>0.20 U/ml</td>
<td>Mix 50 units R/H in 250 mls. NS</td>
</tr>
<tr>
<td>0.50 U/ml</td>
<td>Mix 125 units R/H in 250 mls. NS</td>
</tr>
</tbody>
</table>

3. Maintain administered glucose:insulin ratio at 4-6:1 (grams of intravenous glucose per hour: units of intravenous insulin per hour). The hourly fall in serum glucose concentration should NOT exceed 100 mg/dl/hr. As the patient becomes adequately hydrated and less acidotic, insulin resistance decreases (i.e. insulin sensitivity) and its glycemic effect improves. If the blood glucose falls to 250 mg/dl or less, increase the glucose concentration, rather than decreasing the insulin infusion, to maintain the above ratio. Avoid decreasing the rate of the insulin infusion since this will likely delay the clearance of serum ketones and the correction of the ketoacidosis. Aim to maintain the serum glucose in the 200 - 250 mg/dl range until plasma ketones are cleared and the ketoacidosis resolves.

Note: If the serum glucose is < 200 mg/dl, increase the glucose concentration of the IV fluids. Temporarily hold the insulin infusion and monitor the blood sugar every 30 minutes until it rises above 200 mg/dl. Once the blood sugar is ≥ 200 mg/dl, resume the insulin infusion BUT at a higher hourly glucose to insulin ratio.
Note: Never give intravenous insulin by multiple intermittent injections to treat DKA.

Note: Insulin mixed in saline is stable for approximately 24 hours.

Note: Flush the initial 25 mls. of each mixture to coat the IV tubing and the Soluset/Buratrol.

Note: Continuous intravenous insulin can be piggy-backed into an existing IV BUT should always be given with an IVAC or a similar pump device to ensure its precise administration. When piggy-backed, the insulin tubing should be inserted as close to the venous access site as possible without an inline filter. Using only one extremity for both the necessary fluid replacement and the continuous insulin infusion allows for serial laboratory blood samples to be drawn from the contralateral extremity via a patient-friendly heparin “lock”.

Note: Do NOT administer bicarbonate or calcium in the same intravenous line as the insulin infusion.

4. When the blood glucose is $\leq 400$ mg/dl, add dextrose to the main intravenous, fluid replacement line.

5. If unable to maintain the serum glucose in the 200 - 250 mg/dl range using D$_{10}$ ½ (0.45 %) Normal Saline, then the insulin infusion can be decreased. The insulin infusion, however, should NOT be decreased below 0.05 units/kg/hour if at all possible as low rates of insulin infusion will result in a slower resolution of the ketoacidosis.

6. The insulin drip can generally be discontinued when the patient’s blood pH is $\geq 7.30$ AND the serum bicarbonate is $\geq 20$ mEq/L. The endpoint of therapy for DKA is the correction of the acidosis and NOT the achievement of euglycemia. Thereafter, proceed with insulin therapy using the traditional subcutaneous method.

Note: It is imperative that subcutaneous fast-acting insulin be administered immediately upon (Humalog), or 20-30 minutes prior to (Regular), discontinuation of the intravenous insulin infusion. Otherwise, because of the very short half-life of intravenous insulin, insulin deficiency will quickly develop and could lead to the re-appearance of ketoacidosis.
2. Intermittent Subcutaneous Insulin:

Subcutaneous insulin should be administered to a DKA patient ONLY if vascular volume is adequate since subcutaneous insulin absorption in a dehydrated patient is unpredictable. Do NOT give insulin SQ or IM if patient is in shock.

a. Fast acting (Regular or Humalog) U-100 insulin

<table>
<thead>
<tr>
<th>Severity of DKA</th>
<th>Insulin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate/Severe</td>
<td>1.0 units/kg SQ</td>
</tr>
<tr>
<td>Mild/Moderate</td>
<td>0.5-1.0 units/kg SQ</td>
</tr>
<tr>
<td>Mild</td>
<td>0.25 units/kg SQ</td>
</tr>
</tbody>
</table>

b. Initially can give ½ the calculated dose as an intravenous bolus if hyperglycemia is > 750 mg/dl.

c. An additional bolus of subcutaneous insulin may be given in 1-2 hours if the patient’s blood sugar fails to respond to the initial bolus.

