DKA Pathway of care

DKA is a medical emergency with a significant morbidity and mortality. It should be diagnosed promptly and managed intensively. The specialist diabetes team should always be involved as soon as possible and ideally within 24 hours because this has been demonstrated to be associated with a better patient experience and reduced length of stay.

For young people under the age of 18 years, contact your paediatric diabetes service and use the BSPED DKA guidelines which can be found at http://www.bsped.org.uk/clinical/docs/DKAGuideline.pdf

Assessment of severity

The presence of one or more of the following may indicate severe DKA.

- Blood ketones over 6mmol/L
- Bicarbonate level below 5mmol/L
- Venous/arterial pH below 7.0
- Hypokalaemia on admission (under 3.5mmol/L)
- GCS less than 12 or abnormal AVPU scale
- Oxygen saturation below 92% on air (assuming normal baseline respiratory function)
- Systolic BP below 90mmHg
- Pulse over 100 or below 60bpm
- Anion gap above 16 **[Anion Gap = ($Na^+ + K^+$) – ($Cl^- + HCO_3^-$)]**

If the patient exhibits any of these signs they should be reviewed by a consultant physician and considered for referral to a Level 2/HDU (High Dependency Unit) environment [69]. It may also be necessary to consider a surgical cause for the deterioration. If surgery is required there will need to be an urgent senior multidisciplinary discussion on the optimum time to operate.

Provision of care

Local care pathways should identify the units that are to care for DKA patients. Nursing staff appropriately trained in Level 2/HDU should take the lead in hands on patient care.

New principles

The insulin infusion rate is calculated by weight, which may need to be estimated. Administration by weight allows insulin resistant states to be at least partially accommodated. Reliance on standard VRIII regimens will fail to accommodate for the very obese or the pregnant patient and risks premature reduction of insulin dosage. Where blood ketone measurements are available the adequacy of the insulin regimen is determined by the rate of fall of the ketones and will need revision if this is inadequate. If bedside ketone measurement is not available, the venous bicarbonate level can be used to assess the response to treatment during the first 6 hours, but may be less reliable thereafter due to the confounding influence of the high chloride levels associated with large volumes of 0.9% sodium chloride solution. This is particularly important when glucose levels are relatively normal. Supplementary glucose solution may need to be infused at some stage in treatment to provide substrate. This will permit the FRIII to be maintained, avoid hypoglycaemia and allow the full suppression of ketone production.

A. Hour 1: Immediate management upon diagnosis: 0 to 60 minutes.

T = 0 at time intravenous fluids are commenced. If there is a problem with intravenous access, critical care support should be requested immediately

Aims

- Commence IV 0.9% sodium chloride solution
- Commence a FRIII but only after fluid therapy has been commenced
- Establish monitoring regime appropriate to patient; generally hourly blood glucose (BG) and hourly ketone measurement, with at least 2 hourly serum potassium and bicarbonate for the first six hours
- Clinical and biochemical assessment of the patient
- Involve the diabetes specialist team at the earliest possible stage

Action 1 - Intravenous access and initial investigations

- Rapid ABC (Airway, Breathing, Circulation)
- Large bore IV cannula (use ports to reduce infection risk) and commence IV fluid replacement (See Action 2)
- Clinical assessment
- Respiratory rate; temperature; blood pressure; pulse; oxygen saturation
- Glasgow Coma Scale. NB: a drowsy patient in the context of DKA is serious and the patient requires critical care input. Consider an NG tube with airway protection to prevent aspiration
- Full clinical examination

Initial investigations should include:

- Blood ketones
- Capillary blood glucose
- Venous plasma glucose
- Urea and electrolytes
- Venous blood gases
- Full blood count
- Blood cultures
- ECG
- Chest radiograph if clinically indicated
- Urinalysis and culture
- Continuous cardiac monitoring
- Continuous pulse oximetry
- Consider precipitating causes and treat appropriately
- Establish usual medication for diabetes
- Pregnancy test in women of child bearing age

Action 2 – Restoration of circulating volume

Assess the severity of dehydration using pulse and blood pressure. As a guide 90mmHg may be used as a measure of hydration but take age, gender and concomitant medication into account.

Systolic BP (SBP) on admission below 90mmHg

Hypotension is likely to be due to low circulating volume, but consider other causes such as heart failure, sepsis, etc.

- Give 500ml of 0.9% sodium chloride solution over 10-15 minutes. If SBP remains below 90mmHg this may be repeated **whilst awaiting senior input**. In practice most patients require between 500 to 1000ml given rapidly.
- If there has been no clinical improvement reconsider other causes of hypotension and seek an **immediate senior assessment**. Consider involving the ITU/critical care team.
- Once SBP above 90mmHg follow fluid replacement as shown below

Systolic BP on admission 90mmHg and over

Below is a table outlining a typical fluid replacement regimen for a previously well 70kg adult. This is an illustrative guide only. A slower infusion rate should be considered in young adults (see Controversial Areas).

