Paediatric and adolescent diabetic ketoacidosis

Abstract
Diabetic ketoacidosis (DKA) is one of the two acute emergency situations in those who have diabetes mellitus. DKA should be identifiable and is often preventable. Any associated complications of DKA should also be preventable with proper education and treatment. Awareness of presenting signs and symptoms, on the part of the general public, primary care providers and emergency department personnel, should help minimise the severity of DKA through earlier diagnosis and focusing on appropriate physiologic treatment as well as close, ongoing monitoring to minimise potential lethal DKA complications such as cerebral oedema. Missed diagnosis, late diagnosis, inappropriate treatment, delayed treatment and lack of appropriate monitoring are usually associated with more morbidity and mortality as well as increased hospital costs. Insulin treatment is only one part of DKA management. Fluid and electrolyte monitoring and treatment are often a critical aspect of such management. All aspects of DKA recognition, treatment and prevention must be emphasised to decrease DKA morbidity and mortality around the world. Copyright © 2014 John Wiley & Sons.

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Key words
diabetic ketoacidosis; cerebral oedema; type 1 diabetes mellitus

Introduction
Diabetic ketoacidosis (DKA) is a severe metabolic derangement produced as a result of insulin deficiency and concomitant fluid and electrolyte imbalance. The potential life-threatening consequences of DKA often reflect severe and/or unrecognised fluid, electrolyte and acid-base disturbances not treated properly. Delay in the diagnosis of DKA occurs under certain circumstances, such as in those without a prior history of diabetes, in parts of the world where diabetes is so rare that the possibility is not even entertained or in the very young all around the world where other diagnostic possibilities overshadow the rarity of DKA. In those already diagnosed with diabetes, chronic poor self-care management (including chronic insulin omission due to psychosocial problems such as diabulimia or other eating disorders, and/or inability financially to afford sufficient insulin) increases the risks of DKA. When a secondary illness (e.g., viral, bacterial or other infection) is superimposed on longstanding poor glycaemic control, DKA-associated morbidity and mortality are also increased.1–4

Where access to medical attention is less than ideal, DKA may be completely missed or the patient with DKA may already present severely dehydrated or comatose and die before any confirmatory diagnosis is established. In parts of Africa where malaria, bacterial or parasitic infections or other infectious disease are common, consideration of DKA can be virtually non-existent.5 Because the general public is not very aware of symptoms and signs of diabetes (polyuria, polydipsia, unexplained weight loss, unexplained new-onset enuresis), medical attention may also be delayed. In the very youngest infants and toddlers, onset can be very rapid with fast progression to dehydration and metabolic acidosis if saturated diapers are not recognised; many physicians do not think about the possibility of DKA in such young children and therefore mistake early symptoms for common viral (respiratory or gastrointestinal) illnesses.6,7 In those with known diagnosis, chronic insulin omission1,4 – made acutely worse by miscalculation of when to take insulin or by lack of self-monitoring – hinders early recognition of such decompensation. Misapplication of sick-day guidelines (or never learning them) can also lead to excessive episodes of DKA,9,10 just as lack of DKA treatment protocols, lack of specialty consultation and lack of following established protocols all contribute to preventable DKA morbidity and mortality.11

The goal of therapy of DKA is not returning glucose levels to absolutely normal levels but, rather, the reversal of the underlying ketoacidosis itself.15 ISPAD guidelines for sick-day management10 as well as DKA17 also have been published as supplements in the
ISPAD affiliated journal, *Pediatric Diabetes*, and are freely available from www.ISPAD.org with periodic updates every four to five years based on numerous written reports.\(^{38-46}\)

All stages of ketoacidosis from the earliest increases in blood glucose (BG) through to increasing generation of ketone bodies to ketoacidemia, acidaemia and eventually ketoacidosis may lead to coma and death. Despite appropriate use of insulin and fluids and continuous clinical observation, the mortality rate of DKA has not improved and has remained the same as that reported in the 1970s.\(^{27,28}\)

There is no uniform definition of what constitutes DKA and many authors use idiosyncratic definitions. Diabetic ketoacidosis might be defined with reference to carbon dioxide levels (or serum bicarbonate) \(\leq 10\text{m eq/L}.\)^\(^4\) When comparing what is written, especially concerning outcome and associated problems, it is very important to define pH, acid-base status as well as level of glycaemia. The exact level of hyperglycaemia or ketoacidemia in DKA can be extremely variable. The term ‘diabetic coma’ in the medical literature also can be misleading since most patients with severe DKA are not necessarily ‘unconscious’.

