Management of Diabetic Ketoacidosis (DKA)

Purpose
The purpose of this guideline is to advise the management of children and young people who present in diabetic ketoacidosis.

Intended Audience
This guideline applies to all registered nursing staff and clinicians working within Sheffield Children's Hospital involved in day to day care of children and young people with diabetes.
1. Introduction

This guideline for the management of (diabetic ketoacidosis) DKA in children and young people under the age of 18 years is based on (British Society for paediatric endocrinology and diabetes) BSPED’s latest DKA guideline which was published in January 2020.

These BSPED guidelines are believed to be as safe as possible in the light of current evidence. However, no guidelines can be considered entirely safe as complications may still arise. In particular, the pathophysiology of cerebral oedema is still poorly understood.

Note – New consensus guideline were produced by the BSPED in January 2020. There have therefore been a number of changes compared to the previous guidelines – even if you are very familiar with previous guidelines please check.

Key changes are:

1) The ISPAD definition for DKA with acidosis and a bicarbonate of 15.0 mmol per litre has been adopted. The previous BSPED guideline recommended a bicarbonate of <18mmol/l.

2) This guideline uses pH to categorise the severity of DKA and to determine the degree of dehydration.
   - Mild DKA – venous pH 7.2- 7.29 or bicarbonate < 15 mmol/L. Assume 5% dehydration
   - Moderate DKA – venous pH 7.1-7.19 or bicarbonate < 10 mmol/L. Assume 7% dehydration
   - Severe DKA – venous pH less than 7.1 or serum bicarbonate < 5 mmol/L. Assume 10% dehydration
3) The previous BSPED guideline categorised the severity of diabetic ketoacidosis based on pH, with those individuals with a pH >7.1 defined as having have mild or moderate DKA and those with a pH < 7.1 having severe DKA. Additional stratification has been adopted in this revised guideline with mild, moderate and severe definitions adopted.

4) There is increased emphasis within this guideline on ensuring adequate restoration of the circulation and treatment of shock. The use of inotropes in preference to fluid volume particularly early in resuscitation has been de-emphasised. Careful management of fluid administration remains an important part of the management of diabetic ketoacidosis because of the risk of cerebral edema.

5) Patients presenting with shock should receive a 20 ml/kg bolus of 0.9% Sodium Chloride over 15 minutes. Shock is defined as the APLS definition of tachycardia, prolonged central capillary refill etc. – it is not just poor peripheral perfusion. Following the initial 20 ml/kg bolus patients should be reassessed and further boluses of 10 ml/kg may be given if required to restore adequate circulation up to a total of 40 ml/kg at which stage inotropes should be considered. Boluses given to treat shock should NOT be subtracted from the calculated fluid deficit.

6) The calculation of maintenance fluids should be based on the traditional formula used in paediatrics in the UK. – 100 ml/kg/day for the first 10 kg body weight, plus 50 ml/kg/day for 10 to 20 kg and 20 ml/kg/day for each additional kilogram above 20 kg. This is a more permissive maintenance fluid rate than in the previous DKA guideline and is a significant change.

7) A maximum weight of 80kg should be used for the calculation of fluid replacement and deficit as this ensures that excessive volumes of fluids are not given.

8) Where plasma potassium is above the upper limit of the normal range at presentation it is recommended that Potassium is only added to Intravenous fluids after the patient has passed urine or until after the plasma potassium has fallen to within the upper limit of the normal range.

9) In patients already on long acting insulin this should be continued and in new patients, consideration should be given to starting long acting subcutaneous insulin alongside intravenous insulin.

2. Intended Audience
This guideline applies to all registered nursing staff and clinicians working within
Sheffield Children’s Hospital involved in day to day care of children and young people with diabetes.

3. Guideline Content

A. General

- Always accept any referral and admit children in diabetic ketoacidosis (DKA).
- Always consult with a more senior doctor on-call as soon as you suspect DKA even if you feel confident of your management. There is always a Paediatric Consultant or specialist middle grade doctor on-call for diabetes in Sheffield. Check with switchboard as to who is on duty (Dr C A MacKenzie / Dr N Wright/ Dr A Soni). SHO discuss with Registrar who will discuss with Consultant.

Remember: Children can die from DKA.

They can die from:

**Hypokalaemia** - this is preventable if you are careful.

**Cerebral oedema** - this is unpredictable, occurs more frequently in younger children and new diabetics and has a mortality of around 25%. The causes are not known, but this protocol aims to minimise the risk by facilitating a slow correction of the metabolic abnormalities. The management of cerebral oedema is covered in section 3.3 (F).

**Aspiration Pneumonia** - Consider using a nasogastric tube in semiconscious or unconscious children.

**Inadequate resuscitation** It is important to ensure that children with DKA receive adequate resuscitation if they have shock. Inadequate resuscitation is likely to increase the risk of brain injury and other end organ damage. Cerebral perfusion is influenced both by the circulatory perfusion pressure (blood pressure) and the intracranial pressure in incipient cerebral oedema. (CPP = MAP – ICP)

These are general guidelines for management. Treatment may need to be varied to suit the individual patient and this guideline does not remove the need for frequent detailed reassessments of the individual child or young person’s requirements.