Fluid	Volume
0.9% sodium chloride 1L *	1000ml over 1st hour
0.9% sodium chloride 1L with potassium chloride	1000ml over next 2 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 2 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 4 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 4 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 6 hours
Re-assessment of cardiovascular status at 12 hours is mandatory, further fluid may be required	

*Potassium chloride may be required if more than 1 litre of sodium chloride has been given already to resuscitate hypotensive patients

Exercise caution in the following patients

- Young people aged 18-25 years
- Elderly
- Pregnant
- Heart or kidney failure
- Other serious co-morbidities

In these situations admission to a Level 2/HDU facility should be considered. Fluids should be replaced cautiously, and if appropriate, guided by the central venous pressure measurements.

Action 3 - Potassium replacement

Hypokalaemia and hyperkalaemia are life threatening conditions and are common in DKA. Serum potassium is often high on admission (although total body potassium is low) but falls precipitously upon treatment with insulin. Regular monitoring is mandatory.

Potassium level in first 24 hours (mmol/L)	Potassium replacement in mmol/L of infusion solution
Over 5.5	Nil
3.5-5.5	40
Below 3.5	Senior review as additional potassium needs to be given (see serious complications section)

Action 4 - Commence a fixed rate intravenous insulin infusion (FRIII)

- If a weight is not available from the patient, estimate it in kilograms
- If the patient is pregnant, use her present weight and call for immediate senior obstetric help as well
- Start a continuous FRIII via an infusion pump. This is made of 50 units of human soluble insulin (Actrapid®, Humulin S®) made up to 50ml with 0.9% sodium chloride solution. Ideally this should be provided as a ready-made infusion
- Infuse at a fixed rate of 0.1 unit/kg/hr (i.e. 7ml/hr if weight is 70kg) (See table on page 12)
- Only give a bolus (stat) dose of intramuscular insulin (0.1 unit/kg) if there is a delay in setting up a FRIII
- If the patient normally takes Lantus®, Levemir® or Tresiba® subcutaneously continue this at the usual dose and usual time (although the option exists to continue human basal insulin as well)
- Insulin may be infused in the same line as the intravenous replacement fluid provided that a Y connector with a one way, anti-siphon valve is used and a large-bore cannula has been placed

B. 60 minutes to 6 hours

Aims:

- Clear the blood of ketones and suppress ketogenesis
- Achieve a rate of fall of ketones of at least 0.5mmol/L/hr
- In the absence of ketone measurement, bicarbonate should rise by 3.0mmol/L/hr and blood glucose should fall by 3.0mmol/L/hr
- Maintain serum potassium in the normal range
- Avoid hypoglycaemia

Action 1 – Re-assess patient, monitor vital signs

- During this time, patients should be reviewed hourly initially to ensure that adequate progress is being made in reducing the ketone and/or glucose concentrations
- Consider urinary catheterisation if the patient is incontinent or anuric (i.e. not passed urine by 60 minutes)
- Consider naso-gastric tube insertion if the patient is obtunded or persistently vomiting
- If the oxygen saturation falls, then perform an arterial blood gas measurement and request a repeat chest radiograph

- Regular observations and Early Warning Score (EWS) charting as appropriate
- Maintain an accurate fluid balance chart, the minimum urine output should be no less than 0.5ml/kg/hr
- Continuous cardiac monitoring in those with severe DKA
- Give low molecular weight heparin as per NICE guidance [70]

Action 2 – Review metabolic parameters

- Measure blood ketones and capillary glucose hourly (note: if meter reads "blood glucose over 20mmol/L" or "Hi" venous blood should be sent to the laboratory hourly or measured using venous blood in a blood gas analyser until the bedside meter is within its QA range)
- Review patient's response to FRIII hourly by calculating the rate of change of ketone level fall (or rise in bicarbonate or fall in glucose).
- Assess the resolution of ketoacidosis
    - o If blood ketone measurement is available and blood ketones are not falling by at least 0.5mmol/L/hr call a prescribing clinician to increase the insulin infusion rate by 1.0 unit/hr increments hourly until the ketones are falling at target rates (also check infusion**)
    - o If blood ketone measurement is not available, use venous bicarbonate. If the bicarbonate is not rising by at least 3.0mmol/L/hr call a prescribing clinician to increase the insulin infusion rate by 1 unit/hr increments hourly until the bicarbonate is rising at this rate**
    - o Alternatively use plasma glucose. If the glucose is not falling by at least 3.0mmol/L/hr call a prescribing clinician to increase the insulin infusion rate by 1.0 unit/hr increments hourly until glucose falls at this rate. Glucose level is not an accurate indicator of resolution of acidosis in euglycaemic ketoacidosis, so the acidosis resolution should be verified by venous gas analysis**