Proper early recognition and insulin treatment\(^9\) by the patient and/or their family before hospitalisation remain a therapeutic and educational goal that also has remained elusive.\(^{27,30,31}\) Educational posters in many parts of the world, both rich (e.g. Canada and Italy) and poor (Tanzania and South Africa), which rely on pictographs presenting symptoms of diabetes have raised awareness and reduced DKA morbidity and mortality.\(^{5,32,33}\) Urine glucose monitoring serves the same purpose in situations where BG testing is unavailable. Home blood capillary \(\beta\)-hydroxybutyric acid testing with readily available and relatively inexpensive blood testing strips may provide information to act earlier or more aggressively to head off metabolic decompensation. Urinary acetone/acetocetate test strips provide similar information.\(^{34-38}\)

**Acute hospital or emergency department DKA management**

Table 1 outlines a DKA low dose infusion protocol for children and adolescents.

<table>
<thead>
<tr>
<th>Table 1. Diabetic ketoacidosis low dose insulin infusion protocol for children and adolescents (adapted from Brink SJ. New England Diabetes and Endocrinology Center, 2004(^4))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluids and electrolytes</strong></td>
</tr>
<tr>
<td><strong>Initial sodium and water.</strong> The severity of mental status changes is likely related to serum osmolarity.(^{39}) The weight of the patient can be used for initial estimation of replacement fluids on the assumption that dehydration is mainly reflected by acute body weight loss. Surface area estimations may be used to estimate fluid needs at all ages and are particularly useful in infants and children, but can also be used in adolescents and adults for estimating maintenance needs. The severity of the signs and symptoms of dehydration reflects extracellular fluid loss. With 20% acute volume depletion the patient is, by definition, in profound shock and often moribund. Because extracellular fluid loss represents the loss of sodium and water, immediate restitution of blood volume can be provided using an estimated 10–20cc/kg of body weight.</td>
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</tr>
<tr>
<td><strong>Practice point</strong></td>
</tr>
<tr>
<td>• <strong>ABC.</strong> Maintain airway, breathing and circulation. Consider low-flow nasal oxygen.</td>
</tr>
<tr>
<td>• <strong>Confirm diagnosis</strong> of diabetic ketoacidosis at bedside and consider infections, surgical emergencies and other possible precipitants.</td>
</tr>
<tr>
<td>• Start intravenous (IV) infusion with <em>normal saline</em> 10–20cc/kg to run over 1–2 hours.</td>
</tr>
<tr>
<td>• <strong>Lead II ECG</strong> for potassium status (full ECG in adults to rule out myocardial infarction).</td>
</tr>
</tbody>
</table>
| • Start flow sheet: weight, height, surface area calculations, pulse, BP, respiratory rate and effort, neurologic status including funduscopy, baseline glucose, urine, electrolytes, calcium, phosphate, acid-base data and renal functioning.
| • Determine estimated maintenance and deficit for electrolyte and fluid orders and assume correction over 36–48 hours rather than 24 hours in an effort to minimise cerebral oedema complications. |
| • Attach piggyback短acting insulin infusion system to existing IV line: |
| – Prepare 100 units regular or analogue insulin (1cc) in 100cc of normal saline. |
| – Preflush IV tubing to allow adherence of insulin to plastic; no need for albumin. |
| – Set up piggyback system into existing IV line using available pump or paediatric set. |
| – Start 0.1 unit/kg body weight/hour IV by continuous infusion. |
| – Expect initial drop from rehydration and then approximately 10% of blood glucose hourly (50–70mg [or approximately 3–4mmol/L/hr]). |
| – Monitor blood glucose at 1 hour and then every 2–4 hours to ensure expected response. |
| – Monitor urine for ketone bodies at least every 3–4 hours or, alternatively and if available, monitor blood \(\beta\)-hydroxybutyric acid sequentially every 2–4 hours. |
| – Double rate of infusion or switch to alternative insulin delivery protocol if no response. |
| – Calculate estimated time when blood glucose will reach 250–300mg/dl (or approximately 14–17mmol/L) to avoid hypoglycaemia. |
| – Stop insulin infusion when blood glucose reaches 250mg/dl (or approximately 14mmol/L) and change IV solution to contain 5% dextrose with electrolytes. |
| – After initial 1–2 hours of normal saline infusion, change IV solution to 40mg/L of potassium using 20mg/L KCl plus 20mg/L NaHCO\(_3\) to avoid iatrogenic hypokalaemia in either 0.5 or 0.9% normal saline (see text). |
| – Check electrolytes at 2–4 hours and again as necessary according to clinical monitoring requirements, patient status etc to adjust type of fluids and rate of administration. Evaluate abdominal pain appropriately. If serum electrolyte measurements are not available, consider ECG for evaluation of T-waves as surrogate measure of potassium status. |
| – Must give subcutaneous insulin or intramuscular insulin 15 minutes before IV insulin is discontinued or if line no longer operational because of short half-life of IV insulin to avoid recurrent ketoacidosis. Adjust dosage according to newness of insulin-dependent diabetes mellitus, degree of ketosis and/or acidosis, age of patient, known sensitivity or other factors which will affect amount of insulin needed (pregnancy, renal failure, infection etc). |
| – Identify and treat any underlying problem (i.e. continue antibiotics as needed for urinary infection, streptococcal disease etc). |
| – Keep flow sheet up to date and reassess frequently. |
| – Pay attention to vital signs, abdominal exam, neurologic status (including examination of the optic disk) and electrolyte changes; detect and treat cerebral oedema. Consider cerebral CT or MRI studies to rule out cerebral oedema, cerebrovascular accidents and cerebral venous thrombosis if abnormal neurologic findings occur. |
| – Educate patient and family to prevent recurrence: identify contributing psychosocial problems. |
with normal (0.9%) saline given over the first 1–2 hours of treatment (10–20% dehydration). This effectively removes the patient from the immediate consequences of potential or overt shock and does not cause any delay in searching for special/expensive intravenous (IV) solutions (blood, Ringer’s lactate, albumin etc). Because most young patients will not have pre-existing or serious cardiac or renal problems, there is not much danger in providing such initial hydration. Maintenance water, sodium and potassium then can be estimated according to standard paediatric guidelines based on surface area estimations: water 2000cc/m²/24 hours (1500–2000 range); sodium 40meq/m²/24 hours (30–60 range); and potassium 40meq/m²/24 hours (30–50 range). Total body deficits can be enormous and not always readily reflected via initial laboratory measurements. The initial serum sodium may be high, normal or low, but this is not an accurate measure of the absolute sodium requirement especially if there has been technical artifact because of concomitant hyperlipidaemia. Most centres suggest the use of normal saline (0.9%) IV for the first 1–4 hours with a switch to half normal (0.45%) saline several hours into therapy. More recently, because of the chance that cerebral oedema is more common than appreciated,40 recommendations to continue normal saline for a longer time period have been proposed to allow osmotic re-equilibration in a more leisurely timeframe.41–46 If the total deficit of sodium is sufficiently excessive and if hypovolaemia is great enough, glomerular filtration may decrease and the patient may present with oliguria or progress to acute tubular necrosis.

