JBDS-IP Joint British Diabetes Societies for inpatient care

The Management of Diabetic Ketoacidosis in Adults*

Revised June 2021

*For 16-18 year olds
Use this guideline if managed by the adult diabetes team
but if managed by the paediatric team follow:
https://www.bsped.org.uk/media/1798/bsped-dka-guideline-2020.pdf

ABCD Association of British Clinical Diabetologists
DIABETES UK KNOW DIABETES. FIGHT DIABETES.
DISN UK GROUP
UKCPA CLINICAL PHARMACY ASSOCIATION
Royal College of Nursing
Royal College of Physicians
The Association for Clinical Biochemistry & Laboratory Medicine
Diabetes Network NI
WEDS welsh endocrine and diabetes society
NHS SCOTLAND

This document is coded JBDS 02 in the series of JBDS documents:

Other JBDS documents:

The hospital management of hypoglycaemia in adults with diabetes mellitus	*JBDS 01*
The management of diabetic ketoacidosis in adults	*JBDS 02*
Management of adults with diabetes undergoing surgery and elective procedures: improving standards	*JBDS 03*
Self-management of diabetes in hospital	*JBDS 04*
Glycaemic management during the inpatient enteral feeding of stroke patients with diabetes	*JBDS 05*
The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes	*JBDS 06*
Admissions avoidance and diabetes: guidance for clinical commissioning groups and clinical teams	*JBDS 07*
Management of hyperglycaemia and steroid (glucocorticoid) therapy	*JBDS 08*
The use of variable rate intravenous insulin infusion (VRIII) in medical inpatients	*JBDS 09*
Discharge planning for adult inpatients with diabetes	*JBDS 10*
Management of adults with diabetes on the haemodialysis unit	*JBDS 11*
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A good inpatient diabetes service	*JBDS 14*
Inpatient care of the frail older adult with diabetes	*JBDS 15*
Diabetes at the front door	*JBDS 16*
The Management of Glycaemic Control in Patients with Cancer	*JBDS 17*

These documents are available to download from the ABCD website at https://abcd.care/joint-british-diabetes-societies-jbds-inpatient-care-group , the Diabetes UK website at www.diabetes.org.uk/joint-british-diabetes-society and the chemotherapy board website at www.ukchemotherapyboard.org

These guidelines can also be accessed via the Diabetologists (ABCD) app (need ABCD membership to access the app)

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Statement for inpatient guidelines

These guidelines have been developed to advise the treatment and management of diabetic ketoacidosis in adults.

The guideline recommendations have been developed and reviewed by a multidisciplinary team led by the Joint British Diabetes Society (JBDS) and including representation from Primary Care Diabetes Society, Diabetes UK. People with diabetes have been involved in the development of the guidelines via stakeholder events organised by Diabetes UK.

It is intended that the guideline will be useful to clinicians and service commissioners in planning, organising and delivering high quality diabetes inpatient care. There remains, however, an individual responsibility of healthcare professionals to make decisions appropriate to the circumstance of the individual, informed by them and/or their guardian or carer and taking full account of their medical condition and treatment.

When implementing this guideline full account should be taken of the local context and in line with statutory obligations required of the organisation and individual. No part of the guideline should be interpreted in a way that would knowingly put staff, those with diabetes or anyone else at risk.

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The information contained in this guidance is a consensus of the development and consultation groups' views on current treatment. It should be used in conjunction with any local policies/procedures/guidelines and should be approved for use according to the trust clinical governance process. Care has been taken in the preparation of the information contained in the guidance. Nevertheless, any person seeking to consult the guidance, apply its recommendations or use its content is expected to use independent, personal medical and/or clinical judgement in the context of the individual clinical circumstances, or to seek out the supervision of a qualified clinician. The group makes no representation or guarantee of any kind whatsoever regarding the guidance content or its use or application and disclaim any responsibility for its use or application in any way.

To enable the guideline to stay relevant, it is envisaged that all of the JBDS guidelines will be updated or reviewed each year. As such these are 'living' documents – designed to be updated based on recently published evidence or experience. Thus, feedback on any of the guidelines is welcomed. Please email christine.jones@nnuh.nhs.uk with any comments, suggestions or queries.

Conflict of interest statement

The authors declare no conflicts of interest

Lead authorship
Prof Ketan Dhatariya, Norfolk and Norwich University Hospitals NHS Foundation Trust

Previous authors
Dr Mark Savage, Bendigo Health, Australia

Supporting organisations
Association of British Clinical Diabetologists (ABCD), Chair: Dr Dipesh Patel (Royal Free, London)
Diabetes Inpatient Specialist Nurse (DISN) UK Group, Chair: Erwin Castro (East Sussex)
Diabetes UK: David Jones, Assistant Director Policy, Campaigns and Improvement
Joint British Diabetes Societies (JBDS) for Inpatient Care, Chair: Professor Ketan Dhatariya (Norwich)

Writing group of previous versions
Anne Claydon, Barts Health NHS Trust
Dr Philip Dyer, Heart of England NHS Foundation Trust
Dr Philip Evans, Pontypridd and Rhondda NHS Trust
Dr Atir Khan, Hywel Dda Health Board
Dr Anne Kilvert, Northampton General Hospital NHS Trust
Dr Nicky Leech, The Newcastle upon Tyne Hospitals NHS Foundation Trust
Dr Nicholas Levy, West Suffolk Hospitals NHS Foundation Trust
Dr Gerry Rayman, The Ipswich Hospitals NHS Trust
Dr Alan Rees, Cardiff and Vale University Health Board
Dr Maggie Sinclair-Hammersley, Oxford University Hospitals NHS Trust

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Distributed and incorporated comments from:
Diabetes Inpatient Specialist Nurse (DISN) UK Group membership
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Intensive Care Society
Royal College of Nursing

We would also like to thank the service user representatives whose input has informed the development of these guidelines.

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Foreword

Diabetic ketoacidosis (DKA) is a frequent and potentially life-threatening complication of type 1 diabetes. Though preventable and despite advances in monitoring technologies, insulin therapeutics and insulin delivery systems, the rates of both community and hospital acquired DKA remain largely unchanged. Although mortality today is relatively low it is generally accepted that mismanagement after hospital admission is an important contributory factor to in hospital mortality, morbidity, increased length of stay and high readmission rates. The first Joint British Diabetes Societies (JBDS) guidance document on the management of DKA published in over a decade ago, recognised that there was a large variation in management across the UK with many hospital trusts having no trust wide guidelines and where these existed they were not always followed. The JBDS guidance based on evidence where it existed and consensus opinion from a multidisciplinary group of experienced practicing specialists was welcomed by the diabetes community. It has been almost universally adopted in the United Kingdom, has had world-wide recognition, and together with the updated guidance in 2013 has been downloaded over 100,000 times.

