NHS

Diabetes

Management of Diabetic Ketoacidosis in Adults

October 2009

Supporting, Improving, Caring

Joint British Diabetes Societies
(Association of British Clinical Diabetologists, Diabetes UK, Northern Irish Diabetes Group, Scottish Diabetes Group, Welsh Endocrine and Diabetes Society and Association of Children's Diabetes Clinicians.

These guidelines are based on United Kingdom practice.
Others may find them helpful.

Contents

Introduction

There are several national and international guidelines for the management of Diabetic Ketoacidosis (DKA) in both adults and children (ISPAD 2008, McGeoch 2007, Savage 2006, BSPED 2004, ADA 2001). These guidelines reflect new clinical practice and are intended for use by anyone who manages DKA in adults.

Rationale for Guideline

Diabetic Ketoacidosis fundamentally reflects the accumulation of large quantities of ketone bodies in the blood. This reflects excessive ketone production due to the effect of relative insulin deficiency on lipid metabolism.

In the last decade patients presenting with DKA have changed, technology has developed and the way DKA is managed has evolved. Glucose is no longer the focus of treatment for managing DKA. As DKA is predominantly a disorder of fat metabolism and the target surrogate are ketones.

These guidelines are evidence based where possible but are also drawn from accumulated professional knowledge.

Definition and Diagnosis

DKA consists of the biochemical triad of hyperglycaemia, ketonaemia, and acidaemia.

Glucose > 11 mmol/L or known diabetes

Bicarbonate (HCO_3^-) < 15 mmol/L **and/or** venous pH < 7.3

Ketonaemia > 3 mmol/L **or** significant ketonuria (≥ + + on standard urine sticks)

Epidemiology

The true incidence is difficult to establish. Population-based studies range from 4.6 to 8 episodes per 1,000 patients with diabetes (Johnson 1980, Faich 1983). DKA remains a significant clinical problem in spite of improvements in diabetes care (Fishbein 1995, Umpierrez 1997).

Mortality and Morbidity

Improved understanding of the pathophysiology of DKA with close monitoring and correction of electrolytes has resulted in significant reduction in the overall mortality rate from this life-threatening condition. Mortality rates have fallen significantly in the last 20 years from 7.96% to 0.67% (Lin 2005). Death is predominantly due to underlying morbidity, such as sepsis or acute myocardial infarction (Hamblin 1989), but may occur as a consequence of metabolic disturbance.

The New Paradigm: Rationale for Best Practice

General Management Issues and Therapeutic Goals

Until the recent past the assumption in DKA has been that the blood glucose is elevated and that lowering it with fluids and insulin will reverse the ketosis and acidosis. This assumption has served us well but with recognition that blood glucose is only a surrogate for the underlying metabolic abnormality. However, recent developments permit us now to address both the underlying metabolic abnormality in DKA, ketonaemia, and to treat those presenting with acidosis secondary to ketones who have only moderately elevated blood glucose levels, so-called *euglycaemic diabetic ketoacidosis*.

'Euglycaemic' DKA (Munro 1973, Jenkins 1993) is becoming more common place. Better patient education and increased blood glucose and ketone monitoring has led to partial treatment of DKA prior to admission with lower blood glucose levels.

There is universal agreement that the most important initial therapeutic intervention in DKA is appropriate fluid replacement, followed swiftly by insulin administration.

Specialist involvement should occur as soon as practicable, ideally during the acute phase but this will of course be dependant on local circumstance. and involve an assessment of any precipitating causes and education to help prevent recurrence.

These points are highlighted below:

Fluids:

- Restoration of circulatory volume
- Clearance of ketones
- Correction of electrolyte imbalance

Insulin:

- Suppression of ketogenesis
- Reduction of blood glucose
- Correction of electrolyte imbalance

Patient Considerations:

- Precipitating factor identification
- Prevention of recurrence
- Education

Overview of Acute Management

The recommendations contained within this guideline dictate that bedside monitoring of patients with DKA is mandatory. Not only is blood glucose able to be checked at the bedside, but blood ketones (3-beta-hydroxybutyrate) measured using modern meters have also been shown to be extremely important in the management of DKA (Sheikh-Ali 2008, Bektas 2004, Vaneli 2003, Naunheim 2006). The resolution of DKA depends upon the suppression of ketonaemia and measurement of blood ketones now represents best practice in monitoring the response to treatment.

Level 2/HDU areas in the UK now have access to blood gas and blood electrolyte measurement within a few minutes of blood being taken.

We recommend therefore that glucose, ketones and electrolytes, including bicarbonate and venous pH, be assessed at the bedside.

This recommendation raises a few important issues: firstly meters used must be used by trained staff and also be subject to rigorous Quality Assessment by local biochemistry departments; laboratory results themselves still need to be checked in certain circumstances, such as when blood glucose meters are Out of Range.