Potassium. Because of the acidic state, potassium is usually driven out of the intracellular space while a state of kaliuresis exists as the kidney attempts to save sodium (Bunge effect). Initially, serum potassium levels can be either normal, elevated or low. With treatment as dehydration is corrected, lactic acid production decreases and some potassium begins to shift back intracellularly, fostering peripheral hypokalaemia. Life-threatening hypokalaemia (as potassium returns back into the cell) as well as worsening tissue hypoxia affinity for oxygen can be added to the list of possible bicarbonate treatment complications (see Table 2).

Table 2. Complications associated with bicarbonate administration in diabetic ketoacidosis

<table>
<thead>
<tr>
<th>Complication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life-threatening hypokalaemia</td>
<td>As potassium returns into cell, tissue hypoxia affinity for oxygen can be added.</td>
</tr>
<tr>
<td>Serum potassium levels increase</td>
<td>Within 4–6 hours after insulin administration begins.</td>
</tr>
<tr>
<td>Cerebral oedema, coma and death</td>
<td>Risk is higher with large doses or rapid administration.</td>
</tr>
</tbody>
</table>

With insulin administration, ketoacid production decreases, also fostering entry of potassium intracellularly. Serum potassium should be expected to decrease soon after appropriate DKA treatment begins so an early finding of hypokalaemia can be worrisome if it presages further serious hypokalaemia. Sequential bedside ECG rhythm strips for T or U wave changes or cardiac monitoring allow identification of potential dangerous hypokalaemia necessitating a change in potassium replacement (increasing potassium replacement). Usually, potassium is added in the second to fourth hour of treatment. Potassium can be replaced at a rate of 40meq/L of solution without danger of a rapid rise in blood levels or irritation at the IV site. Half could be given as potassium chloride (20meq/L KCl), and the other half as potassium phosphate (20meq/L K2HPO4) for the first 6–12 hours of replacement therapy, although replacement only with KCl produces as good clinical outcomes in published literature as when half phosphate and half chloride salts are used. After several hours, only potassium chloride should be used so that iatrogenic hypocalcaemia does not occur.