These guidelines are intended for the management of the sick child or young person that has:

- Clinical acidosis (pH < 7.3 or laboratory bicarbonate < 15 mmol/l).
- **and** has ketonemia (indicated by blood ketone level above 3 mmol/litre)*

*Use a near-patient testing method for blood ketone (beta-hydroxybutyrate) level for the diagnosis and monitoring of the treatment of DKA.

- Blood glucose levels are generally high (above 11mmol/l) but children and
young people with known diabetes may develop DKA with normal blood glucose levels.

Children and young people with a blood pH \( 7.2 \)– \( 7.29 \) and/or plasma bicarbonate < \( 15 \) mmol/L have MILD DKA.

Children and young people with a pH less than \( 7.1 \)–\( 7.19 \) and/or plasma bicarbonate < \( 10 \) have MODERATE DKA.

Children and young people with a pH less than \( 7.1 \) and/or plasma bicarb < \( 5 \) have SEVERE DKA.

Children and young people who are not clinically dehydrated, not nauseated or vomiting and not clinically unwell usually tolerate oral rehydration and subcutaneous insulin even if their ketones are high— in this situation you do not necessarily need to treat with intravenous insulin infusions. They require monitoring regularly to ensure that they are improving and their ketone levels are falling.

If a child or young person has plasma hyperosmolarity with a very high blood glucose (BG) level (>\( 30 \) mmol/L), with little or no acidosis or ketones, this is a Hyperosmolar Hyperglycaemic State and requires DIFFERENT treatment. Discuss this with the senior doctor— these children can be very difficult to manage. (see Appendix 2)

You must discuss both groups of children and young people with the senior doctor on-call.

**Weight** - Record the patient’s weight at the earliest opportunity. Wherever possible the patient's actual weight on admission should be used rather than an estimated weight or approximation. Maintenance fluids should be based on the actual weight not an estimate of the likely weight following rehydration.

To avoid excessive amounts of fluid in overweight and obese children it is recommended that consideration be given to using a maximum weight of 80kg or 97th centile weight for age (whichever is lower) when calculating both fluid deficit and maintenance requirements.

**B. EMERGENCY MANAGEMENT**

i. General resuscitation: A, B, C.

ii. Confirm the diagnosis
iii. Initial investigations

i. General Resuscitation: A, B, C

| Airway          | ✚ Ensure that the airway is patent and if the child is comatose, insert oropharyngeal or nasopharyngeal airway if needed.  
|                | ✚ If comatose or has recurrent vomiting, insert a nasogastric tube, aspirate and leave on open drainage with regular aspiration. |
| Breathing       | Give 100% oxygen. |
| Circulation     | Insert an intravenous cannula and take blood samples (see below).  
|                | ✚ If shock (tachycardia, poor peripheral pulse volumes, poor central capillary refill, hypotension) adequate intravenous fluid volume resuscitation is required. A fluid bolus of 20ml/kg of 0.9% Sodium Chloride (Please note that bolus fluid had no potassium in it) or Plasma-Lyte 148 over 15 minutes should be given.  
|                | ✚ Following the initial 20 ml/kg bolus, patients with shock should be reassessed and further intravenous fluid boluses of 10 ml/kg aliquots may be given if required to restore adequate circulation up to a total of 40 ml/kg at which stage vasoactive drug therapy should be considered.  
|                | ✚ All children and young people with mild, moderate or severe DKA who do not have shock and are thought to require IV fluids should receive a 10 ml/kg 0.9% sodium chloride/ Plasma-Lyte 148 bolus over 60 minutes.  
|                | ✚ Whilst excessive intravenous fluid therapy should be avoided because of the risk of cerebral oedema, it is important to ensure that the circulatory volume is adequate and intravenous fluids should be given to support this. Cerebral perfusion is dependent on both perfusion pressure and intracranial pressure and hypotension will exacerbate the risk of brain injury. |

ii. Confirm the Diagnosis

| History       | Polydipsia, polyuria, weight loss |
Clinical Acidotic respiration Dehydration Drowsiness Abdominal pain / vomiting

Biochemical High blood glucose on finger-prick test (>11mmol/L). (It is not always as high as you might expect in DKA – DKA can be present at modestly elevated blood glucose levels) pH < 7.3 and /or plasma bicarbonate < 15mmol/L Finger prick ketones > 3.0 mmol/L

iii. Initial Investigations

- Blood glucose
- Plasma urea, electrolytes and bicarbonate.
- Blood gas (venous or capillary)
- Near patient blood ketone (β- hydroxybutyrate)
- Haematocrit and full blood count
- Blood culture
- Urinalysis, culture and sensitivity
- Continuous electrocardiographic monitoring to observe T waves (hypokalaemia can cause cardiac dysrhythmias). The use of cardiac monitors may be influenced by wider hospital policy. But a child does not necessarily need HDU/ICU admission for cardiac monitoring alone (unless otherwise indicated) if it can safely be performed in the ward environment.
- + Other investigations if indicated, e.g. Chest X-ray, CSF, throat swab, coagulation screen etc.

Note: DKA may be precipitated by sepsis, and fever is not a usual clinical feature of DKA.