FLUIDS: Typical Body deficits of water and electrolytes in DKA

The typical fluid deficit for a 70Kg person presenting with DKA is 7L which should be replaced as crystalloid. In patients with kidney failure or heart failure, as well as the elderly and adolescents, fluid deficit needs to be assessed and replaced with care.

Typical Deficits:	
Water (ml/kg)	100
Na+ (mmol/kg)	7-10
Cl- (mmol/kg)	3-5
K+ (mmol/kg)	3-5

We discuss the type of fluid to be used in Controversial Areas on page *** .

0.9% sodium chloride solution should be the fluid of choice to replace the salt and water deficit. The aim of the first few litres of fluid infusion is to replenish the central compartment deficit and to correct any hypotension as well as to counteract the effects of the osmotic diuresis.

INSULIN:

The rationale for using insulin in DKA are as follows

- Suppression of ketogenesis
- Reduction of blood glucose
- Correction of electrolyte imbalance

This requires insulin to be given at an appropriate dose and we recommend fixed dose per kilogramme infusions, see page ****.

Targets for reducing ketonaemia/glucose and raising bicarbonate:

Suggested targets are to reduce the blood ketone concentration by 0.5-1.0mmol/L/hour, and/or (if blood ketones not available) to increase the serum HCO3- by 3.0 mmol/L/hour and reduce capillary blood glucose by 3.0-5.0mmol/L/hour; if these rates are not achieved then the insulin infusion rate should be increased (see Management of DKA page****).

Glucose Concentration. 5% Glucose vs 10% Glucose: As the suggested paradigm is targeting ketones, and as euglycaemic DKA is no longer uncommon, it may be necessary to administer 10% glucose more frequently than before as the blood glucose falls in order to permit the continuation of intravenous insulin. We recommend 5% glucose when blood glucose is less than 12 mmol/L and 10% if less than 8mmol/L, see page***.

Special Patient Groups:

The following groups of patients need specialist input if at all possible and special attention needs to be paid to fluid balance.

- Elderly
- Pregnant
- Adolescents
- Heart or kidney failure
- Other serious co-morbidities

Controversial Areas:

Whilst the initial assessment and aims are not controversial, the treatment of DKA can lead to disagreement. Some of the more controversial points will now be considered. Our recommendations are given first:

Recommendations:

1. Measure venous rather than arterial bicarbonate and pH
2. Blood ketone meters should be used for near patient testing
3. Do not use bicarbonate routinely
4. Use crystalloids not colloids
5. Subcutaneous long-acting analogue insulin should be continued
6. Intravenous insulin should be administered at a fixed weight-based rate
7. Use 0.9% sodium chloride solution as fluid of choice rather than Hartmann's
8. Do not use phosphate routinely

1. Arterial or venous measurements?

Recent evidence shows that the difference between venous and arterial pH is 0.02-0.15 pH units and the difference between arterial and venous bicarbonate is -1.88 mmol/L (Herrington et all in press, Kelly 2006, Gokel 2000). This will change neither diagnosis nor management of DKA and it is not necessary to use arterial blood to measure acid base status (Ma 2003). Venous blood can be used in portable and fixed blood gas analysers and therefore venous measurements (bicarbonate, pH and K+) are easily obtained in most admitting units.

Arterial line insertion should only be performed if its use will influence management i.e. for frequent arterial oxygen level measurements or monitoring blood pressure in the critically unwell patient.

2. Blood ketone measurement?

Ketonaemia is the hallmark of DKA. Measurement of blood 3-beta-hydroxybutyrate has only recently become a practical option due to the availability of meters which can measure capillary ketone levels. Compelling evidence supports the use of this technology for diagnosis and management of DKA (Sheikh-Ali 2008, Bektas 2004, Vaneli 2003, Naunheim 2006). The resolution of DKA depends upon the suppression of ketonaemia and measurement of blood ketones now represents best practice in monitoring the response to treatment.

3. Intravenous Bicarbonate?

The acidosis in DKA resolves with adequate fluid and insulin therapy. The use of bicarbonate is not indicated (Morris 1986, Hale 1984). The acidosis may be an adaptive response as it improves oxygen delivery to the tissues by a right shift of the oxygen dissociation curve. Excessive bicarbonate may cause a rise in the CO2 partial pressure in the cerebro-spinal fluid (CSF) and may lead to a paradoxical increase in CSF acidosis (Ohman 1974 ** to check manually not on-line). In addition, the use of bicarbonate in DKA may delay the fall in blood lactate: pyruvate ratio and ketones when compared to intravenous sodium chloride solution infusion (Hale 1984). Several studies suggest that bicarbonate treatment may be implicated in the development of cerebral oedema in children and young adults (ref**).