Bicarbonate. Since acetocetate and beta-hydroxybutyrate are metabolisable anions, restoration of serum bicarbonate concentration usually will follow insulin administration in the absence of treatment with alkali containing solutions. Acidosis results from a combination of: (1) release of fatty acids secondary to insulin deficiency; (2) generation of ‘ketone bodies’; (3) starvation from poor food intake; and, in some instances, (4) excessive production of lactic acid because of plasma volume depletion, poor tissue perfusion and an increase in anaerobic glycolysis in muscles. Concerns for the consequences of severe metabolic acidosis have been balanced by fears of cerebral oedema and respiratory arrest when bicarbonate is replaced ‘too quickly’.46,47 Life-threatening hypokalaemia (as potassium returns back into the cell) as well as worsening tissue hypoxia affinity for oxygen can be added to the list of possible bicarbonate treatment complications (see Table 2). Treatment with sodium bicarbonate should be restricted to patients with a severe metabolic acidosis as indicated by an arterial pH of 7.0–7.1 or less, or a bicarbonate value of <5meq/L. When sodium bicarbonate is used, it should be given by slow IV infusion over several hours.48–50,52 Frequent serial pH and/or bicarbonate determinations should be obtained so that the administration of bicarbonate can be discontinued when the pH reaches 7.2–7.25.

Phosphate and oxygen. Patients with DKA sustain intracellular phosphate depletion. Serum phosphate often follows a pattern similar to that of potassium. Although initial serum phosphate values may be normal or elevated, within 4–6 hours after insulin treatment has begun, these values may often fall dramatically as glycogen deposition resumes and phosphate moves intracellularly. The consequences of hypophosphataemia may be reflected in red blood cell levels of 2,3-diphosphoglycerate (2,3-DPG), an intermediary metabolite of glycolysis associated with tissue and cerebral hypoxia in DKA. Hence the recommendation that most patients being treated for DKA should receive oxygen at least for the first few hours of treatment. In any patient with known or suspected cardiac, renal and/or cerebrovascular compromise, there is more potential benefit in ensuring adequate oxygen supply and minimal risk using nasal oxygen delivery under such circumstances.

This author suggests replenishment of phosphate losses by providing 50% of the needed potassium replacement and maintenance as phosphate salts and 50% as chloride salts (see potassium section above). This is provided for the first 6–12 hours of IV fluid therapy so that changes in calcium phosphate ratios are not excessive.
Insulin: bolus, intramuscular, continuous IV protocols

The best route of administration and the dose of insulin necessary for treatment of DKA are unknown. Successful results have been published with differing insulin regimens for several decades, although most experts currently recommend continuous low dose infusion insulin. All patients in ketoacidosis have an immediate need for insulin and, no matter which protocol is followed, fluid and electrolyte replacement as well as recognition of underlying precipitating events must remain high on the list of priorities to decrease morbidity and mortality. Table 3.

Table 3. Diabetic acidosis flow sheet

<table>
<thead>
<tr>
<th>Examination</th>
<th>Blood work</th>
<th>Ketones</th>
<th>Fluids</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>BP</td>
<td>Resp</td>
<td>CNS. 1 = alert; 2 = lethargic (easily aroused); 3 = stupor (aroused with difficulty); 4 = comatose/ unresponsive</td>
<td>Pupils</td>
</tr>
</tbody>
</table>

Insulin: bolus, intramuscular, continuous IV protocols

The giving of ‘enough’ insulin should be the aim. This should be guided by initial and subsequent BG levels as well as clinical follow up, duration of symptomatology, severity of dehydration etc. Blood acetocetate and acetone levels should be expected to rise initially despite a much greater fall in β-hydroxybutyric acid as a result of acid-base changes and insulin treatment involved with fat metabolic effects. Strips for rapid blood β-hydroxybutyric acid level determination may help adjust treatment needs more physiologically compared with urine ketone determinations.46

Too vigorous insulin administration may lead to too rapid decreases in BG and therefore excessive osmotic changes; the risks of cerebral oedema might increase if this crucial metabolic fact is ignored. The newer human insulins work faster than the animal-based insulin and the newest three analogues even a bit faster than the synthetic regular insulins when administered subcutaneously (SC), but there is little difference clinically among all these fast-acting insulin preparations when given IV.