The 2021 guidance is a welcome and a timely update as there has been much new learning since previous publications.

Recently attention has been drawn to the extremely high prevalence of DKA in adolescence. In the UK young people aged between 16 and 18 may be admitted to a paediatric or adult unit. The paediatric and adult guidelines differ particularly around fluid replacement. This has led to confusion amongst admitting staff as to which guidance should be followed. In this updated guidance there is a useful discussion as to which guideline should be followed, with a sensible recommendation that the guidance used should be determined by the ward to which the person with diabetes is admitted. This will ensure that that the staff only use guidance they are familiar with, so reducing the potential for mistakes.

The updated guidance includes the new recommendation to consider de-escalating the insulin infusion rate from 0.1units/kg/hr to 0.05 units/kg/hr once the blood glucose falls below 14 mmol/L as a UK wide based on audit of the previous guidelines that found hypoglycaemia and hypokalaemia were not infrequent if the infusion rate was kept at 0.1 unit/kg/hr ever though 10% glucose had been commenced.

This guidance also addresses the new problem of DKA and particularly euglycaemic DKA in those treated with SGLT-2 inhibitors. It also for the first time considers ketosis prone type 2 diabetes and the complex issue of the management of DKA in people with end stage renal failure or on dialysis.

As with the previous guidelines this is clearly written and at the beginning of the document there is a very easy to follow single page treatment pathway.
Again the authors should be congratulated on their important contribution to the care of people with diabetes who suffer this life threating complication and for their commitment to continuing to update the guidelines in the light of further evidence. The widespread use of this guidance should significantly improve the care of people admitted with DKA.

Dr G Rayman
GIRFT co-lead for Diabetes and Diabetes UK Clinical Lead for Inpatient Diabetes Care
April 2021

Acronyms:

NPSA - National Patients Safety Agency

ISPAD – International Society for Pediatric and Adolescent Diabetes

BSPED - British Society of Paediatric Endocrinology and Diabetes

FRIII – Fixed rate intravenous insulin infusion

VRIII – Variable rate intravenous insulin infusion

Nursing management

This guideline should be used in conjunction with the document entitled "Nursing management for Diabetic Ketoacidosis (DKA)" which can also be found on the ABCD or Diabetes UK websites.

Changes since the 2013 guidance

- The expansion of the age group for which this guideline can be used if they are looked after by adult diabetes teams – i.e. for young people aged 16-18 years, it is considered appropriate for them to be managed using local adult guidelines that the teams are familiar with rather than using potentially unfamiliar paediatric guidelines.
  Where individuals aged 16-18 are managed by paediatric teams, the paediatric guidelines should be followed.https://www.bsped.org.uk/media/1798/bsped-dka-guideline-2020.pdf
- When the glucose concentrations drops to ≤14.0 mmol/L **consider** reducing the rate of intravenous insulin infusion to 0.05 units/kg/hour to reduce the risk of developing hypoglycaemia and / or hypokalaemia
- A short section on managing DKA in those with end stage renal failure or on dialysis has been added
- The algorithm for the management of DKA is now near the front of the guideline to make it easier to access

Uptake of the 2010 and 2013 guidelines

By 2018, the 2010 and 2013 versions of this guideline had been viewed almost 107,000 times (1). The websites for ABCD and Diabetes UK show that further views and download since then number in the tens of thousands. A survey of 50 UK clinical teams in 2018 showed that this guideline had been adopted or adapted by 92% of them and 91% rated them as good or very good (1). As of February 2021, they have been cited by others over 350 times.

Single page treatment pathway for DKA

Where individuals aged 16-18 are managed by paediatric teams, the paediatric guidelines should be followed: https://www.bsped.org.uk/media/1798/bsped-dka-guideline-2020.pdf

Diagnostic criteria: **all three of the following must be present**

- capillary blood glucose above 11 mmol/L
- capillary ketones above 3 mmol/L or urine ketones ++ or more
- venous pH less than 7.3 and/or bicarbonate less than 15 mmol/L

BOX 1: Immediate management: time 0 to 60 minutes

(T=0 at time intravenous fluids are commenced)

If intravenous access cannot be obtained request critical care support immediately

Action 1: Commence 0.9% sodium chloride solution (use a large bore cannula) via an infusion pump
See Box 2 for rate of fluid replacement

Action 2: Commence a fixed rate intravenous insulin infusion (FRIII). (0.1unit/kg/hr based on estimate of weight) 50 units human soluble insulin (Actrapid® or Humulin S®) made up to 50ml with0.9% sodium chloride solution. If patient normally takes long acting insulin analogue (glargine, detemir, degludec) continue at usual dose and time

Action 3: Assess patient
- Respiratory rate; temperature; blood pressure; pulse; oxygensaturation
- Glasgow Coma Scale
- Full clinical examination

Action 4: Further investigations
- Capillary and laboratory glucose
- Venous BG
- U&E and FBC
- Blood cultures
- ECG
- CXR
- MSU

Action 5: Establish monitoring regimen
- Hourly capillary blood glucose
- Hourly capillary ketone measurement if available
- Venous bicarbonate and potassium at 60 minutes, 2hours and 2 hourly thereafter
- 4 hourly plasma electrolytes
- Continuous cardiac monitoring if required
- Continuous pulse oximetry if required

Action 6: Consider and precipitating causes and treat appropria

HDU/level 2 facility and/or insertion of central line may be required in following circumstances (request urgent senior review)

- Young people aged 18-25 years
- Elderly
- Pregnant
- Heart or kidney failure
- Other serious co-morbidities
- Severe DKA by following criteria
  - Blood ketones above 6 mmol/L
  - Venous bicarbonate below 5 mmol/L
- Venous pH below 7.1
- Hypokalaemia on admission (below 3.5 mmol/L)
- GCS less than 12
- Oxygen saturation below 92% on air (Arterial blood gases required)
- Systolic BP below 90 mmHg
- Pulse over 100 or below 60 bpm
- Anion gap above16 [Anion Gap = $(Na^+ + K^+) - (Cl^- + HCO_3^-)$]

BOX 2: Initial fluid replacement

Restoration of circulating volume is priority

Systolic BP (SBP) below 90mmHg

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

- Give 500mls 0.9% sodium chloride solution over 10-15 minutes. If SBP remains <90mmHg repeat whilst awaiting senior input. Most people require between 500-1000mls given rapidly
- Consider involving the ITU / critical care team
- Once SBP is >90mmHg, give 1L 0.9% sodium chloride over the next 60 minutes. The addition of potassium is likely to be required in this second litre of fluid