4. Colloid versus crystalloid fluid?

Many guidelines suggest that in shocked patients initial fluid resuscitation should be with colloid. However, a recent Cochrane review did not support the use of colloid in preference to crystalloid fluid (Perel 2007).

5. Continuation of long-acting insulin analogues?

In the last few years the use of long acting basal insulin analogues has become widespread.

Continuation of long acting analogues during the initial management of DKA provides background insulin when the IV insulin is discontinued. This avoids rebound hyperglycaemia when IV insulin is stopped and should avoid excess length of stay.

6. Fixed-rate intravenous insulin infusion versus variable rate?

Patient demographics are changing and patients with DKA are now more likely to be obese, pregnant or suffering with other insulin-resistant states. Evidence has led to the re-emergence of fixed rate insulin infusions (ADA 2009). There is much to recommend this approach as fixed dose(s) per kilogramme weight, can be dove-tailed with the use of bed-side ketone measurement. Moreover it has had widespread acceptance in the management of paediatric cases (BSPED 2009).

The benefit of the fixed dose insulin regime by providing higher insulin doses throughout the treatment of DKA is a more rapid resolution of ketosis (Need Hammersley data). The fixed rate may, however, need to be adjusted if the ketone concentration is not falling fast enough, and/or if the bicarbonate level is not rising fast enough.

7. 0.9% Sodium chloride solution or Hartmann's solution?

There has been much debate in the recent past about the relative merits of these 2 solutions (Dhatariya 2007 and Rapid Responses).

0.9% Sodium chloride solution

Advantages

- Replaces sodium and chloride and deficiency
- Decades of clinical experience without adverse effects
- Ubiquity of availability
- Cost effectiveness

Disadvantages

- Hyperchloraemic metabolic acidosis with large volumes
- No buffer

Hartmann's solution

Advantages

- Contains a buffer
- Replaces potassium
- Provides an energy substrate

Disadvantages

- Cost
- Lack of familiarity in the non-emergency care environment
- Inadequate electrolyte and substrate replacement if used alone

On balance, whilst neither solution offers ideal electrolyte replacement, we feel that 0.9% sodium chloride solution should be the fluid of choice.

8. USE OF PHOSPHATE

Whole-body phosphate deficits in DKA are substantial, averaging 1 mmol/kg of body weight. There is no evidence of benefit of phosphate replacement (Wilson 1982) thus we do not recommend the routine measurement of phosphate, or use of phosphate replacement.

Complications of severe hypophosphatemia may include respiratory and skeletal muscle weakness, cardiomyopathy, and haemolytic anemia. In such patients with very low phosphate levels, replacement may be considered.

Serious Complications of DKA or its treatment

Hypokalemia and hyperkalemia

Hypokalemia and hyperkalemia are potentially life-threatening conditions during the management of DKA. There is a risk of acute pre-renal failure associated with severe dehydration and it is, therefore, recommended that no potassium be prescribed with the initial fluid resuscitation or if initial serum potassium level is >5.5mmol/L. Potassium will almost always fall, thus thereafter, it is recommended that 40 mmol KCl is added to each litre if K+ is < 5.5 mmol/L and the patient is passing urine. More may be required if K+ falls below 3.5 mmol/L. Potassium solutions should not be made up on the ward/unit by nursing or medical staff, unless it is a level 2/HDU environment and procedures in place to ensure safe administration of potassium-rich fluids. U&E's can be obtained from most modern blood gas analysers i.e. venous blood should be used and this will allow measurement of sodium, potassium and venous bicarbonate. Beware of K+ result if venepuncture was difficult.

Cerebral Oedema

Cerebral oedema causing symptoms is a relatively uncommon event in adults during DKA although asymptomatic cerebral oedema may be a common occurrence (Rosenbloom 1990). The observation that cerebral oedema usually occurs within a few hours of initiation of treatment has led to the speculation that it is iatrogenic (Hillman 1987), however, this is disputed since subclinical cerebral oedema may be present before treatment is started Hoffmann 1988). The exact cause of this phenomenon is unknown; recent studies suggest that cerebral hypoperfusion with subsequent re-perfusion may be the mechanism operating (Glaser 2001, Glaser 2008, Yuen 2008).

Cerebral oedema in DKA is more common in children than in adults. Indeed in the UK around 70 to 80% of diabetes-related deaths in children under 12 years of age are the result of cerebral oedema (Edge 1999). The UK case control study of cerebral oedema complicating DKA showed that children who developed cerebral oedema were more acidotic and after severity of acidosis was corrected for, insulin administration in the first hour (OR 12.7 [1.41–114.5], p=0.02) and volume of fluid administered over the first 4 h (OR 6.55 [1.38–30.97], p=0.01) were associated with risk (Edge 2006).