Many factors determine the amounts of insulin required, as summarised in Table 4. The largest doses are generally needed in older, more overweight patients who have had diabetes for some time, particularly when insulin has not been administered regularly (i.e. chronically omitted) or when insulin has incorrectly not been given during the initial hours of an illness. Newly-diagnosed patients who are very acidic may require larger amounts of insulin, whereas others are exquisitely sensitive. The new ‘epidemic’ of overweight adolescents presenting in DKA, but who soon look more like patients with type 2 diabetes/Syndrome X/non-insulin dependent diabetes mellitus,52 has presented peculiar challenges to health care providers because of the often enormous amounts of insulin required in the first few days of DKA and subsequent treatment – until insulin resistance wanes; dramatic reductions of insulin are then needed with resolution of initial ‘glucose toxicity’.53 Smaller children, infants and toddlers are often relatively more sensitive to insulin than older children and teenagers.

Table 4. When to modify insulin dose in diabetic ketoacidosis treatment45

<table>
<thead>
<tr>
<th>Time to modify insulin dose when:</th>
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</tr>
</thead>
<tbody>
<tr>
<td>• Increase dose when:</td>
<td>• Decrease dose when:</td>
</tr>
<tr>
<td>– Very high usual insulin dose</td>
<td>– Blood glucose below 400mg/dl</td>
</tr>
<tr>
<td>– Longer duration of diabetes</td>
<td>(approximately 22mmol/L)</td>
</tr>
<tr>
<td>– Severe infection</td>
<td>– Very thin person</td>
</tr>
<tr>
<td>– Extreme obesity</td>
<td>– Young infant or child</td>
</tr>
<tr>
<td>– Insulin resistance</td>
<td>– History of skipping insulin</td>
</tr>
<tr>
<td>– Severe acidosis</td>
<td>– History of insulin sensitivity (i.e. very low insulin dose)</td>
</tr>
<tr>
<td>– Decrease dose when:</td>
<td>– Renal insufficiency</td>
</tr>
<tr>
<td>– Newly-diagnosed patient</td>
<td>– Hypokalaemia</td>
</tr>
<tr>
<td>– Not unconscious</td>
<td>– Extreme hyperosmolality</td>
</tr>
</tbody>
</table>

IV low dose continuous infusion

IV low dose regular insulin infusion has become the standard method of treating DKA as long as IV access can occur.14–21 Although the original reports from Germany were in 194654 and then again in 1960,55 it was not until 1972 when interest was stirred and enthusiasm generated for low dose insulin infusions for ketoacidosis based on studies56 where such treatment was ‘rediscovered’.57 The slow and predictable decrease in BG has been viewed as a marked improvement compared to larger bolus insulin treatments previously used. Generally, BG falls by approximately 10% hourly once the initial ‘dehydrated’ BG value is corrected (with the first few hours of hydration). Correction of acidemia and restoration of electrolyte status and lipid profiles presumably occur at a slightly slower rate compared to earlier IV insulin protocols because of the smaller amounts of insulin being given; in some studies, no significant differences among the three types of insulin dosing protocols could be found.31,58,59 Early fears of insulin resistance have not been confirmed nor has there been any noticeable increase in mortality.60–65

One protocol for use of low dose continuous insulin infusion is
presented in Table 1. If insulin actually is being delivered and the blood sugars remain elevated, the dose should either be doubled or an alternative protocol utilised. As in all other treatment regimens, uncorrected severe dehydration and resulting/persistent hypovolaemic shock remain a potential cause for non-response, especially from underestimated ongoing losses. The presence of documented infection seems to slow down return of all parameters of metabolic control but is not significantly different clinically in low dose vs high dose protocol comparisons.