C. Full Clinical Assessment and Observations

Assess and record in the medical notes to allow serial assessments.

i. Conscious level
ii. Full clinical examination
iii. Assess need for HDU/ICU admission
iv. Observations
v. Weight

Patients with shock will require high dependency care and should be discussed with the most senior Paediatrician or Critical Care Consultant at the earliest opportunity.
Conscious Level

Commence hourly neurological observations and record Glasgow Coma Score in all patients (whether alert or with impaired consciousness).

If impaired conscious level on admission, or any subsequent deterioration in conscious level transfer to PCCU.

Consider instituting cerebral oedema management (section [F]), only after discussion with a senior member of staff. Irritability, confusion or headache can be the earliest sign of cerebral oedema and it is important to respond promptly.

Full examination

Look particularly for evidence of:

- Cerebral oedema:
  - Irritability
  - Confusion or reduced conscious level may be the earliest sign of cerebral oedema.
  - Variation in deep tendon reflexes and plantar responses
  - N.B. Examine pupillary responses and fundi
  - Slow pulse with high blood pressure and papilloedema are very late signs

- Infection

- Ileus

Does the child need to be on PCCU?

- YES
  
  If reduced conscious level, or >10% dehydration with shock, or staffing levels on the wards are insufficient to allow adequate monitoring.

| Children and young people with DKA must have hourly observations and close monitoring if They are younger than 2 years OR They have severe DKA (blood pH below 7.1) Consideration must be given to admission to HDU in this situation |

Observations

- Ensure full instructions are given to the senior nursing staff emphasising the need for:
  - Strict fluid balance record
  - Testing of every sample of urine
D. Management

i. Fluids
   a. Volume
   b. Type
   c. Oral fluids
   d. Fluid losses

ii. Bicarbonate

iii. Potassium

iv. Insulin

v. Hyperchloraemic metabolic acidosis

vi. Phosphate

vii. Anticoagulant prophylaxis

NB. It is essential that all fluids given are documented carefully, particularly the fluid which is given in the Emergency Department and during transfer between departments, as this is where most mistakes occur.

a. Volume of Fluid
   By this stage, the circulating volume should have been restored and child no longer in shock. If not, give a further 10ml/kg colloid or (up to max of 20ml/kg in total – if already received 20ml/kg discuss with consultant).

   Otherwise, once the circulating blood volume has been restored, calculate fluid requirements as follows:

   \[
   \text{Requirement} = \text{Maintenance} + \text{Fluid deficit}
   \]

Fluid Deficit-
It is not possible to assess the degree of clinical dehydration accurately to work out the deficit. Therefore-

Assume a 5% fluid deficit in children and young people in mild DKA (indicated by

- Hourly capillary blood glucose measurements
- Capillary ketones
- Twice daily weight
- Half hourly Glasgow come score measurements initially
- Reporting any change in neurology immediately to the medical staff: symptoms of headache or any change in either conscious level or behavior.
- Reporting any changes in the electrocardiogram trace, especially T wave changes.
Management of Diabetic Ketoacidosis

**a blood pH 7.2 - 7.29 and/or plasma bicarbonate <15 mmol/L**

Assume a 7% fluid deficit in children and young people in moderate DKA (indicated by a blood pH of 7.1-7.19 and/or plasma bicarbonate <10 mmol/L)

Assume a 10% fluid deficit in children and young people in severe DKA (indicated by a blood pH <7.1 and/or plasma bicarbonate <5 mmol/L)

**Resuscitation fluid:**

The volume of any fluid boluses given for resuscitation in children with shock should **NOT** be subtracted from the estimated fluid deficit.

The initial 10ml/kg bolus given to all patients not in shock requiring intravenous fluids **SHOULD** be subtracted from total calculated fluid deficit.

The fluid deficit should be replaced over 48 hours alongside appropriate maintenance fluids.

**Maintenance Fluids:**

Maintenance fluid volumes should be calculated using the Holliday – Segar formula (the traditional method of calculating fluid volume in children in the UK)

Maintenance Fluid:
- 100 ml/kg/day for the first 10 kg of body weight
- 50 ml/kg/day for the next 10 to 20 kg
- 20 ml/kg/day for each additional kilogram above 20 kg

**N.B.** Neonatal DKA will require special consideration and larger volumes of fluid than those quoted may be required, usually 100-150 ml/kg/24 hours

**Fluid Calculations:**

Calculate the fluid deficit (either 5%, 7% or 10% dehydration depending on whether the patient has mild, moderate or severe DKA), subtract the initial 10ml/kg bolus then divide this over 48 hours and add to the hourly rate of maintenance fluid volume, giving the total volume evenly over the next 48 hours. i.e.,

**Hourly rate = ((Deficit – initial bolus) / 48hr) + Maintenance per hour**
Examples of how to work out deficit fluids:

A 20 kg 6 year old boy who has a pH of 7.15 (Moderate DKA = > 7% Dehydrated) will receive a 10ml/kg bolus (200mls fluid) over 60 minutes as part of his initial management. His ongoing fluids will comprise:

<table>
<thead>
<tr>
<th>Deficit 7% x 20 kg</th>
<th>= 1400 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtract initial bolus</td>
<td>= 1400-200 = 1200ml to be replaced over 48 hours</td>
</tr>
<tr>
<td>Maintenance</td>
<td>= 10 x 100 = 1000 ml per day for 1st 10 kg</td>
</tr>
<tr>
<td></td>
<td>= 10 x 50 = 500ml per day for next 10 kg (weighs 20kg)</td>
</tr>
<tr>
<td></td>
<td>= 1500 ml per day total (over 24 hours)</td>
</tr>
<tr>
<td>Total fluid</td>
<td>= 25ml/hour - Deficit of 7% minus bolus over 48 hours</td>
</tr>
<tr>
<td></td>
<td>+ 62 ml/hr – Maintenance fluids</td>
</tr>
<tr>
<td></td>
<td>= 87 ml/hour</td>
</tr>
</tbody>
</table>

A 60 kg 15 year old girl with a pH of 6.9 who was in shock at presentation has received 30ml/kg of 0.9% sodium chloride for resuscitation. These fluid boluses are not subtracted from ongoing maintenance fluids. Her ongoing fluids will comprise:

<table>
<thead>
<tr>
<th>Deficit 10% x 60 kg</th>
<th>= 6000 ml to be replaced over 48 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance</td>
<td>= 10 x 100 = 1000 ml per day for 1st 10 kg</td>
</tr>
<tr>
<td></td>
<td>= 10 x 50 = 500ml per day for next 10 kg (10-20kg)</td>
</tr>
<tr>
<td></td>
<td>= 40 x 20 = 800ml per day for next 40kg</td>
</tr>
<tr>
<td></td>
<td>= 2300 ml per day total (over 24 hours)</td>
</tr>
<tr>
<td>Total fluid</td>
<td>= 125 ml/hour - Deficit of 10% over 48 hours</td>
</tr>
<tr>
<td></td>
<td>+ 96 ml/hr – Maintenance fluids</td>
</tr>
<tr>
<td></td>
<td>= 221 ml/hour</td>
</tr>
</tbody>
</table>

A fluid calculator which can be printed out for the child’s medical records is being developed and will be available soon – It will link to the BSPED audit which will capture data for ongoing audit of outcomes in DKA in children and young people. The link to the calculator should be available by early March 2020.

Do not give additional intravenous fluid to replace urinary losses. Urinary catheterisation should be avoided but may be useful in the child with impaired consciousness and/or shock.
b. **Type of fluid**

Initially use 0.9% sodium chloride with 20 mmol potassium chloride in each 500ml bag and continue this sodium concentration until blood glucose levels are less than 14 mmol/l. “Protocol for concentrated potassium containing injection solutions” available on the Trust intranet states the ready-made potassium bags that are available. Once the blood glucose has fallen to 14 mmol/l, use a bag containing glucose 5%, potassium chloride 20mmol and 0.9% sodium chloride in 500ml. This fluid is available from AUU, A & E, ICU, Ward 3, Ward 4, and Ward 6. Only if these readymade bags are not available should concentrated potassium be added to a bag of fluid in ICU. – see Protocol for Concentrated Potassium ContainingInjection Solutions on the trust intranet.

Alternatively, Plasma-Lyte 148 with 40mmol/L potassium chloride may be used.

**Sodium(Na) and Corrected Sodium (Na\textsuperscript{corr}) and Effective Osmolality**

Some experts have suggested that Corrected Sodium levels give an indication of the risk of cerebral oedema with rapidly falling corrected sodium indicating an excess of free water and an increased risk of cerebral oedema. Serum Na concentration falls as a consequence of “dilution” of the extracellular fluid. It is recommended that the corrected sodium levels are monitored during the management of DKA. The corrected sodium (Na\textsuperscript{corr}) represents the expected serum sodium in the absence of hyperglycaemia.

**Corrected sodium = plasma sodium + (0.3x (glucose - 5.5)**

Several formulae exist, this is a simplified version. Expect corrected sodium levels (and actual sodium levels) to rise as blood glucose levels fall with treatment.

Consider adjusting the total fluid rate using corrected Sodium (Na\textsuperscript{corr}) taking into account the circulation and patient’s general condition and state of hydration:

- A rise in Na\textsuperscript{corr} of >5mmol/L in 4-8 hours suggests increased fluid loss or insufficient replacement. Consider increasing the fluid administration rate.
- A fall in Na\textsuperscript{corr} of >5mmol/L in 4-8 hours suggests too much fluid gain or too rapid replacement. Consider reducing the fluid administration rate.

Check urea and electrolytes two hours after resuscitation is begun and then at least four hourly. Corrected sodium levels should be calculated on laboratory sodium results not on blood gas results every four hours.

**If corrected sodium levels do not rise during treatment, discuss with the consultant on call.**
c. Oral Fluids
- Do not give oral fluids to a child or young person who is receiving intravenous fluids for DKA until ketosis is resolving and there is no nausea of vomiting.
- A nasogastric tube may be necessary in the case of gastric paresis.
- If clinical improvement occurs before the 48 hours rehydration period is finished, oral intake may commence then with reduction of intravenous fluid intake.

d. Fluid Losses
If a massive diuresis continues for several hours fluid input may need to be increased if the corrected sodium is rising rapidly.