**** If ketones and glucose are not falling as expected always check the insulin infusion pump is working and connected and that the correct insulin residual volume is present (to check for pump malfunction)**

- Measure venous blood gas for pH, bicarbonate and potassium at 60 minutes, 2 hours and 2 hourly thereafter
- If the potassium is outside the reference range, assess the appropriateness of the potassium replacement and check it hourly. If it remains abnormal after a further hour, seek immediate senior medical advice (see Action 3 p20)
- Continue the FRIII until the ketone measurement is less than 0.6mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18mmol/L (see section C)
- Do not rely on urinary ketone clearance to indicate resolution of DKA, because these will still be present when the DKA has resolved
- If the glucose falls below 14.0mmol/L, commence 10% glucose given at 125ml/hour alongside the 0.9% sodium chloride solution
- Monitor and replace potassium because it may fall rapidly

Action 3 – Identify and treat precipitating factors

Action 4

Patients presenting with newly diagnosed type 1 diabetes should be given Lantus® or Levemir® (or human NPH insulin, depending on local policy) at a dose of 0.25 units/Kg subcutaneously once daily to mitigate against rebound ketosis when they are taken off the FRIII [49].

C. 6 to 12 hours.

Aim:

The aim within this time period is to:

- Ensure that clinical and biochemical parameters are improving
- Continue IV fluid replacement
- Continue insulin administration
- Assess for complications of treatment e.g. fluid overload, cerebral oedema

- Continue to treat precipitating factors as necessary
- Avoid hypoglycaemia

Action 1 – Re-assess patient, monitor vital signs

- If the patient is not improving then seek senior advice
- Ensure a referral has been made to the specialist diabetes team

Action 2 – Review biochemical and metabolic parameters

- At 6 hours check the venous pH, bicarbonate, potassium, as well as blood ketones and glucose
- Resolution of DKA is defined as ketones less than 0.6mmol/L and venous pH over 7.3 (do not use bicarbonate as a surrogate at this stage because the hyperchloraemic acidosis associated with large volumes of 0.9% sodium chloride will lower bicarbonate levels)

If DKA resolved go to section E.

If DKA not resolved refer to Action 2 in Section B.

D. 12 to 24 HOURS

Expectation:

By 24 hours the ketonaemia and acidosis should have resolved

Aim:

- Ensure that the clinical and biochemical parameters are improving or have normalised
- Continue IV fluids if the patient is not eating and drinking
- If the patient is not eating and drinking and there is no ketonaemia move to a VRIII as per local guidelines
- Re-assess for complications of treatment e.g. fluid overload, cerebral oedema
- Continue to treat any precipitating factors as necessary
- Transfer to subcutaneous insulin if the patient is eating and drinking normally. Ensure that the subcutaneous insulin is started before the IV insulin is discontinued. Ideally give the subcutaneous fast acting insulin at a meal and discontinue IV insulin one hour later

Action 1 – Re-assess patient, monitor vital signs

Action 2 – Review biochemical and metabolic parameters

- At 12 hours check venous pH, bicarbonate, potassium, as well as blood ketones and glucose
- Resolution of DKA is defined as ketones less than 0.6mmol/L, and venous pH over 7.3

If DKA resolved go to section E.

If DKA not resolved refer to Action 2 in Section B and seek senior specialist advice as a matter of urgency.

NB: Do not rely on bicarbonate alone to assess the resolution of DKA at this point due to the possible hyperchloraemia secondary to high volumes of 0.9% sodium chloride solution. The hyperchloraemic acidosis will lower the bicarbonate and thus lead to difficulty is assessing whether the ketosis has resolved. The hyperchloraemic acidosis may cause renal vasoconstriction and be a cause of oliguria.

Expectation: Patients should be eating and drinking and back on normal insulin. If this expectation is not met within this time period it is important to identify and treat the reasons for the failure to respond to treatment. **It is unusual for DKA not to have resolved by 24 hours with appropriate treatment** and requires senior and specialist input.

E. Conversion to subcutaneous insulin

The patient should be converted to an appropriate subcutaneous regime when biochemically stable (blood ketones less than 0.6mmol/L, pH over 7.3) and the patient is ready and able to eat. Conversion to subcutaneous insulin is ideally managed by the diabetes specialist team. If the team is not available see Appendix 1. If the patient is newly diagnosed, it is essential they are seen by a member of the specialist team prior to discharge.

Specialist diabetes team input

In line with the Best Practice Tariff, if they are not already involved, the local diabetes team should be informed and the patient reviewed within 24 hours of admission [32]. Specialist diabetes team input is important to allow re-education, to reduce the chance of recurrence, and to facilitate appropriate follow up.