Systolic BP on admission 90 mmHg and over

- Give 1L 0.9% sodium chloride over the first 60 minutes

Potassium replacement Potassium level (mmol/L)	Potassium replacement mmol/L of infusion solution
> 5.5	Nil
3.5-5.5	40 mmol/L
< 3.5	senior review – additional potassium required

BOX 3: 60 minutes to 6 hours

Aims of treatment:
- Rate of fall of ketones of at least 0.5 mmol/L/hr OR bicarbonate rise 3 mmol/L/hrand blood glucose fall 3 mmol/L/hr
- Maintain serum potassium in normal range
- Avoid hypoglycaemia

Action 1: Re-assess patient, monitor vital signs
- Hourly blood glucose (lab blood glucose if meter reading 'HI')
- Hourly blood ketones if meter available
- Venous blood gas for pH, bicarbonate and potassium at 60 minutes, 2 hours and 2 hourly thereafter
- If potassium is outside normal range, re-assess potassium replacement and checkhourly. If abnormal after further hour seek immediate senior medical advice

Action 2: Continue fluid replacement via infusion pump as follows:
- 0.9% sodium chloride 1L with potassium chloride over next 2 hours
- 0.9% sodium chloride 1L with potassium chloride over next 2 hours
- 0.9% sodium chloride 1L with potassium chloride over next 4 hours
- Add 10% glucose 125ml/hr if blood glucose falls below 14 mmol/L
- **Consider** reducing the rate of intravenous insulin infusion to 0.05 units/ kg/hour when glucose falls below 14 mmol/L

More cautious fluid replacement in young people aged 18-25 years, elderly, pregnant, heart or renal failure. (Consider HDU and/or central line)

Action 3: Assess response to treatment

Insulin infusion rate may need review if
- Capillary ketones not falling by at least 0.5 mmol/L/hr
- Venous bicarbonate not rising by at least 3 mmol/L/hr
- Plasma glucose not falling by at least 3 mmol/L/hr
- Continue FRIII until ketones less than 0.6 mmol/L, venous pH >7.3 and/or venous bicarbonate over 18 mmol/L

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

If equipment working but response to treatment is inadequate, increase insulin infusionrate by 1 unit/hr increments hourly until targets achieved.

Additional measures
- Regular observations and Early Warning Score (NEWS2)
- Accurate fluid balance chart, minimum urine output 0.5ml/kg/hr
- Consider urinary catheterisation if incontinent or anuric (not passed urine) by 60 minutes
- Nasogastric tube with airway protection if patient obtunded or persistently vomiting
- Measure arterial blood gases and repeat chest radiograph if oxygen saturation less than 92%
- Thromboprophylaxis with low molecular weight heparin
- Consider ECG monitoring if potassium abnormal or concerns about cardiac status

BOX 4: 6 to 12 hours

Aims:
- Ensure clinical and biochemical parameters improving
- Continue IV fluid replacement
- Avoid hypoglycaemia
- Assess for complications of treatment e.g. fluid overload, cerebral oedema
- Treat precipitating factors as necessary

Action 1: Re-assess patient, monitor vital signs
- If patient not improving by criteria in Box 3, seek senior advice
- Continue IV fluid via infusion pump at reduced rate
  - 0.9% sodium chloride 1L with KCl over 4 hours
  - 0.9% sodium chloride with KCl over 6 hours
- Add 10% dextrose 125mls/hr if the glucose falls below 14 mmol/L
- **Consider** reducing the rate of intravenous insulin infusion to 0.05 units/ kg/hour when glucose falls below 14 mmol/L

Reassess cardiovascular status at 12 hours; further fluidmay be required

Check for fluid overload

Action 2 – Review biochemical and metabolic parameters
- At 6 hours check venous pH, bicarbonate, potassium, capillary ketones and glucose
- Resolution of DKA is defined at ketones <0.6 mmol/L **AND** venous pH >7.3 (do not use bicarbonate as a marker at this stage)
- Ensure a referral has been made to the diabetes team
- **If DKA not resolved review insulin infusion (see BOX 3Action 3)**
- **If DKA resolved go to BOX 6**

BOX 5: 12 to 24 HOURS

Expectation: By 24 hours the ketonaemia and acidosis should have resolved. Request senior review is not improving

Aim:
- Ensure that clinical and biochemical parameters are continuing to improve or are normal
- Continue IV fluid replacement if not eating and drinking
- If ketonaemia has cleared and the person is not eating or drinking, move to a variable rate intravenous insulin infusion (VRIII) as per local guidelines
- Reassess for complications of treatment, e.g. fluid overload, cerebral oedema
- Continue to treat precipitating factors
- Transfer to subcutaneous insulin if the person is eating and drinking normally and biochemistry is normal

Action 1 – Re-assess patient, monitor vital signs

Action 2 – Review biochemical and metabolic parameters
- At 12 hours check venous pH, bicarbonate, potassium, capillary ketones and glucose
- Resolution is defined as ketones <0.6 mmol/L, venous pH>7.3
- If not resolved review fluid **Box 4 Action 1** and insulin infusion **Box 3 Action 3**

If DKA resolved go to Box 6

BOX 6: Resolution of DKA

Expectation: Patient should be eating and drinking and back on normal insulin

If DKA not resolved identify and treat the reasons for failure to respond. **This situation is unusual** and requires senior and specialist input

Transfer to subcutaneous insulin

Convert to subcutaneous regime when biochemically stable (capillary ketones less than 0.6 mmol/L **AND** pH over 7.3) and the patient is ready and able to eat. **Do not discontinue intravenous insulin infusion until 30 minutes after subcutaneous short acting insulin has been given** Conversion to subcutaneous insulin should be managed by the Specialist Diabetes Team. If the team is not available use local guidelines. If the patient is newly diagnosed it is essential they are seen by a member of the specialist team prior to discharge

Arrange follow up with specialist team

Represented: Association of British Clinical Diabetologists; British Society for Endocrinology and Diabetes and Association of Children's Diabetes Clinicians; Diabetes Inpatient Specialist Nurse (DISN) Group; Diabetes UK; Diabetes Network Northern Ireland; Society of Acute Medicine; Welsh Endocrine and Diabetes Society, Scottish Diabetes Group.