Note: check patient’s vascular volume/hydration status prior to any additional bolus to ensure adequate subcutaneous absorption of insulin. If dehydration persists, give additional fluids (see section IV.A.2.a above) and consider administering insulin intravenously as a continuous infusion (see section IV.E.2 below).

d. Subsequent doses of fast acting insulin (U-100) are usually given q 3 to 4 hours after the initial bolus(es) at doses of 0.25-1.0 units per kilogram of body weight subcutaneously.

Note: subsequent doses of subcutaneous insulin will need to be adjusted on the basis of follow-up lab studies and the clinical response of the individual patient

e. Once oral intake is tolerated, subcutaneous injections of fast-acting insulin (Regular or Humalog) are given prior to each main meal and at bedtime at a dose of 0.1-0.2 units per kilogram of body weight. If the patient is stable, an intermediate (NPH) or long-acting insulin (Ultra-Lente) may be substituted for the bedtime dose of fast-acting insulin.
f. With continued improvement, combinations of rapid (Regular or Humalog) and intermediate/long acting insulins in multiple doses may be given as follows:

Total Daily Dose: 0.6-1.2 units per kilogram of body weight per day divided as follows:

<table>
<thead>
<tr>
<th>Time</th>
<th>Total Daily Dose</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-breakfast</td>
<td>2/3 - 3/4</td>
<td>NPH:Regular or Humalog (2:1 ratio)</td>
</tr>
<tr>
<td>Pre-dinner</td>
<td>1/6 - 1/8</td>
<td>Regular or Humalog</td>
</tr>
<tr>
<td>Pre-bedtime snack</td>
<td>1/6 - 1/8</td>
<td>NPH or Ultra-Lente</td>
</tr>
</tbody>
</table>

Note: If the patient is to receive only a b.i.d. insulin injection regimen at home, the bedtime intermediate or long-acting insulin may be combined with the pre-dinner fast-acting insulin and administered together as a single injection.

Note: Subcutaneous Regular insulin **must** be administered 20 to 30 minutes before the scheduled meal for maximal effectiveness. Alternatively, Humalog need only be given 5 to 10 minutes before the scheduled meal. The bedtime intermediate or long-acting insulin may be given immediately prior to the bedtime snack without affecting its efficacy. However, if the bedtime snack exceeds 35 grams of carbohydrates, a small dose of short-acting insulin (Regular or Humalog) may be necessary to avoid significant post-prandial hyperglycemia.

Note: Regular insulin may be combined with NPH but NOT with Ultra-Lente as the latter combination may significantly delay the Regular insulin’s absorption characteristics and result in post-prandial hyperglycemia and a delayed hypoglycemia. In contrast, the rate of subcutaneous absorption of Humalog has been shown to remain unaffected when combined with Ultra-Lente and may thus, be administered in combination without causing adverse effects on the patient’s diabetes control. As of this writing, January 1999, data is limited as to the effects of combining Humalog and NPH on the former’s absorption characteristics. The consensus, however, is that the combination of Humalog and NPH may adversely delay the glucose lowering effects of Humalog and should, therefore, be given in the same syringe with NPH only with caution and close monitoring of its glycemic effect.
3. Intramuscular Insulin

   a. Dosages are generally similar to those used with an intermittent subcutaneous insulin regimen.

   b. Because of the shorter half-life of intramuscularly administered insulin, it is given on an hourly schedule.
V. FOLLOW-UP:

A. Sugar-free oral fluids

* can usually be given 6 to 12 hours after the start of therapy depending on the patient’s level of consciousness, lack of nausea and success of treatment (i.e. correction of acidosis and dehydration).

B. Diet

Initially, patient should be placed n.p.o. especially if nausea or vomiting is present or if mental status/sensorium is depressed.

* as the patient continues to improve, advance diet from clear liquids to a Constant Carbohydrate Diet regimen with three main meals plus snacks.

* snacks should be included as follows:

<table>
<thead>
<tr>
<th>Age</th>
<th>Snacks per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>preschool</td>
<td>3 (a.m., p.m. and h.s.)</td>
</tr>
<tr>
<td>school</td>
<td>2 (p.m. and h.s.)</td>
</tr>
</tbody>
</table>

Note: Although not offered right away, the patient’s special diet may need to be offered 12 or more hours in advance to allow its preparation by the hospital’s kitchen staff.