Pulmonary Oedema

Pulmonary oedema has only been rarely reported in DKA, however far from being a rare complication of DKA pulmonary oedema in children appears to be common but usually a subclinical phenomenon (Goldstein 1976). Similar to cerebral oedema the observation that pulmonary oedema usually occurs within a few hours of initiation of treatment has led to the speculation that the complication is iatrogenic and that rapid infusion of crystalloids over a short period of time increases the likelihood of this complication (Dixon 2006).

Management of Diabetic Ketoacidosis

Diabetic Ketoacidosis 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 at least within 24 hours as this improves outcomes and reduces length of stay.

Diagnosis of Diabetic Ketoacidosis

DKA consists of the biochemical triad of hyperglycemia, ketonaemia, and acidaemia.

Glucose > 11 mmol/L

HCO3- <15 mmol/L

If HCO3- not measured, venous pH <7.3

Presence of ketonaemia > 3mmol/L (see below for discussion of capillary ketone measurement)

If no blood ketone measurement available: Presence of significant ketonuria (usually 2 or more + on standard urine sticks)

Assessment of Severity

Factors that would indicate severe DKA and should prompt consideration of central line and urinary catheter insertion as well as admission to a Level 2 (High Dependency Unit) environment include:

Any of the following are surrogate markers of severity and should lead to consideration of admission to a Level 2/HDU environment and senior review:

- Ketonaemia >6 mmol/L
- Bicarbonate level < 5 mmol/L
- Venous/Arterial pH<7.1
- Hypokalaemia on admission (below local reference range)
- Abnormal GCS or AVPU score
- Oxygen saturation <92% on air (assuming normal baseline respiratory function)
- Systolic BP <100 mmHg
- Pulse >100 or <60 bpm
- Large anion gap e.g. >16 (The anion gap should be calculated in all patients presenting with hyperglycaemia and acidosis because a normal anion gap **excludes** the diagnosis of DKA). Anion Gap = (**Na^+** + **K^+**) – (**Cl^-** + **$HCO3^-$**)

Aim of Management

1. To restore circulatory volume
2. To reverse the ketonaemia
3. To treat and reverse the acidosis/electrolyte imbalance
4. To lower the blood glucose
5. To treat any co-existing illnesses or conditions that might have precipitated the DKA.

Provision of care

We recommend that local care pathways identify which units care for DKA patients and that nursing staff appropriately trained in level 2 care (High Dependency Unit-level) take the lead in hands-on patient care.

DKA Care Pathway

A: Hour 1 – Immediate management upon diagnosis

T=0 at insulin start/administration

Aims:

- Commence 0.9% sodium chloride solution
- Commence intravenous infusion of insulin
- Monitor ketones, potassium, glucose, bicarbonate, venous pH
- Establish monitoring regimen appropriate to patient
- Inform specialist diabetes team

Action 1 - Intravenous Access and Initial Investigations

- Rapid ABCDE (Airway, Breathing, Circulation, Drowsy, Environment) assessment
- Large bore IV cannulae
- Clinical assessment should include: respiratory rate; temperature; blood pressure; pulse; oxygen saturation; AVPU (A = Alert; V = Responding to voice; P = Responding to pain; U = Unconscious) or Glasgow coma scale or Early Warning Score as appropriate to local circumstance.
- Initial investigations in all patients unless deemed unnecessary
  - o capillary blood glucose
  - o capillary ketones
  - o venous plasma glucose
  - o urea and electrolytes
  - o full blood count
  - o venous blood gases
  - o blood cultures
  - o ECG
  - o chest radiograph
  - o urinalysis and culture
- Continuous cardiac monitoring
- Continuous pulse oximetry
- Consider precipitating diagnoses.

Action 2 - Restoration of Circulating Volume

Systolic BP on admission < 90mmHg

- Estimate patient weight (in Kg).
- Give 10 ml/kg aliquots of 0.9% sodium chloride solution over 10-15 minutes up to a maximum of 30 ml/kg. In practice this equates to 500 to 1000 mls given stat. If there has been no clinical improvement seek immediate senior assessment and consider involving the ITU/critical care team.
- Once SBP > 100 mmHg follow fluid replacement as below

Systolic BP on admission > 90 mmHg

Fluid	Rate (mls/hr)	Time
0.9% Sodium chloride 1L	1000	1 hours
0.9% Sodium chloride 1L With potassium chloride	500	2 hours
0.9% Sodium chloride 1L With potassium chloride	500	2 hours
0.9% Sodium chloride 1L With potassium chloride	250	4 hours
0.9% Sodium chloride 1L With potassium chloride	250	4 hours
0.9% Sodium chloride 1L With potassium chloride	250	4 hours
0.9% Sodium chloride 1L With potassium chloride	125	8 hours
Total	**7 Litres**	**25 hours**

For a 70kg patient > 100mL/kg deficit = 7L

All fluid after the 1st bag for the next 24hours should contain KCl unless urine output is less than 0.5ml/kg/hr (<30mls/h if unable to calculate) or serum potassium remains in excess of 5.5mmol/L

In the following groups, caution needs to be exercised:

- Elderly
- Pregnant
- Adolescents
- Heart or kidney failure
- Other serious co-morbidities

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

Action 3 - Potassium Replacement

Hypo and hyperkalaemia are life threatening conditions 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.