Introduction

Since it was first published in 2010, this guideline, and its update published in 2013, have been widely adopted or adapted across the UK and other parts of the world. It is often seen as the standard of care for the condition. Together with the guideline from the American Diabetes Association (ADA) (2), this remains one of the most frequently cited guidelines on the management of DKA. By 2018, the original version had been accessed, read or downloaded over 100,000 times from the ABCD and Diabetes UK websites. In addition the published concise version has remained in the top 10 most downloaded articles from the Diabetic Medicine website for many years. This document introduced a change from glucose based management of the metabolic disorder to ketone based. Although controversial at the time this has resulted in faster resolution of ketoacidosis and shorter length of stay in repeated audits.

When it was first written, whilst most of the advice was evidence based, some of the recommendations were consensus based. They were based on the collective experiences of the writing group. Since then, more evidence has become available to suggest that many of those recommendations were appropriate, but also that a few may need to be amended.

This new edition aims to update the guidance using evidence that has become available. In other places, changes have been suggested based on expert consensus. These are highlighted in the controversial areas section.

To enable the guideline to stay relevant, it is envisaged that all of the JBDS guidelines will be updated or reviewed each year. As such these are 'living' documents – designed to be updated based on recently published evidence or experience. Thus, feedback on any of the guidelines is welcomed.

Diagnosis of DKA

All of these must be present to make the diagnosis

The 'D' – a blood glucose concentration of >11.0 mmol/L **or known to have diabetes mellitus**

The 'K' – **The 'K'** – a capillary or blood ketone concentration of >3.0 mmol/L or significant ketonuria (2+ **or** more on standard urine sticks)

The 'A' – a bicarbonate concentration of <15.0 mmol/L **and/or** venous pH <7.3

The ADA definition is slightly different, and it also uses the anion gap as part of the diagnostic criteria to judge severity (2). The most common equation to calculate anion gap is $([Na^+] + [K^+]) - ([Cl^-] + [HCO3^-])$. There has been a call to update the ADA guideline (3).

Rationale for current practice

Ketones and acidosis

With a greater understanding of acid base chemistry and physiology, it is now well established that venous blood gas measurements alongside capillary ketone and glucose measurements are key to guiding the management of DKA.

Data from a national survey carried out in 2014 in the UK showed that 76% of institutions had the ability to measure ketone concentrations using point of care testing (4). The 2020 report of the 2019 National Inpatient Diabetes Audit (NaDIA) showed that 71.3% or hospitals used remote (networked) glucose meters (5). Diabetes UK also recommended the use of remote glucose and ketone monitors in their 2018 report entitled "Making Hospitals Safe for People with Diabetes" (6).

Euglycaemic DKA

This is the development of DKA in people known to have diabetes but where the glucose is normal, or not particularly raised. Improved education for those with diabetes with increased home capillary glucose and ketone monitoring has led to partial treatment of DKA prior to admission with consequent lower blood glucose levels at presentation. **This condition is treated in exactly the same way as hyperglycaemic DKA.**

1) **Initiate glucose 10% straight away at 125 ml/hr because the glucose is <14 mmol/L**
2) **Begin with 0.1units/kg/hr insulin rate**
3) **If glucose falling despite 10% glucose reduce to 0.05 units/kg/hr to avoid hypoglycaemia**

With the widespread use of the sodium-glucose cotransporter (SGLT) inhibitor class of drugs (e.g. dapagliflozin, canagliflozin, empagliflozin, ertugliflozin, sotagliflozin) people with type 2 diabetes, and increasingly in those with type 1, has highlighted the importance of using pH and ketones (rather than the older 'glucose-centric' care) to guide the diagnosis and management. This is because of the risk of developing euglycaemic DKA with these agents (7). The rates of euglycaemic DKA prior to the widespread use of SGLT inhibitors showed that it was not uncommon (8). However, the rates of SGLT associated DKA in the 'real world', i.e. outside of the trial population are not yet known, but may be higher than the trial data suggest. This is because of the careful selection, education and follow up of trial participants as well as the differing definitions of DKA used in the trials (9; 10).

If DKA occurs with SGLT inhibitor use, they should be stopped. A 'Yellow Card' should also be completed. Whether the drugs should be restarted once the individual has recovered should be discussed with the diabetes team.

Ketosis prone type 2 diabetes

DKA does not exclusively occur in people with type 1 diabetes, and people with type 2 diabetes may also develop DKA – so called 'ketosis prone type 2 diabetes' (11). This most often occurs in people of Afro-Caribbean or Hispanic descent. The treatment for this condition is the same as for others with DKA, but they often come off insulin quickly after the resolution of the DKA and underlying precipitating condition.

Differential diagnosis

It is important to exclude other cause of ketoacidosis, such as alcoholic ketoacidosis and starvation ketosis.

In alcoholic ketoacidosis, the normal glucose concentration glucose is the key difference with DKA – however, a careful history needs to be taken to differentiate it from euglycaemic DKA. Ketoacidosis without a raised glucose in a person with alcoholism is virtually diagnostic of alcoholic ketoacidosis (12). If alcoholic ketoacidosis is suspected, then ß-hydroxybutyrate should be measured and not urine ketones, because acetoacetate production can be supressed in alcoholic ketoacidosis. In addition, acetoacetate is measured by urinary dipstick.

Starvation ketosis occurs due to a lack of carbohydrate intake and usually develops over several days. The low carbohydrate intake will lead to low insulin secretion, subsequent lipolysis and ketosis. Ketone concentrations can rise to over 6 mmol/L (13). However, because this condition arises over a prolonged period, renal compensation for the acidosis means that (as long as other nutrients are eaten) acid base and electrolyte disturbances are often minimal (14).

Point of care testing ('bedside monitoring')

These guidelines recommend that management be based on point of care testing of those admitted with DKA. Blood glucose is routinely checked using point of care testing, but portable ketone meters now also allow point of care testing of 3-beta-hydroxybutyrate, the main blood ketone. Blood ketone measurement represents best practice in monitoring the response to treatment (15). There have been some concerns raised about their accuracy (16), but to date no harm has been reported from their use, and the data from these meters is just one of the measurements that helps to guide therapy and diagnose resolution.

Access to blood gas and blood electrolyte measurement is now relatively easy and available within a few minutes of blood being taken. Venous blood gas can be used safely (17-19). Therefore glucose, ketones and electrolytes, including bicarbonate and venous pH, should be assessed at or near the bedside using point of care testing.