If large volumes of gastric aspirate continue, these may need to be replaced with 0.45% Sodium chloride with 20 mmol/L potassium chloride.

ii. Sodium bicarbonate
Do not give intravenous sodium bicarbonate to children and young people with DKA to treat metabolic acidosis routinely. Consider giving sodium bicarbonate after discussion with a Critical Care Consultant in the following situations:
- Life threatening hyperkalaemia
- Severe acidosis with impaired myocardial contractility.

iii. Potassium
Potassium intake should be commenced immediately after the bolus fluid unless anuria is confirmed after urinary catheterisation or there are peaked T waves on a 12-lead electrocardiogram. Potassium is mainly an intracellular ion, and there is always massive depletion of total body potassium although initial plasma levels may be low, normal or even high. Levels in the blood will fall once insulin is commenced and metabolic acidosis is corrected.

Therefore, add 20 mmol potassium chloride to every 500 ml bag of fluid (40 mmol per litre).

Intravenous fluids are now available with 20 mmol Potassium in 500ml (including 5% Dextrose & 0.9% Sodium chloride. Readymade potassium bags should be used. The above strength of fluid is available from AAU, A & E, ICU, Ward 3, Ward 4 and Ward 6. Please refer to Protocol for Concentrated Potassium Containing Injection Solutions for information on various potassium containing fluids available in the trust and their location. Potassium containing fluids should only be made up on ICU when pharmacy is closed and when a suitable readymade bag is not available.

Check urea and electrolytes 2 hours after resuscitation is begun and then at least 4 hourly, and alter potassium replacements accordingly.

If hypokalaemia develops (serum potassium below 3 mmol/litre):
- Consider reducing the insulin infusion rate
- Discuss urgently with a critical care specialist, a central venous catheter may be required to give intravenous potassium solutions concentrations >40 mmol/litre.

Use a cardiac monitor and observe frequently for T wave changes:
- Flat = hypokalaemia.
- Peaked = hyperkalaemia.

**iv. Insulin**

Once rehydration has been commenced, blood glucose levels will start to fall. There is some evidence that cerebral oedema is more likely if insulin is started early.

**DO NOT start insulin until intravenous fluids therapy has been administered for at least one hour.**

Continuous low-dose intravenous infusion is the preferred method. Do not give bolus doses of intravenous insulin.

Pharmacy has prefilled pre-prepared insulin syringes to avoid errors. If these are not available, make up a solution of 1 unit per ml of human soluble insulin (e.g. Actrapid) by adding 50 units (0.5ml) insulin to 49.5ml 0.9% Sodium chloride in a syringe pump to make a final volume of 50ml. Attach this to the intravenous fluids on flow using a Y-connector. Do not add insulin directly to the fluid bags.

Administer the insulin solution at **0.1 unit/kg/hour** (0.1ml/kg/hour).

Some paediatricians believe that 0.05 units/kg/hour is an adequate dose. There is no firm evidence to support this.

Continue with 0.9% sodium chloride with 20 mmol potassium chloride in 500ml until blood glucose levels have fallen to 14 mmol/L. **(in children <5 years of age, consider reducing insulin to 0.05 U/kg/hr if the blood glucose is falling rapidly)**

If the blood ketone level does not decrease within 6–8 hours, continue the insulin dosage at 0.1 units/kg/hour or more.

Once the blood glucose level falls to 14mmol/L, change the fluid to contain 5% glucose (generally 0.9% Sodium Chloride with 5% glucose and potassium, see 1b above for type of fluid). Amend the insulin infusion rate, as follows –
If ketone levels are less than 3 mmol/l
- Change the fluid to contain 5% glucose; use 500 ml bags of 0.9% sodium chloride with 5% glucose and 20 mmol potassium chloride in 500ml which are available from Pharmacy. (Plasma-Lyte 148 with 5% glucose and potassium chloride 20 mmol/ 500mls may be used.)
- Reduce to, or maintain at an insulin infusion rate of 0.05 unit/kg/hr

If ketone levels are above 3 mmol/l
- Maintain the insulin infusion rate at 0.1 unit/kg/hour to switch off ketogenesis
- Change the intravenous maintenance fluid to contain 10% glucose rather than 5% glucose, in order to prevent hypoglycaemia when the higher dose of insulin is continued e.g. (0.9% Sodium Chloride with 10% dextrose and 20 mmol potassium per 500 ml) should be used.

- **DO NOT** stop the insulin infusion while glucose is being infused, as insulin is required to switch off ketone production. If the blood glucose falls below 4 mmol/L, give a bolus of 2 ml/kg of 10% glucose and increase the glucose concentration of the infusion. Insulin may be temporarily be reduced for 1 hour.

- Once the blood pH is above 7.3, the blood glucose has decreased to 14 mmol/l or less, and a glucose-containing fluid has been started, consider reducing the insulin infusion rate, but to no less than 0.05 units/kg/hour.

If the blood glucose rises out of control, or the pH level is not improving after 4-6 hours consult senior medical staff and re-evaluate (errors in prescription of fluid and/or insulin therapy, errors in administration of fluid and/or insulin therapy, problems with intravenous infusions, possible sepsis, or other conditions).