Initial Potassium level (mmol/L)	Replacement per litre 0.9% sodium chloride solution
>5.5	Nil
3.5-5.5	40mmol/L
<3.5	Admit to Level2 /HDU/ITU facility

Action 4 - Commence Intravenous Insulin Infusion

- Start an insulin infusion pump with 50units of soluble or rapid-acting Human Analogue insulin (i.e.. Actrapid®, Humulin S®, Novorapid®, Humalog® or Apidra®) made up to 50ml with 0.9% sodium chloride solution
- Infuse IV at fixed rate of 0.1unit/kg/hr (i.e. 7mls/hr if weight is 70Kg)
- Only give a stat dose of insulin if there is a delay in setting up an insulin infusion.
- If the patient normally receives insulin glargine (Lantus®) or insulin detemir (Levemir®) subcutaneously continue this at the usual dose

B: 60 minutes to 6 hours (insulin start = 0).

NEW PRINCIPLES:
The insulin infusion rate is estimated by weight. Assessment of the adequacy of the insulin regimen is determined by the rate of fall of the ketones. However, this may need revision if the rate of fall of ketones is inadequate. Nevertheless, in the absence of ketone measurement, within the first 6 hours, one can usually use blood glucose levels to assess response to therapy. If glucose is relatively normal use venous bicarbonate as the surrogate.

If ketone measurement is available the glucose level does not influence the rate of insulin infusion.

Supplementary glucose solution may need to be infused to permit the fixed dose insulin infusion rate to be maintained, and avoid hypoglycaemia, to allow the full suppression of ketone production.

Aims:

- clear the blood of ketones and suppress ketogenesis
- ketones to fall by at least 0.5 mmol/L/hr
- blood glucose to fall by 3-5 mmol/L/hr
- maintain serum potassium in normal range

Action 1 - Re-assess patient, monitor vital signs

- Consider urinary catheterisation if appropriate
- Consider naso-gastric tube if patient obtunded or if persistently vomiting
- If oxygen saturation falling perform arterial blood gases and request repeat chest radiograph

Action 2 - Review metabolic parameters

- Measure capillary blood ketones and capillary glucose hourly (note if meters read blood glucose >20 mmol/L or "HI" then venous blood should be

sent to the laboratory hourly until meter is within its QA range)

- Review patient's response to intravenous insulin infusion hourly by calculating rate of change of ketone level fall (or glucose).
    - o If capillary ketones not falling by at least 0.5 mmol/L/hr call a prescribing clinician to increase insulin infusion rate by 1 unit/hr increments hourly until ketones falling falls at target rates
    - o If, due to unforeseen circumstances, capillary ketones are not available use plasma glucose. If it is not falling by at least 3 mmol/L/hr call a prescribing clinician to increase insulin infusion rate by 1 unit/hr increments hourly until glucose falling falls at target rates.
- Venous blood gas for pH, bicarbonate and potassium at 60 minutes and 2 hours and 2 hourly thereafter
- If potassium outside reference range, assess appropriateness of potassium replacement and check it hourly. If abnormal next hour seek immediate senior medical advice.
- Continue fixed rate intravenous insulin infusion until ketones <0.3 mmol/L, venous pH >7.3 and/or venous bicarbonate>18 mmol/L
- NB: If ketones and glucose 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)
- In the unlikely event of glucose becoming < 12 mmol/L add in 5% glucose with 40 mmol/litre KCl 125mls/hour

In order to avoid hypoglycaemia (and iatrogenic morbidity/mortality):

Glucose monitoring	Fluids
If capillary blood glucose < 12 mmol/L in first 16 hours	Start 5% glucose with KCl infusion via 2nd line at rate of 125 ml/hr
If capillary blood glucose < 8mmol/L in first 16 hours	Change to 10% glucose with KCl at rate of 125 ml/hr

** WE GOT TO HERE!!!! ** further edits below need to be confirmed

Action 3 - Consider Precipitating Factors

- If precipitating factor identified, treat.

Action 4 - Monitoring

- Regular observations and Early Warning Score (EWS) charting as appropriate
- Fluid balance chart
- Monitor conscious level – AVPU or Glasgow coma scale
- Continuous cardiac monitoring in those with severe DKA
- Nasogastric tube if protracted vomiting and/or unprotected airway (GCS <8)
- Consider the use of low molecular weight heparin, this is primarily a clinical decision.

C: 6 to 12 hours.