The data informing these recommendations raise important issues (4):

- Staff must be trained in the use of point of care blood glucose and ketone meters in line with local point of care testing policy and demonstrate continuing competence in their use
- The meters should be subject to rigorous quality assurance
- Laboratory measurement will be required in certain circumstances, such as when blood glucose or ketone meters are 'out of range'
- Staff should be made aware of the interferences affecting glucose meters and of the pre-analytical effects such as peripheral shutdown and shock

Furthermore, initial training with regular updates and/or revalidation should be implemented for all healthcare staff using POCT equipment and managed in line with local laboratory guidance. Additionally, point of care testing meters must be regularly checked with internal quality control material and a subscription to an external quality assessment scheme must be undertaken to ensure correct functionality of the meters.

It is recognised that almost all units now have access to ketone meters. However, guidance is also given on monitoring treatment using the rate of rise of bicarbonate and fall in blood glucose as alternative measures.

The involvement of diabetes specialist teams

The diabetes specialist team must always be involved in the care of those admitted to hospital with DKA. Their involvement shortens hospital stay and improves safety (20; 21). This should occur as soon as possible during the acute phase but will depend on local circumstances. In line with the Best Practice Tariff for DKA, specialists must also be involved in the assessment of the precipitating cause of DKA, management, discharge, and follow up (22; 23). This should include assessment of the understanding of the condition by person with diabetes (PWD) plus their attitudes and beliefs as well as ensuring the provision of structured education. Specialist involvement is essential to ensure regular audit and continuous quality improvement in the implementation of DKA guidelines. The practice of admitting, treating and discharging those with DKA without the involvement of the diabetes specialist team is likely to compromise safe patient care. Regular auditing and monitoring of DKA outcomes and performance of specialist and non-specialist teams may not be routinely done (4).

General management issues

Fluid administration and deficits

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

The main aims for fluid replacement are:

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

The typical fluid and electrolyte deficits are shown in the table below. For example, an adult weighing 70 kg presenting with DKA may be up to 7 litres in deficit. This should be replaced as crystalloid. In people with kidney failure or heart failure, as well as the elderly and adolescents, the rate and volume of fluid replacement may need to be modified. The aim of the first few litres of fluid is to correct any hypotension, replenish the intravascular deficit, and counteract the effects of the osmotic diuresis with correction of the electrolyte disturbance.

Table: Typical deficits in DKA in adults

Water - 100 ml/kg

Sodium - 7-10 mmol/kg

Chloride - 3-5 mmol/kg

Potassium - 3-5 mmol/kg

The type of fluid to be used is discussed in detail in Controversial Areas.

Insulin therapy

A fixed rate intravenous insulin infusion (FRIII) calculated on 0.1 units/per kilogram body weight is recommended (see table below to assist). It may be necessary to estimate the weight of the individual. Insulin has several effects, but the following are the most important when treating DKA:

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

The insulin infusion is made up of 50 units of soluble human insulin in 49.5 ml 0.9% sodium chloride solution (i.e. 1 unit /ml). A table has been introduced to assist in the calculation of the insulin dose for weight:

WEIGHT in kg	INSULIN DOSE PER HOUR (units) at 0.1 units/kg/hour if glucose ≥14 mmol/L
40-49	4
50-59	5
60-69	6
70-79	7
80-89	8
90-99	9
100-109	10
110-119	11
120-130	12
130-139	13
140-150	14
>150	15 (any dose higher than this should be on the advice of the Diabetes Specialist Team)

Once the glucose drops to <14 mmol/L then in addition to adding a 10% dextrose infusion **consider** reducing the rate of intravenous insulin infusion to 0.05 units/kg/hr to avoid the risk of developing hypoglycaemia and hypokalaemia.

WEIGHT in kg	INSULIN DOSE PER HOUR (units) at 0.05 units/kg/hour if glucose <14 mmol/L
40-49	2
50-59	2.5
60-69	3
70-79	3.5
80-89	4
90-99	4.5
100-109	5
110-119	5.5
120-130	6
130-139	6.5
140-150	7
>150	7.5

Metabolic treatment targets

The recommended targets are

- Reduction of the blood ketone concentration by 0.5 mmol/L/hour
- Increase the venous bicarbonate by 3.0 mmol/L/hour
- Reduce capillary blood glucose by 3.0 mmol/L/hour
- Maintain potassium between 4.0 and 5.5 mmol/L

If these targets are not achieved, then the FRIII rate should be increased (see Management of DKA Section B, Action 2).

Intravenous glucose concentration

To ensure that ketones are cleared, an FRIII should be continued as well as an infusion of 0.9% sodium chloride solution to maintain fluid replacement. But once the blood glucose falls below 14.0 mmol/L, a 10% dextrose infusion should be added to act as the substrate for the insulin, to prevent hypoglycaemia. It is quite often necessary to infuse 0.9% sodium chloride solution and 10% dextrose concurrently (Section B, Action 2). The intravenous insulin and dextrose should not be discontinued until the person with diabetes is eating and drinking normally.

In those already on long acting basal insulin, it should continue to be prescribed at their usual dose. In those newly diagnosed, then a long acting basal insulin should be commenced, at a dose of 0.25 units/Kg subcutaneously once daily.

Special groups

The following groups need specialist input as soon as possible and special attention needs to be paid to their fluid balance:

- Elderly
- Pregnant
- Young people 18 to 25 years of age (see section on cerebral oedema)
- Heart or kidney failure
- Other serious co-morbidities

Other considerations

In line with several aspects of the Best Practice Tariff, people with diabetes who are admitted with DKA should be referred to the diabetes specialist team within one working day. Every opportunity should be taken to educate the person with diabetes. In particular, they should be counselled about the precipitating causes and early warning symptoms. Things to consider are:

- Identification of precipitating factor(s) e.g. intercurrent illness or omission of insulin injections
- Review of their usual glycaemic control
- Review of their injection technique / blood glucose monitoring / equipment / injection sites
- For those on insulin pumps, review of their use of the device and provision of further education in the use of such technology, as necessary
- Prevention of recurrence e.g. provision of written sick day rules
- Insulin effectiveness e.g. their own insulin may be expired or denatured. This should be checked prior to reuse
- Assess the need for, and where necessary, provision of handheld ketone meters for use at home – this should be the default position
- Provision of a contact number on how to contact the diabetes specialist team out of hours
- Education of health care professionals on the management of ketonaemia
- Provision of a written care plan – allowing the person with diabetes to have an active role in their own diabetes management, with a copy of this going to their GP
- For those with recurrent admissions, there is often a psychological element (e.g. eating disorders, other undiagnosed mental health disorders), that is likely to benefit from formal mental health team involvement

Recurrent DKA

People who present with recurrent episodes of DKA comprise a significant proportion of all DKA admissions – in the UK accounting for 66% of those with type 1 diabetes and 35% of those with type 2 (24). Many of these individuals have fragmented care, social, behavioural or psychological considerations that need to be accounted for (25; 26). Other risk factors for recurrent episodes include female sex, adolescence, low socioeconomic status, and previous DKA admissions. Recurrent episodes of DKA re associated with increased risk of long term cognitive decline and premature mortality (27; 28). Strategies to help individuals may include frequent telephone contacts, formal referral to psychology, supervised insulin administration – e.g. using ultra long acting insulin analogues.