When BG falls to ~250 mg/dl (~14 mmol/L), 5% dextrose is added to the IV fluids and SC insulin is started. The benefits of continuous IV insulin treatment for DKA are the same as those for intramuscular (IM) treatment compared to the older bolus protocols: (1) more gentle osmotic correction of hyperosmolar state; (2) reduced risk of hypoglycaemia because the decrease is more predictable; (3) decreased severe hypokalaemia; (4) decreased theoretical risk of cerebral oedema; and (5) elimination of guessing re dose required. Repeated IM injections are obviously not necessary, an especially important benefit when dealing with small children scared of needles anyway. The major drawback may be the need to ensure a continuous IV route, especially a problem in the severely dehydrated patient or in the child who is difficult to restrain and keep quiet, or in parts of the world where such equipment may be unavailable. One additional advantage of the low dose continuous insulin infusion method is that the infusion rate can be titrated against changes in the BG in an almost instantaneous fashion because of the very short plasma half-life of insulin and the fact that no depot insulin is in use. It would be difficult to argue that low dose treatment methods are more effective than others, but they appear to be simpler to use, easier to teach, and, for these reasons, better treatment for DKA as well as less hypoglycaemia.

Carbohydrates
Carbohydrate is necessary as a substrate for insulin action if fatty acid breakdown is to be rapidly halted. Under many conditions of DKA presentation, lack of appetite or lack of food and caloric intake is part of the presenting picture so that starvation ketosis may add to the dilemma of ketoacidosis (insulin deficiency) and lactic acidosis (tissue dehydration). This author suggests that glucose be added to the IV fluids when the BG is in the 250–300 mg/dl (approximately 14–17 mmol/L) range. For some patients whose problems of ketoacidosis are secondary to dehydration and vomiting, and who enter with BGs in the low 300 mg/dl (approximately 17 mmol/L) range, this means giving 5% dextrose with the initial fluid solution. For other patients, this means adding 5–10% dextrose at 5–12 hours after initiating treatment with fluids, electrolytes and insulin. Deciding when to add glucose is facilitated with the more predictable decreases in glycaemia (~10% BG drop per hour after initial rehydration BG is known) that occur using low dose insulin infusion protocols and the availability of accurate bedside capillary BG equipment.

Subsequent treatment
Oral feeding should be reinstituted starting with clear liquids and progressing to soft solids and then more complex foods. Early refedding can hasten recovery as it may allow increased potassium replenishment in a safe manner in addition to avoiding the body’s need to continue to break down fats with attendant ketosis.

Subsequent insulin dosage remains a clinical guesstimate which takes into account many factors such as: the age and weight of the patient; duration of known diabetes; prior usual dose of insulin (unless newly diagnosed); and other potential confounding factors (pregnancy, renal failure, use of other drugs etc). Since average daily insulin doses are ~0.5–0.8 units/kg in the prepubertal and postpubertal periods and ~0.8–1.2 units/kg/day in the midst of the pubertal growth spurt, these values can be used to arrive at an estimated insulin dosage and can then be divided into prandial and basal insulin. Adults generally require about 0.5–0.8 units/kg as well, although the more obese children, teens and adults may need significantly more insulin because of insulin resistance. Newly-diagnosed patients may require much more insulin for several days to several weeks after diagnosis. In any individual patient, such higher doses of insulin may be needed for 24–48 hours after resolution of the ketoacidotic crisis. Sequential BG determinations are the best guide to insulin dose and help determine when to change to intermediate or longer-acting basal insulins since there are no hard and fast, dogmatic rules in such circumstances and each patient must be treated in an individualised fashion based upon their actual BG responses.

Financial costs, availability and philosophy of insulinisation dictate which protocols are to be considered for moving to twice, three or four times daily insulin SC and ultimate home treatment.

DKA complications
Table 5 lists frequent errors and complications of DKA.

Problems reflecting sodium, potassium, water, acid-base status, calcium/phosphate balance and glucose
as well as insulin orders all occur; they are often caused by errors in initial or subsequent orders, compounded by lack of appropriate monitoring and attention to the fact that DKA is a dynamic state with its treatment adding to changing circumstances. Missing the underlying precipitating factors – whether they are patient and family lack of knowledge concerning home recognition of impending DKA, psychosocial turmoil or comorbid events such as malaria, pyelonephritis or appendicitis – can certainly increase morbidity and mortality significantly. Similarly, in an adult population, attention to cardiovascular and cerebrovascular events as precipitants of DKA or co-existing conditions deserves the attention of the health care team. Gastric lavage should be considered for any patient truly unconscious because of the frequent association of gastric atony with ketoacidosis. Used judiciously, however, nasogastric tubes can certainly help to prevent aspiration in the patient who is critically ill (i.e. unconscious or semi-conscious) at presentation. Abdominal pain can be diffuse and severe, and perhaps suggests the need for surgical consideration. Amylase elevation, usually of pancreatic origin, is common and sometimes extremely high whereas serum lipase values are often not abnormal. Leukocytosis also can cause concern about underlying bacterial infection when most often both the hyperamylasaemia and leukocytosis resolve spontaneously with correction of the metabolic acidosis and dehydration. Insulin oedema