C. Calories

* caloric requirement may be estimated as follows:

\[
1000 \text{ kcal/day} + [(100 \times \text{Age in years})] = \text{Total daily calories}
\]

* distribution of calories should be as follows:

<table>
<thead>
<tr>
<th></th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO</td>
<td>55</td>
</tr>
<tr>
<td>Protein</td>
<td>15</td>
</tr>
<tr>
<td>Fat</td>
<td>30</td>
</tr>
</tbody>
</table>

D. Insulin

1. If patient is an established, previously diagnosed diabetic child or adolescent, simply resume his/her outpatient insulin regimen and monitor its glycemic effect via frequent capillary blood sugars prior to discharge. Supplemental Regular or Humalog insulin may be given for significant pre-prandial hyperglycemia.
2. If patient is newly diagnosed, start him/her on a b.i.d. or t.i.d. subcutaneous insulin injection regimen as follows:

* Total daily dose 0.6 – 1.2 units per kilogram of body weight per day given as

  a.m. pre-breakfast  
  2/3 – 3/4 of total, calculated daily dose with  
  1/4 – 1/3 as fast-acting Humalog and  
  2/3 – 3/4 as intermediate acting NPH

  p.m. pre-dinner  
  1/8 – 1/6 of total, calculated daily dose as  
  fast-acting Humalog

  h.s. pre-bedtime snack  
  1/8 – 1/6 of total, calculated daily dose as  
  intermediate acting NPH or long-acting Ultra-Lente

Note: If the patient is to receive only a b.i.d. insulin injection regimen after discharge, the bedtime intermediate NPH may be combined with the pre-dinner fast-acting Humalog and administered together as a single pre-dinner injection.

Note: The above dosage recommendations are only rough guidelines and should individualized for each patient’s unique requirements.

Note: Most newly diagnosed patients with diabetes are relatively insulin resistant, even after the diabetic ketoacidosis has resolved. As a result, the insulin dose they are discharged on is often higher than the daily insulin dose they require after a few weeks.
VI. COMPLICATIONS OF DKA THERAPY

A. Cerebral Edema

Most patients with diabetic ketoacidosis recover without complications when properly treated. Poor prognostic signs at the time of admission include hypotension, azotemia, seizures, coma and the presence of an associated illness. In children, cerebral edema during DKA and its therapy is STILL a too common cause of death.

A decrease in the level of consciousness may occur normally during the course of appropriate therapy for DKA but it is always a potential cause for concern. Computed tomography and magnetic resonance studies of patients with DKA have demonstrated the existence of mild cerebral edema in almost all patients often before intravenous fluid replacement has been started. If clinically significant cerebral edema occurs, it is often after a period of clinical improvement and often in the first 6 to 12 hours after institution of therapy.

The cause of the deranged CNS function is multifactorial and has been related to (1) the degree of cerebral edema, (2) the degree or severity of the acidosis, (3) the degree of dehydration and (4) to various other factors including the degree of hypoxemia. Although the etiology of this devastating complication of DKA remains unknown, theories include:

a. osmotic disequilibrium between the brain and plasma as the blood glucose is rapidly lowered (i.e. glucose lowered at > 100 mg/dl/hr). Rapid falls in plasma glucose or osmolality during fluid replacement therapy have both been associated with the occurrence of cerebral edema. In one study, the development of coma was correlated with serum osmolalities $\geq 320$ but NOT with the degree of acidosis.

b. decreased plasma osmotic pressure due to infusion of large amounts of free water (i.e. fluid intake $> 4000$ ml/m²/day). The failure of the corrected sodium to rise during rehydration indicates the excessive administration of free water.

c. insulin-induced ion flux across the blood-brain barrier. Administration of bolus bicarbonate therapy has been related to the occurrence of a worsening mental status/sensorium.
The diagnoses of cerebral edema is suspected clinically when any of the following symptoms or signs are present:

**EARLY SIGNS:**
- Coma scale ≤ 10
- Headache, recurrent and severe
- Decreasing mental status (disorientation, decreased cooperation, decreased level of consciousness)
- Increased blood pressure with decreased pulse rate and respiratory insufficiency (Cushing’s Triad)

**LATE PHENOMENA:**
- Papilledema
- Unilateral pupil dilation and other focal neurologic signs
- Vomiting, recurrent and persistent

Treatment:

To be of benefit, treatment must be initiated STAT as soon as the patient’s clinical course suggests the presence of increased intracranial pressure and cerebral edema (i.e. altered mental state and coma scale ≤ 10).