Controversial areas

Whilst the clinical assessment and aims of treatment in the management of DKA are not controversial, there is still disagreement about the optimum treatment regimen. Where the evidence base is not strong, recommendations are based on consensus and experience. Some of the more controversial points will now be considered and good practice recommendations are made. The recommendations are given first followed by the rationale. Differences between the US and UK guidelines are discussed elsewhere (29).

There were a number of issues that were considered 'controversial' in the previous versions of this document, which have now become standard practice. These have been removed from this section. These are:

1. Measure venous rather than arterial bicarbonate and pH
2. Blood ketone meters should be used for point of care testing
3. 0.9% sodium chloride solution is the recommended fluid of choice on the general medical ward (recommended as it is commercially available with premixed potassium chloride, and therefore complies with NPSA recommendation)
4. Subcutaneous long-acting analogue/human insulin should be continued
5. Insulin should be administered as a FRIII calculated on body weight
6. Do not use a priming (bolus) dose of insulin

Should they wish to, interested readers can still access the discussions about these controversial areas by looking at previous versions of this document that can be found at: https://abcd.care/resource/management-diabetic-ketoacidosis-dka-adults

Recommendations

1. Reduce rate of insulin infusion to 0.05 units/kg/hr when glucose drops to <14 mmol/L
2. Crystalloid rather than colloid solutions are recommended for fluid resuscitation
3. 0.9% sodium chloride solution ('normal saline') is the fluid resuscitation of choice
4. Cautious fluid replacement in young adults
5. Bicarbonate administration is not recommended routinely
6. Phosphate should not be supplemented routinely
7. The rate of glucose lowering should be least 3.0 mmol/L/hr

1. Reduce the rate of insulin infusion to 0.05 units/kg/hr when glucose drops to <14.0 mmol/L

A national survey of DKA management following earlier version of this guideline found that the rates of hypoglycaemia (<4.0 mmol/L) and hypokalaemia (<4.0 mmol/L) were 27.6% and 67% respectively. Whilst it may have been that these occurred due to 10% dextrose not being added in a timely manner, or that potassium containing fluids were not given correctly, the main driver for both of these biochemical abnormalities is the use of insulin. Thus, when glucose drops below 14 mmol/L, **consider** reducing the rate of intravenous insulin infusion to 0.05 units/kg/hr. This is already an option in the adult guidelines elsewhere (25), and several paediatric studies have suggested that the rate of resolution of DKA is not longer compared to 0.1 units/kg/hr (30-32). It is thus also included in the UK paediatric guidelines (33).

2. Colloid versus crystalloid?

A 2007 Cochrane review also did not support the use of colloid in preference to crystalloid fluid (34). A further 2013 consensus document suggested that colloids should be avoided where possible, due to a potential risk of increased mortality and morbidity associated with their use (35). Therefore, we recommend the use of crystalloid fluid as the initial fluid of choice.

3. 0.9% sodium chloride solution or balanced crystalloid solution for resuscitation?

There has been much debate about the relative merits of these two solutions (36). Two randomised trials have compared 0.9% sodium chloride solution to Hartmann's solution (37; 38). Neither has shown the superiority of one fluid over the other in terms of clinical outcomes. More recently, a post hoc secondary subgroup analysis of 2 trials suggested that balanced crystalloid may lead to faster resolution of DKA than 0.9% sodium chloride, but not when given in a general ward environment (39). This limits crystalloid use to environments where central venous access is available, and higher potassium concentrations may be given (39). The result of a systematic review on the choice of crystalloid fluid replacement in hyperglycaemic emergencies is awaited (40). Until then, we continue to recommend that 0.9% sodium chloride with pre-mixed potassium chloride be the default solution for fluid resuscitation because it is compliant with NPSA recommendations. Furthermore, diabetes specialists and physicians have a vast experience in the safe use of this fluid. We also recognise that many critical care units will prefer to use balanced crystalloids such as Hartmann's solution. This is acceptable provided local policies are followed for the safe administration of additional potassium chloride.

Infusion solution	Advantages	Disadvantages
0.9% sodium chloride	• Decades of clinical experience • Readily available in clinical areas • Commercially available ready mixed with potassium at required concentrations, 20 mmol/L (0.15%) or 40 mmol/L (0.3%) • Supports safe practice with injectable potassium (NPSA compliant (NPSA alert 2002))	• Hyperchloraemic metabolic acidosis which may cause renal arteriolar vasoconstriction leading to oliguria and a slowing of resolution of acidosis
Compound sodium	• Balanced crystalloid with minimal tendency to hyperchloraemic metabolic acidosis	• Insufficient potassium if used alone • Not commercially available with adequate pre-mixed potassium. Potassium addition in general clinical areas is unsafe. (NPSA alert 2002) • Unfamiliar and not routinely kept on medical wards

4. Rate of fluid replacement?

For many years there has been concern that rapid fluid replacement may lead to cerebral oedema in children and young adults. Until 2018, no randomised controlled trials existed to guide decision making in this area. However, a large randomised controlled trial of 1389 episodes of DKA randomised children between 0 and 18 years of age to either 0.45% or 0.9% sodium chloride solution given fast or slow (i.e. a 2 by 2 factorial trial) (41). Reassuringly, these authors found no differences in neurological outcomes in children with DKA treated with rapid versus slower volume correction or with the use of 0.9% versus 0.45% sodium chloride. It is felt that the development of cerebral oedema is multifactorial, but often idiosyncratic.

5. Intravenous bicarbonate?

Adequate fluid and insulin therapy will resolve the acidosis in DKA and the use of bicarbonate is not indicated (42-45). The acidosis may be an adaptive response as it improves oxygen delivery to the tissues by causing a right shift of the oxygen dissociation curve. Excessive bicarbonate may cause a rise in the CO_2 partial pressure in the cerebrospinal fluid (CSF) and may lead to a paradoxical increase in CSF acidosis (42). In addition, the use of bicarbonate in DKA may delay the fall in blood lactate:pyruvate ratio and ketones when compared to intravenous 0.9% sodium chloride infusion (43). Intensive care teams may occasionally use intravenous bicarbonate if the pH remains low and inotropes are required.