Aim: The aim within this time period is to continue clearing the blood of ketones and suppress ketogenesis and continue ongoing rehydration.

- ketones to fall by at least 0.5 mmol/L/hr
- blood glucose to fall by 3-5 mmol/L/hr and then be maintained between 8 and 12 mmol/L
- maintain serum potassium in normal range

Action 1 - Re-assess Patient, Monitor Vital Signs

- Catheterise if oliguric

Action 2 - Review biochemical and metabolic parameters

- U&Es and laboratory glucose at end of ***Hour 8***
- Heparinised venous sample for pH, bicarbonate and potassium at 6, 8, 10 and 12hrs, aiming to keep K^+ between 4.0-5.0mmol/L
- Review patient response to insulin infusion pump
- Measure capillary blood glucose and ketones hourly
- If capillary blood glucose not dropping by 5mmol/L/hr and capillary ketones by 0.5-1.0mmol/L/hr, increase infusion rate by 0.05 units/kg/hr
- Repeat increase hourly if necessary to achieve reduction in capillary blood glucose and capillary ketones
- Continue fixed rate insulin until blood ketone level <0.3mmol/L, venous pH>7.3 and venous bicarbonate>18mmol/L
- Add in or continue 5% glucose with 40mmol/litre KCl 125mls/hour when capillary blood glucose less than 12.0mmol/L
- When capillary blood glucose less than 8.0mmol/L start, or continue, 500ml 10% glucose with KCl as appropriate at 125mls/hour.
- Maintain capillary blood glucose between 8.0 and 12.0mmol/L
- Glucose to run concurrently with 0.9% sodium chloride in the first 24 hours
- Continue insulin at established rate
- NB: If ketones and glucose 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)

D: 12 to 24 HOURS

Aim: The aim within this time period is to continue clearing the blood of ketones and suppress ketogenesis, continue ongoing rehydration and consideration for converting to subcutaneous insulin.

- ketones to fall by at least 0.5 mmol/L/hr and be cleared by 24 hours
- blood glucose to fall by 3-5 mmol/L/hr and then be aminteained between 8 and 123 mmol/L
- maintain serum potassium in normal range

Action 1 - Re-assess Patient, Monitor Vital Signs

Action 2 - Review biochemical and metabolic parameters

- As in Stage 3, except U&Es and laboratory glucose at end of ***Hour 24***
- NB: If ketones and glucose 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)

E: Subsequent management greater than 24 hours.

Aim: The aim within this time period is to identify and treat reasons for the inability to convert to subcutaneous insulin.

Action 1- Re-assess Patient, Monitor Vital Signs

Action 2 - Review biochemical and metabolic parameters

If the patient is eating and drinking a variable insulin infusion ("sliding scale") could be started, so long as pH>7.3, ketones <0.3 mmol/L and capillary blood glucose <15 mmol/L

- However, if the patient is eating and drinking, consideration may be given to starting on subcutaneous insulin directly, see below.
- Check laboratory U&Es daily
- Measure capillary blood glucose 1-2 hourly while on IV insulin
- Continue 5% or 10% glucose with 20 mmol KCl (unless hyperkalaemic)125mls/hour and maintain capillary blood glucose between 8.0 - 12.0mmol/L
- Supplemental 0.9% sodium chloride solution may be needed to prevent hyponatraemia in some cases

Action 3 - Identify and treat conditions preventing conversion to subcutaneous insulin

F: Conversion o subcutaneous insulin.

- Convert back to an appropriate subcutaneous regime when biochemically stable (capillary ketones<0.3, pH>7.3) and the patient is ready and able to eat.

Calculating subcutaneous insulin dose in insulin-naïve patients

1. On fixed rate of insulin regime (0.1 units/kg)

The Total Daily Dose (TDD) of insulin - this estimate is based on several factors, including the patient's sensitivity to insulin, degree of glycaemic control, insulin resistance, weight, and age. The TDD can be calculated by multiplying the patient's weight (in kg) by **0.5 to 0.75 units**. Use 0.75units/kg for those thought to be more insulin resistant i.e. teens, obese.

Example, a 72kg person would require approximately 72 x 0.5 units or 36 units in 24 hours

Calculating a Basal Bolus (QDS) Regimen:

Give 50% of total dose with the evening meal in the form of long acting insulin and divide remaining dose equally between pre-breakfast, pre-lunch and pre-evening meal.

	Pre-breakfast	Pre-lunch	Pre-evening meal	Bedtime
Rapid acting insulin, e.g Apidra®/Humalog®/NovoRapid®	6 units	6 units	6 units	
Long acting insulin, e.g. Lantus®/Levemir®			18 units	

Administer 1st dose of s/c insulin prior to breakfast or lunch preferably. Administer before evening meal if monitoring can be guaranteed, **NEVER BEFORE BED**. Continue intravenous insulin for 60 minutes after the subcutaneous injection.