Treatment consists of:

1. Bolus infusion of 1cc of D₅₀W per kilogram of body weight (maximum 50cc/dose).
2. Bolus infusion of 20 % mannitol at 0.5 - 1.0 gram per kilogram of body weight given over 30 to 60 seconds. Bolus may be repeated every 2 to 4 hours as clinically indicated.
3. Decrease total IV fluid administration to 100 - 150 % of maintenance.
4. Elevate head of bed to 30 degrees. Perform frequent neuro checks (i.e. every 30 minutes).
5. Intravenous Dexamethasone at 0.5 – 1.5 mg per kilogram of body weight IV push over 30 to 60 seconds.
6. Control airway and intubation with hyperventilation to an arterial pCO₂ of 28 to 30 mm. Lower values of pCO₂ should be avoided since such values can result in cerebral ischemia.
7. Re-evaluate insulin requirements.
B. Other complications of diabetic ketoacidosis include:

a. vascular thrombosis from volume depletion, hyperosmolality, increased blood viscosity and changes in clotting factors favoring thrombosis

b. adult respiratory distress syndrome (ARDS). Although its cause is unknown ARDS in DKA is most likely related to the metabolic acidosis

Diabetes is a complex disorder that requires a multidisciplinary team to interact with the patient in order to achieve maximum benefit. It is crucial that the child and family receive appropriate education from a Pediatric Diabetes Team after the initial metabolic problem has resolved and the patient’s status is stable.
NUTS and BOLTS of DKA MANAGEMENT

I. Initial Evaluation

History:
Presence of concurrent illness; missed/omitted insulin dosages

Physical:
ABCs; mental status/coma scale
vital signs; weight
hydration status; fruity breath/Kussmaul’s respirations
concurrent infection

Laboratory:
glucose, at bedside and by laboratory
pH and pCO₂
urine/serum ketones (β-hydroxybutyrate)
calculated serum osmolality and anion gap
Na/K/Cl/CO₂
BUN/Creat/Ca/Phos/Mg
CBC with differential
new IDDM (islet cell antibodies, anti-GAD antibodies, insulin, C-peptide, Hemoglobin A₁C)

II. Fluids

a. Estimate fluid deficit (5,10,15%) and 48 hours maintenance requirements.
b. Give initial bolus: isotonic (0.9%) NaCl 10-20 ml/kg. May repeat as indicated by patient’s clinical status. Continue replacement with isotonic (0.9%) NaCl until IV dextrose added, then change to ½ (0.45%) normal saline unless patient remains hyponatremic.
c. Rehydrate over 48 hours. Give ½ calculated fluid deficit over first 24 hours. Give the remainder over next 24 hours.
d. Maintain total fluids at < 4000 ml/day or < 250 % of maintenance unless clinical findings dictates otherwise.
e. Continuously assess ongoing fluid losses and replace as needed.
f. Potassium supplementation added after renal function status established and if initial serum K ≤ 5.0 mEq/L. Give 20-40 mEq/L as ½ KCl and ½ KPO₄. Increase concentration to 60 mEq/L if patient hypokalemic.
g. Start IV dextrose when blood glucose ≤ 400 mg/dl OR if blood glucose falling at greater than 100 mg/dl/hour. Give IV dextrose to maintain serum glucose between 200-250 mg/dl and the glucose (grams per hour) to insulin (units per hour) ratio at 4-6 to 1 by raising amount of dextrose administered.
h. Caution with chloride overloading which may promote a non-anion gap metabolic acidosis.
i. Use of bicarbonate reserved for when initial pH < 7.10 and repeat pH fails to improve after initial fluid bolus(es) resuscitation (i.e. repeat pH < 7.10 one hour after initial results). Give bicarbonate at 0.5 mEq/kg over 1-2 hours AND NEVER as a bolus unless patient in full cardiorespiratory arrest.

III. Insulin

a. Standard therapy:
   1. give initial loading dose of 0.25-1.0 units/kg SQ or IM. May repeat in 1-2 hours if blood glucose remains > 500 mg/dl.
   2. maintenance: 0.25-1.0 units/kg SQ every 3-4 hours until ketones clear.
   3. do NOT give insulin SQ if vascular perfusion is compromised.

b. Low-dose insulin infusion therapy:
   1. initial bolus: 0.025-0.1 units/kg IVP unless initial pH > 7.15 or blood glucose level < 400 mg/dl.
   2. maintenance: mix fast-acting (Regular or Humalog) insulin in isotonic (0.9%) normal saline at desired concentration. Change solution every 24 hours. Piggyback insulin infusion unto IV fluids given for hydration. Do NOT, however, administer insulin in the same IV tubing as calcium. Do NOT mix the bicarbonate directly into the insulin infusion IV bag. Give continuous insulin infusion at 0.1 units/kg/hour.
      If serum glucose decreases to ≤ 200 mg/dl, raise IV dextrose infusion rate or concentration AND hold insulin infusion until hypoglycemia resolves. Once serum glucose rises > 200 mg/dl, restart insulin infusion but at a greater hourly glucose to insulin ratio.
      It is important that when insulin infusion is terminated that patient receive SQ fast-acting insulin 20-30 minutes prior to (Regular), or immediately (Humalog) upon discontinuation of the insulin infusion.