6. Use of intravenous phosphate?

Phosphate concentrations are often done as standard when a 'bone profile' is requested. Despite initial serum concentrations appearing normal significant intracellular depletion means that whole-body phosphate deficits in DKA are substantial, averaging 1 mmol/kg of body weight. However, severe phosphate deficiency can worsen respiratory failure, precipitate cardiac arrhythmias and cause rhabdomyolysis. If any of these are present phosphate measurement and replacement should be considered as per local guidance (25; 46). In general, however, there is no evidence of benefit of routine phosphate replacement (47). Therefore we do not recommend the routine replacement of phosphate.

7. What should the rate of glucose lowering be?

The data from the studies published in the 1970s (48; 49) showed that using low dose insulin infusions (i.e. 0.1 units/Kg/hr) resulted in glucose levels coming down at about the same rate as the high dose insulin given in the preceding decades, with glucose levels coming down by about 50-60% in the first 4 hours. The theoretical risk of large osmotic shifts due to rapid changes in plasma glucose is very rare in DKA, and thus the safety of using 0.1 unit/kg/hr outweighs any risk.

Complications of DKA and its treatment

1. Hypokalaemia and hyperkalaemia

Due to the dehydration, lack of insulin and metabolic acidosis, hyperkalaemia should be sought when DKA is initially diagnosed. In a UK national survey 283 people treated with the 2013 edition of this guideline, the mean admission potassium was 4.8 (±1.0) mmol/L (45). Hypokalaemia and hyperkalaemia are potentially life-threatening conditions during the management of DKA. Because of the risk of acute pre-renal kidney injury associated with severe dehydration, it is recommended that no potassium be prescribed with the initial fluid resuscitation or if the serum potassium level remains above 5.5 mmol/L. A normal or even elevated serum potassium concentration may be seen due to the extracellular shift of potassium in acidotic conditions, and this very poorly reflects total potassium stores. However, potassium will almost always fall as the DKA is treated with insulin and the UK survey showed that 67.1% developed hypokalaemia (<4.0 mmol/L) at 24 hours after admission (45).

Thus it is recommended that 0.9% sodium chloride solution with potassium 40 mmol/L (ready-mixed) is prescribed as long as the serum potassium level is below 5.5 mmol/L and the person is passing urine. If the serum potassium level falls below 3.5 mmol/L the potassium regimen needs review. Where the fluid balance permits, an increase in the rate of the infusion of 0.9% sodium chloride solution with potassium 40 mmol/L is possible. Otherwise, a more concentrated potassium infusion will be needed and to ensure safe practice, all aspects of its use must comply with local and national guidance (50; 51).

In addition to inadequate replacement, the main driver for hypokalaemia is the use of insulin. Thus, when glucose drops below 14 mmol/L, **consider** reducing the rate of intravenous insulin infusion to 0.05 units/kg/hr.

Trusts need to ensure that they have local protocols in place which allow for the safe administration of concentrated potassium solutions. This may require transfer to a Level 2 or Level 3 environment.

2. Hypoglycaemia

The blood glucose may fall very rapidly as ketoacidosis is corrected and a common mistake is to allow the blood glucose to drop to hypoglycaemic levels. In the UK national survey of 283 people treated with the 2013 edition of this guideline, glucose dropped to <4.0 mmol/L in 27.6% of people (45). Severe hypoglycaemia (i.e. requiring third party assistance) is also associated with increased length of stay, cardiac arrhythmias, acute brain injury and death (52). The main driver for hypoglycaemia is the use of insulin. Thus, in addition to commencing 10% dextrose to run alongside the 0.9% sodium chloride solution, when glucose drops below 14 mmol/L, consider reducing the rate of intravenous insulin infusion to 0.05 units/kg/hr.

3. Cerebral oedema

Cerebral oedema causing symptoms is relatively uncommon in adults, although may occur in those who are physically slight or in younger adults. Asymptomatic cerebral oedema may be a common occurrence, and may exist prior to treatment starting (25; 53). The exact cause of this phenomenon is unknown. Reassuringly a large randomised controlled trial of 0.9% sodium chloride solution vs 0.45% sodium chloride solution each given either rapidly or slowly, showed no differences in the rates of developing neurological injury (41). It is thus possibly an idiosyncratic response to the metabolic injury and subsequent treatment. However, any deterioration in Glasgow Coma Scale score should prompt urgent treatment and imaging. If cerebral oedema is suspected, urgent treatment with mannitol or hypertonic saline to induce osmotic fluid shifts should be started and not be delayed whilst awaiting imaging (25).

4. Other complications

Several other complications may occur with some being relatively common, generally mild and easily treated. However, others may be more serious. These include the development of venous thromboembolic disease, particularly if central venous catheters are used. Transient acute kidney injury may occur in up to 50% of adults (25). Other, rare complications include pulmonary oedema; a rise in pancreatic enzymes, with or without acute pancreatitis; cardiomyopathy; rhabdomyolysis; and, gastrointestinal bleeding (25).

The management of DKA in people with end stage renal failure or on dialysis

Fortunately this is a relatively rare occurrence. There are limited data on the management of DKA in this circumstance (54-57). The lack of renal insulin clearance means that DKA is much less likely to occur. It may also be difficult to determine because of the chronic metabolic acidosis associated with advanced chronic kidney disease (stages 4 and 5). Recent data suggest that those presenting in DKA with end stage renal disease have lower ß-hydroxybutyrate concentrations, and higher glucose and anion gap than those with preserved renal function (58). Bicarbonate and pH were not significantly different (58). When DKA does occur in end stage renal disease, several issues need to be considered.

Fluid replacement

The inability to develop an osmotic diuresis means that dialysis associated hyperglycaemia and ketosis can occur without much dehydration. A mixed picture of DKA and HHS may also occur because of the high serum tonicity (56). In addition, the circulating intravascular volume may increase at the expense of intracellular volume that resolves as the glucose and ketosis normalises. Therefore there may be no need for fluid replacement in those with end stage renal failure or those on dialysis. However, for those who are deemed hypovolaemic, aliquots of 250 ml (0.9% sodium chloride or 10% dextrose) may be given with frequent clinical assessments.

Insulin treatment

For people with end stage renal failure or those on dialysis, insulin replacement is the mainstay of treatment. This should be given as a FRIII at an initial rate of 0.1 units/kg/hr, but may need to increase if the required rate of glucose fall is not achieved. However, the failure to renally clear insulin increases the risk of hypoglycaemia. However, the rate of glucose reduction is the same as for people with preserved renal function – i.e. 3.0 mmol/L/hour. If the rate of fall is faster, or the glucose falls to <14.0 mmol/L strongly **consider** reducing the rate of intravenous insulin infusion to 0.05 units/kg/hr.