Calculate and start treatment from the beginning with fresh fluid and insulin infusions.

For **children who are already on long-acting insulin** (eg Glargine/Lantus and Detemir/Levemir), you may want this to continue at the usual dose and time throughout the DKA treatment, in addition to the IV insulin infusion, in order to shorten length of stay after recovery from DKA.

For children on continuous subcutaneous insulin infusion (CSII) pump therapy, stop the pump when starting DKA treatment.

v. **Hyperchloreaemic metabolic acidosis**
Hyperchloraemic metabolic acidosis may occur following the administration of large amounts of chloride containing fluids given during the management of DKA. Direct monitoring of ketones and calculation of the component of the base deficit due to chloride will help differentiate whether persisting acidosis is due to ongoing ketosis that may need additional treatment (adjustment to insulin infusion or fluids) or due to hyperchloraemia. Acidosis due to hyperchloraemia will correct spontaneously and doesn’t need specific treatment. Acidosis due to hyperchloraemia need not delay the transition to oral fluids and subcutaneous insulin. It needs to be differentiated from ongoing ketoacidosis.

**Anion gap:**
If the clinical picture is not improving calculate the anion gap. The anion gap is typically 20-30 mmol/L in a patient with ketoacidosis. However, an anion gap >35 mmol/L may suggest concomitant lactic acidosis due to sepsis or poor perfusion and should prompt a review of the overall clinical picture. It is not required for routine monitoring but may be helpful if the clinical picture or biochemistry is not improving.

**vi. Phosphate**
There is always depletion of phosphate, this is a predominantly intracellular ion. Plasma levels may be very low. There is no evidence in adults or children and young people that replacement has any clinical benefit. Note: phosphate administration may lead to hypocalcaemia.

**vii. Anticoagulant Prophylaxis**
Be aware that there is a significant risk of femoral vein thrombosis in young and very sick children with DKA who have femoral venous catheters inserted. Femoral venous catheters should remain in situ for as short a time as possible.

Thromboembolic prophylaxis should be considered in young people >16 years (in line with NICE guidance), in young women taking the combined oral contraceptive pill and sick patients with femoral venous catheters. (Enoxaparin is the low molecular weight heparin of choice.)

**Continuing Management**
- Strict fluid balance including oral fluids and urine output.
- **Hourly capillary blood glucose measurements** (these may be inaccurate with severe dehydration/acidosis but useful in documenting the trends. Do not rely on any sudden changes but check with a venous laboratory glucose measurement)
- Capillary blood ketone levels every 1-2 hours
- Hourly blood pressure, pulse, respiratory rate observations
- Hourly level of consciousness initially, using the modified Glasgow coma score
- Hourly neurological observations, including level of consciousness (using the
modified Glasgow coma score) and heart rate, in children under the age of 2, or in children and young people with a pH less than 7.1, because they are at increased risk of cerebral oedema

- Reporting immediately to the medical staff if any symptoms of headache, change in either conscious level or behaviour, change in pulse rate or blood pressure
- Report any changes in the electrocardiogram trace, especially signs of hypokalaemia (flat T waves). ST-segment depression and prominent U-waves
- Check urea and electrolytes, blood pH, and laboratory blood glucose two hours after the start of resuscitation, and then 4-6 hourly.
- Review the fluid composition and rate according to each set of electrolyte results.
- A full medical review is warranted hourly for two hours after starting treatment, and then at least 4 hourly. This includes assessment of clinical status including vital signs and neurological examination. Blood results must be noted, trends must be reviewed and fluid, electrolyte and insulin therapy must be reviewed and documented in the medical notes.
- More frequent reviews may be needed for children under two years of age, for those who have severe DKA or there are other reasons for special concern.

If acidosis is not correcting, consider the following

- insufficient insulin to switch off ketones
- inadequate resuscitation
- sepsis
- hyperchloremic acidosis
- salicylate or other prescription or recreational drugs poisoning

Use near-patient blood ketone testing to confirm that ketone levels are falling adequately. Urine ketone testing is not the preferred method for ketone monitoring but may be used in rare circumstances when blood ketones cannot be measured. If blood ketones are not falling, then check infusion lines, the calculation and dose of insulin. Consider giving more insulin.

Consider sepsis, inadequate fluid input and other causes if sufficient insulin is being given.

Insulin management once ketoacidosis resolved –

Do not change from intravenous insulin to subcutaneous insulin until ketosis is resolving (for example, blood beta-hydroxybutyrate level below 1.0 mmol/litre) and the child or young person with DKA is alert and is tolerating fluids without nausea or vomiting.

Start subcutaneous insulin at least 30 minutes before stopping intravenous insulin to avoid rebound hyperglycaemia.
For a child or young person with DKA who is using insulin pump therapy, restart the pump at least 60 minutes before stopping intravenous insulin.