IV. Monitoring

a. Clinical:
   1. perform vital signs including blood pressure and Neuro checks every 1-4 hours until ketoacidosis resolves and patient is stable.
   2. maintain strict Intake and Output while patient on IV fluids.
   3. check weight.

b. Laboratory:
   1. hourly bedside capillary glucoses with intermittent corroborating serum glucose sampling by hospital laboratory.
   2. pH and pCO₂ every 2 hours until pH > 7.25.
   3. lytes/CO₂/calculated osmolality and anion gap every 2-4 hours.
   4. urine ketones q8-12 hours. Serum β-hydroxybutyrate every 8-12 hours if rapidly available.
   5. BUN/Creat/Ca/Phos/Mg q8-12 hours.
V. Complications

a. Cerebral edema:
   1. to be beneficial, treatment must be initiated AS SOON AS the patient’s clinical course suggests the presence of an increased intracranial pressure and cerebral edema (i.e. altered mental status, coma scale < 12, Cushing’s triad [increased blood pressure, decreased heart rate and respiratory insufficiency], papilledema or focal neurological signs such as unilateral pupil dilation).
   2. treatment consists of:
      bolus infusion of 1cc/kg D50W (maximum 50cc/dose)
      bolus infusion of 20% mannitol at 0.5-1.0 gr/kg over 30 seconds
      lowering IV fluid rate to 100-150% of maintenance
      elevating head of bed to 30 degrees
      controlling airway and intubation with hyperventilation

b. Thrombosis from volume depletion, hyperosmolality and increased blood viscosity.

c. Adult respiratory distress syndrome (ARDS).

VI. Evaluate and treat for an underlying inciting condition that may have precipitated the DKA (i.e. infection; psychosocial instability; non-compliance)

VII. Please see DKA protocol for complete details.
I. Definition
* blood pH < 7.30
* serum bicarbonate < 15 mEq/L

II. Goals of Treatment
* correct volume depletion
* correct acidosis/abolish ketosis
* replace electrolyte losses
* avoid complications

III. Initial Evaluation

History
* presence of concurrent illness
* missed/omitted insulin doses

Physical
* ABCs
* mental status/coma scale
* vital signs
* weight
* fruity breath/Kussmaul’s
* hydration status
* concurrent infection

Laboratory
* glucose, bedside and laboratory
* pH and pCO₂
* urine/serum ketones (β-OHbutyrate)
* calculated serum Osmo/anion gap
* Na/K/Cl/CO₂
* BUN, Creat, Ca, PO₄, Mg
* CBC with diff.
* new IDDM (ICA, anti-GAD, Hgb A₁C, insulin, C-peptide)

IV. Fluids
* estimate deficit and maintenance requirements
* initial bolus: 10-20 ml/kg NS may repeat as indicated
* rehydrate over 48 hrs: give ½ over first 24 hrs, remainder over next 24 hrs.
* assess ongoing losses
* maintain total fluids < 4L/day unless higher volumes indicated
* give initial fluids as NS; change to ½ NS when adding dextrose to IV
* add IV dextrose when blood glucose < 400 mg/dl OR dropping by ≥ 100 mg/dl/hr
* add K at 20-40 mEq/L to IV (½ KCl and ½ KPO₄) once know serum K conc. and renal function status

V. Insulin Infusion
* initial bolus 0.025-0.1 u/kg unless pH > 7.15 or blood glucose < 400 mg/dl
* insulin drip 0.05-0.1 u/kg/hr
* maintain glucose:insulin ratio at 4 to 6 grams/hr per unit/hr

VI. Monitor
* bedside glucose hourly
* pH/pCO₂ q2hrs till pH > 7.25
* lytes/CO₂ q2-4hrs
* calc. osmo/anion gap q2-4hrs
* urine ketones q8-12hrs
* serum β-OHbutyrate (if avail)
* BUN/Creat q8-12hrs
* Ca/Phos/Mg q8-12 hrs
* I/Os while on IV fluids
* Neuro checks q1-4hrs till DKA resolves