If starting basal-bolus ensure long-acting analogue and rapid acting insulin are given together before the intravenous insulin is taken down and thereafter give the long acting analogue at the time prescribed.

Calculating a Twice daily (BD) Regimen

Give 50% of total dose pre-breakfast and 50% pre-evening meal, using a pre-mixed insulin.

	Pre-breakfast	Pre-lunch	Pre-evening meal	Pre-supper
Pre-mixed Insulins e.g.Humalog Mix 25 or 50, NovoMix 30, Mixtard 30, Humulin M3	18 units		18 units	

Administer 1st dose of s/c insulin prior to breakfast preferably or evening meal if monitoring can be guaranteed, **NOT BEFORE BED**. Continue insulin sliding scale for 30 minutes then discontinue sliding scale.

2. On patients on iv sliding scale

Add up the total amount of insulin required in 24hrs on IV insulin sliding scale not on the fixed rate insulin regime. Divide the insulin dose as described above for basal bolus regime or bd regime as above.

Restarting insulin for patients already on it.

- Before automatically putting the patient on their previous regime, check the HbA_{1c} (if not in the last 3 months)
- If ≤7.5% restart their usual insulin regime as above for basal bolus or bd regimen.
- If >7.5% discuss the appropriate insulin regime with the Diabetes Team.
- If there is a delay in the response from the Diabetes Team, calculate the insulin dose from the 24hr IV insulin from the sliding scale requirement as above.
- If previously on a long acting insulin analogue such as Lantus® or Levemir®,this should not have been stopped and thus it will be a matter of restarting the rapid analogue analogue insulin if glycaemic control is acceptable.

Specialist Diabetes team Input

If not already involved the local diabetes team should be informed and the patient reviewed as soon as possible. Diabetes team input is important to allow re-education, to reduce the chance of recurrence and to facilitate follow up.

Implementation of the Guidelines

Repeated audits by many diabetes units in all constituent UK countries have repeatedly demonstrated poor adherence to local (or national) guidelines for the management of DKA. There are therefore 2 main problems are faced:

1. the guidelines need to be updated as required
2. the guideline must be implemented

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Commissioning of Care

Diabetic Ketoacidosis is a recognised common medical emergency and as such must be treated appropriately.

For this to occur the various Health Economies within the United Kingdom must address its' management in the context of provision of expert medical and nursing input within the secondary care sector. Commissioners, Primary Care Providers, Local Diabetes Networks and Diabetes Directorates within the Acute Trusts, should co-operate and ensure the Quality Indicators and Audit Standards set out below are met.

Quality Indicators

Every Acute Trust should have a local management plan in place based upon these, or other authoritive guidelines, that are not out of date (i.e. guidelines must be current and be valid and not be used after their Review Date, if there is no review date, they should not be used).

Every Acute Trust should have nominated Care Areas for Diabetic Ketoacidotic Patients

Every Acute Trust should have trained Health Care Workers available to measure capillary ketone levels 24 hours per day.

Every Acute Trust should have a Quality Assurance Scheme in place to ensure accuracy of blood glucose and ketone meters.

We recommend that every Acute Trust uses a Treatment Pathway document as adherence to guidelines for this condition is very poor and integrated Pathway Documents will help adherence to guidelines (example given in Appendix ***).

Name .....

Hospital Number .....

Ward ..... Site .....

Date .....

Patient Name:

Hospital Number:

DoB:

Diabetic Ketoacidosis – Results

Diagnostic Tests

Date:

Time:

Name of Clinician entering test results (PRINT):

Signature:

Capillary glucose	Lab glucose	Capillary ketones	Ketonuria (if no capillary ketones available)	pH	HCO3-	Na+	K+	Cl-	Anion gap

Name .....

Hospital Number .....

Ward ..... Site .....

Date .....

Monitoring

Time (Hours from insulin)	First results	0	1	2	3	4	5	6	8	10	12	16	20	24
Glucose														
Ketones (blood)														
Ketones (Urine)														
Urea														
Sodium														
Potassium														
Creatinine														
Bicarbonate														
Urine output														

Name .....

Hospital Number .....

Ward ..... Site .....

Date .....

Add Potassium using pre-prepared bags only as follows:
>5.5 mmols/l None 4 – 5.4mmol/l 10 mmol in each 500 ml
<4mmol/l 20 mmol in each 500ml

PREVIOUS DAY INTAKE | PREVIOUS DAY OUTPUT | BALANCE

THE INTAKE RECORD MUST ONLY DETAIL COMPLETED VOLUMES OF DRINKS/INFUSIONS

Intake		**Output**
	Device no.	
1.....	.....	1.....
2.....	.....	2.....
3.....	.....	3.....
4.....	.....	
5.....	.....	