Subcutaneous insulin should be started according to the protocol for the child with newly diagnosed diabetes, or the child should be started back onto their usual insulin regimen at an appropriate time (discuss with senior staff). **Ideally long acting insulin should be prescribed and administrated on arrival to the ward.**

**E. Cerebral Oedema**

Risk factors include:
- Young age
- New diagnosis
- Falling Na\textsuperscript{corr} on treatment
- Low pCO\textsubscript{2}
- High urea

The signs and symptoms of cerebral oedema include:
- headache
- change in neurological status (restlessness, irritability, increased drowsiness, incontinence)
- specific neurological signs (e.g., cranial nerve palsies), change in deep tendon reflexes and plantar responses
- abnormal posturing
- rising blood, decreased heart rate, decreased O\textsubscript{2} saturation –late signs

More dramatic changes such as convulsions, papilloedema, respiratory arrest may be pre-terminal events and are associated with extremely poor prognosis.

**MANAGEMENT OF CEREBRAL ODEMA**

If cerebral oedema is suspected inform senior medical and nursing staff immediately.

The following measures should be taken immediately while arranging transfer to PICU. First exclude hypoglycaemia as a possible cause of any behaviour change.

Treat immediately for cerebral oedema if a child or young person develops any of these signs –
- Deterioration in level of consciousness, headache or irritability
- Abnormalities of breathing pattern, e.g., respiratory pauses and/or fall in SaO\textsubscript{2}
- Oculomotor palsies
- Abnormal posturing
• Pupillary inequality or dilatation.

Give hypertonic (2.7%) Sodium Chloride (5mls/kg over 5-10 mins)

• Restrict intravenous fluid intake to half of regular maintenance and replace deficit over 72 rather than 48 hours.
• Discuss with PICU consultant. The child will need to be moved to PICU (if not there already)
• Do not intubate and ventilate unless advised by a PICU consultant.
• Endotracheal intubation must be performed by the most experienced practitioner
• When the child is stable, exclude other diagnoses by CT scan - other intracerebral events may occur (thrombosis, hemorrhage or infarction) and present similarly
• **Treatment of suspected cerebral oedema should not be delayed. A CT scan is not needed to suspect or commence treatment of cerebral oedema.**
• If hypertonic Sodium Chloride is not readily available, mannitol 0.5 – 1.0 g/kg should be given immediately (20% mannitol 2.5 - 5 ml/kg over 20 minutes). The effect of mannitol should be apparent within 15 minutes and typically lasts for 120 minutes. If there is no improvement with mannitol within 30 minutes a repeated dose of mannitol may be given (or 2.7% sodium Chloride may be preferred). Mannitol may promote a brisk diuresis due to its osmotic effect and renal excretion
• Document all events (with dates and times) very carefully in medical records

**Other Complications**

• Hypoglycaemia and hypokalaemia – avoid by careful monitoring and adjustment of infusion rates. Consideration should be given to adding more glucose if blood glucose is falling quickly even if it is above 4 mmol/L.
• Systemic Infections – antibiotics are not given routinely unless a severe bacterial infection is suspected
• Aspiration pneumonia – avoid by inserting a nasogastric tube in vomiting children and young people with impaired consciousness

Other associations with DKA require specific management:

• Continuing abdominal pain is common and may be due to liver swelling, gastritis, bladder retention or ileus. However, beware of appendicitis and ask for a surgical opinion if in doubt. A raised serum amylase is common in DKA.
• Other problems are pneumothorax ± pneumo-mediastinum, interstitial pulmonary oedema, unusual infections (e.g., tuberculosis, fungal infections), hyperosmolar hyperglycaemic non–ketotic coma, ketosis in type 2 diabetes.
• Discuss complications with the consultant on-call
4. References

BSPED recommended guidelines on diabetic ketoacidosis 2020-

NICE Guideline – https://www.nice.org.uk/guidance/ng18

A Consensus Statement from the International Society for Pediatric and Adolescent Diabetes: Diabetic ketoacidosis and hyperglycemic hyperosmolar state.

Ng SM, Edge JA, Timmis AE. Practical Management of Hyperglycaemic Hyperosmolar State (HHS) in children. 2017 [cited 2020 Apr 14]; Available from:
Appendix 1: Algorithm for the Management of Diabetic Ketoacidosis

Algorithm for the Management of Diabetic Ketoacidosis

**Clinical History**
- polyuria
- polydipsia
- weight loss
- abdominal pain
- weakness
- vomiting
- confusion

**Clinical Signs**
- assess dehydration
- deep sighing respiration (Kussmaul)
- smell of ketones
- lethargy, drowsiness

**Biochemistry**
- elevated blood glucose (>11mmol/L)
- acidaemia (pH<7.3)
- ketones in blood >3mmol/L
- take blood also for electrolytes, urea
- perform other investigations if indicated

**Confirm Diagnosis**
**Diabetic Ketoacidosis**
Call Senior Staff

**Shock**
- Reduced peripheral pulse
- volume
- Reduced conscious level, coma

**Resuscitation**
- Airway + N/G tube
- Breathing (100% O2)
- Circulation (20ml/kg 0.9% sodium chloride. Repeated 10ml/kg boluses until circulation restored, max 40 ml/kg dose before discussion with senior doctor)

**Observations**
- hourly blood glucose
- neurological status at least hourly
- hourly fluid input/output
- electrolytes 2 hours after start of IV-therapy, then 4-hourly
- 1-2 hourly blood ketone levels