The rapid appearance of oedema, significant weight gain, abdominal bloating and blurred vision can occur shortly after treatment of DKA is begun. These clinical events are most often noted during or after aggressive treatment of patients with ketoacidosis, or in patients in whom the diagnosis of diabetes has been made recently but who have had asymptomatic diabetes for a much longer duration. Unless underlying cardiovascular or renal disease is present, not often the case in paediatric or adolescent diabetes mellitus, these symptoms usually abate spontaneously and have been called ‘insulin oedema’ for lack of a better explanation.  

- Progressive CNS deterioration despite improvement of laboratory parameters
  - Headache
  - Increasing lethargy
  - Failure to regain consciousness
  - Increased CSF pressure
  - Abnormal reflexes
- Eye changes
  - Papilloedema
  - Unequal intraocular pressure
- Increasing intraocular pressure
- Decreasing pupillary light reflex
- Hyperpyrexia
- Hypertension
- Diabetes insipidus
- Abnormal electroencephalogram
- Abnormal computerised tomography or magnetic resonance imaging consistent with cerebral oedema

<table>
<thead>
<tr>
<th>Table 6. Cerebral oedema symptoms and signs</th>
</tr>
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</table>
| Unexpected or unusual neurologic abnormalities including changes in sensorium as well as abnormalities of vital signs (e.g. elevated temperature, hypertension) should warrant consideration of either cerebral oedema or cerebral venous thrombosis. Imaging with computerised tomography or magnetic resonance may be the only way to confirm these diagnoses, but Table 6 presents some symptoms and signs that should raise the index of suspicion and warrant fundoscopy as well as closer medical attention so that appropriate treatment can be instituted. Concordance of DKA with cerebral oedema raises the stakes and is associated with significant morbidity and mortality. While major treatment errors in fluid, electrolyte or insulin administration may be contributory, most cases of cerebral oedema remain unexplainable. Table 6 lists a series of clinical events which should lead one to be suspicious of the possibility of cerebral oedema, especially if the patient seems to be improving by laboratory parameters but worsening on clinical grounds. Any delay in diagnosis, error in treatment or worsening of acid base, fluid or electrolyte status of the patient, if left unrecognised (or if treated incorrectly), could be invoked as a possible explanation for inadequate delivery of oxygen to the brain. Brain infarction can occur associated with or after cerebral oedema. Autopsy findings thought to be similar to those seen in the brains of victims of asphyxia and cerebral anoxia have been reported. Low-flow oxygen delivery may help decrease cerebral oedema associated with DKA – just as early recognition via sequential neurologic examination (presence or absence of venous pulsations and sharp disk margins on fundoscopy) by the primary health care professional supervising the DKA treatment is important. Fundoscopy must be done and documented initially and at intervals during treatment to make sure that cerebral oedema is recognised. Early consultation by a neurologist, neurosurgeon and/or ophthalmologist might be indicated if fundoscopy cannot be accomplished by the primary treating health care team. Treatment, once cerebral oedema is recognised, is supportive and includes measures to maintain cardiorespiratory function, oxygenation and normal body temperature. The possible benefits of corticosteroids to reduce intracranial pressure and the use of diuretics like mannitol have not been scientifically proven but are often used once cerebral oedema occurs. If cerebral oedema is diagnosed, the IV fluid rate should be reduced dramatically, mannitol should be considered at a dose of 1g/kg IV (10–20g/m2) and hyperventilation may all be helpful in reducing intracranial pressure or its effects on the brain.

Conclusions

DKA is a true paediatric, adolescent and adult metabolic medical emergency but, like many other disease entities, prevention of DKA decreases morbidity and mortality, saving enormous hospital and emergency department costs. Teaching health care professionals to understand the pathophysiology of DKA helps them provide better patient education and better treatment when DKA occurs.

Declaration of interests

There are no conflicts of interest declared.

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References are available online at www.practicaldiabetes.com.
Paediatric and adolescent diabetic ketoacidosis

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