	INTAKE (mls)							**OUTPUT (mls)**					
B/F													
Time	Oral						Running Total	Urine					Running Total
01.00													
02.00													
03.00													
04.00													
05.00													
06.00													
07.00													
08.00													
09.00													
10.00													

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18.00													
19.00													
20.00													
21.00													
22.00													
23.00													
24.00													
24hr													

Name .....

Hospital Number .....

Ward ..... Site ..... Date .....

The Pennine Acute Hospitals NHS
NHS Trust

APPENDIX X

INTRAVENOUS INSULIN INFUSION
Add 50 units soluble insulin (Actrapid®/Humulin S®/NovoRapid®Humalog®) to 49.5ml 0.9% sodium chloride solution in a syringe. Patients weight Kg
Use new column (delete previous prescription) each time insulin prescription is changed

PRESCRIPTION				ADMINISTRATION				
	Insulin units/Kg/hour	Insulin units/hour		Batch number	Start time	Signature	Finish time	Signature
Name								
Signature								
Bleep number								
Date								
Time								

Name .....

Hospital Number .....

Ward ..... Site .....

Date .....

The Pennine Acute Hospitals NHS
NHS Trust

TO BE COMPLETED BY NAMED NURSE							
SYRINGE DRIVER CONTROLLED INSULIN INFUSION (record hourly)							
Time	Meter Blood ketone mmol/L	Meter blood glucose mmol/L	Rate units/ hour	Volume left in syringe (ml)	Volume infused in one hour (ml)	Total volume infused (ml)	Signature

Management of Diabetic Ketoacidosis in Adults (>70 kgs)

Stage 1 – Immediate Management

1 Initial investigations

- Monitor observations including sats, resp rate, GCS, urine output **hourly** ☐
- FBC, U&Es, Chloride, Bicarb, Glc ☐
- Capillary blood ketones and glucose ☐
- ECG (consider cardiac monitoring) ☐
- Consider blood cultures/CXR/MSSU ☐

2 Interventions

- IV cannula x 2 (consider central line) ☐
- Catheter ± central line if oliguric or evidence of poor LV/renal function ☐
- NG tube if vomiting or ,GCS ☐

3 Insulin

Fixed rate infusion 0.1units/kg/h
Delay insulin treatment for 1 hour after fluids if under 26 years of age ☐

4 Fluids

0.9% Sodium chloride solution: 1000ml over 1h ☐

Stage 2 – On-going Management – 2-6 hours

1 Investigations

Re-assess patient hourly ☐

Capillary glucose & ketones, Venous Na+, K+ & bicarb

- Hour 1 ☐ Hour 4 ☐
- Hour 2 ☐ Hour 5 ☐
- Hour 3 ☐ Hour 6 ☐

2 Insulin

Continue fixed rate infusion unless glucose/ketones nor improving ☐

3 Fluids ☐

0.9% sodium chloride solution + KCl 1000ml/1-2h
then 0.9% Sodium chloride solution + KCl 1000ml/2-4h then depending on clinical response

Once blood glucose <15mmol/L, **10% glucose** 100ml/h

Reduce fluid rate for < 25yrs ☐

4 Potassium from 2nd bag of fluid ☐

if K > 6.0, recheck urgently

if K > 5.5, no potassium I

if K 3.5-5.5, add 40mmol/L KCl

if K <3.5, add 60mmol/L KCl

Max rate of KCl infusion 20mmol/h

Refer to Diabetes Team ASAP ☐

In-patient review ☐

?Precipitating factor ☐

Out-patient follow-up ☐

No improvement?

Insulin added to pump?
Pump/infusion set/cannula working?
Glucose should fall by 4-6mmol/h

D/W SpR/Cons - ?increase insulin

Bicarbonate usually unnecessary
Only use on HDU/ITU
with Consultant approval

Cerebral oedema
Monitor for headaches or, ↓ GCS
If suspicion, call consultant

Consider **ARDS** if increasing hypoxia

Consider HDU/ITU referral if
↓ level of consciousness
airway or fluid balance problems

Stage 3 – Subsequent Management (timing varies)

1 Investigations

Re-assess patient hourly ☐

Capillary glucose & ketones, Venous Na+, K+ & bicarb

- Hour 8 ☐ Hour 16 ☐
- Hour 10 ☐ Hour 20 ☐
- Hour 12 ☐ Hour 24 ☐

2 Insulin

Continue fixed rate insulin until biochemistry satisfactory ☐

If venous pH <7.3, bicarb >18mmol/L, capillary ketones <0.3mmol/L ☐

Not eating	Variable rate insulin "sliding scale" ☐
Eating & Drinking	Back to subcutaneous insulin ☐

3 Fluids

Continue 0.9% sodium chloride solution + KCL until fluid resuscitation complete

Continue 10% glucose until DKA has resolved