When blood glucose < 14 mmol/L

**Intravenous therapy**
1. Once blood glucose < 14mmol add
   - add 5% glucose to 0.9% sodium chloride with 20 mmol KCl per 500 ml. Reduce insulin infusion to 0.05 units/kg/hr
2. If continuing with 0.1 units/kg/hr
   - add 10% glucose to 0.9% sodium chloride with 20 mmol KCl per 500 ml

**Resolution of DKA**
- clinically well, drinking well, tolerating food
- blood ketones < 1.0 mmol/L or pH normal
- urine ketones may still be positive

**Insulin**
- start subcutaneous insulin then stop intravenous insulin 1 hour later

*Updated January 2020*

**No improvement (eg pH static/no reduction in ketones/BG)**

Re-evaluate
- fluid balance + IV-therapy
- if continued acidosis, may require further resuscitation fluid
- check insulin dose correct and running properly
- consider sepsis
- consider restarting protocol

**When blood glucose < 6 mmol/L**

- Add more glucose to 0.9% sodium chloride
- DO not reduce insulin below 0.05 units/kg/hr if ketones >1 mmol/L

**Intravenous therapy**
- give 5 ml/kg 2.7% sodium chloride or mannitol 0.5 - 1.0 g/kg
- dose may be repeated if needed
- call senior staff
- restrict I.V. fluids by 1/2
- discuss further care with paediatric critical care specialist

**Neurological deterioration**
- Warning signs: headache, irritability, slowing heart rate, reduced conscious level, specific signs raised ICP
- Exclude hypoglycaemia
- Is it cerebral oedema?

**Management**
- give 5 ml/kg 2.7% sodium chloride or mannitol 0.5 - 1.0 g/kg
- dose may be repeated if needed
- call senior staff
- restrict I.V. fluids by 1/2
- discuss further care with paediatric critical care specialist
Appendix 2: Initial Management of Hyperosmolar Hyperglycaemic State (HHS)

Definition
Features which differentiate it from other hyperglycaemic states such as DKA are:
- Marked hyperglycaemia (33.3 mmol/L or more)
- Absent to mild ketonaemia (blood pH >7.3, serum bicarbonate >15 mmol/L)
- Osmolality usually 320 mosmol/kg or more
- Hypovolemia

This picture usually occurs in Type 2 diabetes, especially where there are learning difficulties or other factors preventing adequate hydration. HHS has a high mortality rate.

Goals of treatment
The goals of treatment of HHS are to treat the underlying cause and to gradually and safely:
- Normalise the osmolality
- Replace fluid and electrolyte losses
- Normalise blood glucose

Other goals include prevention of arterial or venous thrombosis and other potential complications e.g., cerebral oedema and central pontine myelinolysis

Fluid therapy
The goal of initial fluid therapy is to expand the intra and extravascular volume and restore normal renal perfusion. The rate of fluid replacement should be more rapid than is recommended for DKA.
- Give an initial bolus should be of 20 mL/kg of 0.9% sodium chloride.
- Assume a fluid deficit of approximately 12–15% of body weight.
- Additional fluid boluses should be given, if necessary, to restore peripheral perfusion.
- Thereafter, 0.9% -0.45% Sodium chloride should be used aiming for a reduction in plasma sodium of 0.5 mmol/l per hour. (ISPAD recommendations). The goal is to promote a gradual decline in serum sodium concentration and osmolality.
- **As isotonic fluids are more effective in maintaining circulatory volume**, 0.9% sodium Chloride should be restarted if perfusion and hemodynamic status appear inadequate as serum osmolality declines.
- Serum sodium concentrations should be measured frequently and the sodium concentration in fluids adjusted to promote a gradual decline in corrected serum sodium concentration. Mortality has been associated with failure of the corrected serum sodium concentration to decline with treatment. This may be an indication for renal replacement therapy.
- Replace potassium (40mmol/litre of rehydration fluid) once renal function is known.
Prior to insulin starting, potassium replacement is probably only needed if plasma potassium concentration is less than 5.5 mmol/l.

- Plasma glucose should fall by around 4-6 mmol/L per hour with adequate rehydration. If there is a continued rapid fall in serum glucose (>5 mmol/l per hour) after the first few hours, consider adding 5% glucose to the rehydration fluid.
- Failure of the expected decrease of plasma glucose concentration should prompt reassessment and evaluation of renal function.

Unlike treatment of DKA, replacement of urinary losses is recommended. The typical urine sodium concentration during an osmotic diuresis approximates 0.45% Sodium chloride; however, when there is concern about the adequacy of circulatory volume, urinary losses may be replaced with a fluid containing a higher sodium concentration.

**Insulin therapy**

- Blood glucose levels will fall with fluid therapy alone and insulin is **NOT** required early in treatment.
- Insulin administration should be initiated when serum glucose concentration is no longer declining at a rate of at least 3 mmol/l per hour with fluid administration alone.

**Potassium**

Patients with HHS also have extreme potassium deficits; a rapid insulin-induced shift of potassium to the intracellular space may trigger cardiac arrhythmias. Therefore Potassium chloride **MUST** be included in all fluids as explained above. For further information see ISPAD Guidelines 2014 Chapter