Potassium

Potassium supplementation is not usually required because the lack of the osmotic diuresis means that there is significantly less potassium loss that for those with preserved renal function. However, the acidosis may lead to significant hyperkalaemia, and this is more common in those with renal failure (54). In this circumstance, continuous cardiac monitoring is essential and critical care or the specialist renal team should be involved to consider urgent haemodialysis / haemofiltration.

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 experience for the person with diabetes and reduced length of stay (59).

Where young people aged 16-18 years are managed by adult medical teams because of local arrangements, it is considered appropriate for them to be managed using local adult guidelines that the teams are familiar with rather than using potentially unfamiliar paediatric guidelines.

Where individuals aged 16-18 years are managed by paediatric teams the paediatric guidelines should be followed. https://www.bsped.org.uk/media/1798/bsped-dka-guideline-2020.pdf

Assessment of severity

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

- Blood ketones over 6.0 mmol/L
- Bicarbonate level below 5.0 mmol/L
- Venous/arterial pH below 7.0
- Hypokalaemia on admission (under 3.5 mmol/L)
- GCS less than 12 or abnormal AVPU scale
- Oxygen saturation below 92% on air (assuming normal baseline respiratory function)
- Systolic BP below 90 mmHg
- Pulse over 100 or below 60 bpm
- Anion gap above 16 **[Anion Gap = (Na^+ + K^+) – (Cl^- + $HCO3^-$)]**

If the individual exhibits any of these signs, resuscitation and treatment should be started without delay, and an intensive monitoring regimen put in place. **Depending on local circumstances** individuals who fulfil the criteria for severity or who require intensive monitoring should be reviewed by a consultant physician and considered for swift referral to a Level 2/HDU (High Dependency Unit) environment, or if the individual has failed to improve after initial resuscitation measures (60). 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.

In those using an insulin pump, if transfer to a Level 2 / HDU or ITU is necessary, then the pump should be stopped, removed and stored safely.

The use of flash glucose monitoring (e.g. Freestyle Libre®, Dexcom G6®, etc) in these circumstances is not known. Further work is necessary to determine their utility in critical illness. Until such data are available, they may be left on, but data from them should not be used to guide treatment.

0 to 60 minutes: Immediate management upon diagnosis

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 for the person with diabetes; generally hourly blood glucose (BG) and hourly ketone measurement, with at least 2 hourly serum/blood potassium and bicarbonate for the first six hours
- Clinical and biochemical assessment of the individual
- Involve the diabetes specialist team at the earliest possible stage
- Consider referral to a Level 2 / HDU environment if criteria for severity are met or if facilities for intensive monitoring are unavailable

Action 1 - Intravenous access and initial investigations

- Rapid ABC (Airway, Breathing, Circulation)
- Large bore IV cannula, and commence IV fluid replacement (See Action 2)
- Clinical assessment
- Respiratory rate; temperature; blood pressure; pulse; oxygen saturation
- Glasgow Coma Scale. N.B.: a drowsy individual in the context of DKA is seriously concerning and the person requires critical care assessment. 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 (including phosphate if necessary)
- 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
- COVID-19 testing - particularly in those not known to have a prior diagnosis of diabetes

Action 2 – Restoration of circulating volume

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

Systolic BP (SBP) on admission below 90 mmHg

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

- Give 500 ml of 0.9% sodium chloride solution over 10-15 minutes. If SBP remains below 90 mmHg this may be repeated **whilst awaiting senior input**. In practice most individuals require between 500 to 1000 ml 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 90 mmHg follow fluid replacement as shown below

Systolic BP on admission 90 mmHg and over

Below is a table outlining a typical fluid replacement regimen for a previously well 70 kg 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 1 L *	1000 ml over 1st hour
0.9% sodium chloride 1 L with potassium chloride	1000 ml over next 2 hours
0.9% sodium chloride 1 L with potassium chloride	1000 ml over next 2 hours
0.9% sodium chloride 1 L with potassium chloride	1000 ml over next 4 hours
0.9% sodium chloride 1 L with potassium chloride	1000 ml over next 4 hours
0.9% sodium chloride 1 L with potassium chloride	1000 ml 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 those who are hypotensive.

Exercise caution in the following groups

- 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.

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 the person is unable to state their weight, or it is not available, estimate it in kilograms
- If it is a pregnant woman, use her present weight and call for immediate additional senior obstetric help
- Start a continuous FRIII via an infusion pump. This is made of 50 units of human soluble insulin (Actrapid®, Humulin S®) made up to 50 ml with 0.9% sodium chloride solution. Ideally this should be provided as a ready-made solution
- Infuse at a fixed rate of 0.1 unit/kg/hr (i.e. 7 ml/hr if weight is 70 kg) (See table on page 14)
- 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 individual normally takes long acting basal insulin (e.g. glargine, degludec, detemir, or human isophane insulin) continue this at the usual dose and usual time
- 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. However, two large bore intravenous catheters are advisable

60 minutes to 6 hours

Aims:

- Clear the blood of ketones and suppress ketogenesis
- Achieve a rate of fall of ketones of at least 0.5 mmol/L/hr
- In the absence of ketone measurement, bicarbonate should rise by 3.0 mmol/L/hr and blood glucose should fall by 3.0 mmol/L/hr
- Maintain serum potassium in the normal range
- Avoid hypoglycaemia
- Consider referral to a Level 2 (HDU) environment if criteria for severity are met after initial resuscitation or if facilities for intensive monitoring are unavailable.

Action 1 – Re-assess and monitor vital signs

- During this time, individuals 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 person is incontinent or anuric (i.e. not passed urine by 60 minutes)
- Consider naso-gastric tube insertion if the person 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
- Regular assessment of Glasgow Coma Scale score, if this drops then urgent brain imaging should be considered
- Maintain an accurate fluid balance chart, the minimum urine output should be no less than 0.5 ml/kg/hr
- Continuous cardiac monitoring in those with severe DKA
- Give prophylactic low molecular weight heparin as per NICE guidance (61)

Action 2 – Review metabolic parameters

- Measure blood ketones and capillary glucose hourly (note: if meter reads "blood glucose over 20 mmol/L" or "Hi" venous blood should be sent to the laboratory hourly or measured using venous blood in a blood gas analyser until the point of care testing meter is within its QA range)
- The hourly glucose readings should be recorded directly into the hospital pathology system. Where this is not possible (e.g. with non-networked glucose meters), the results should be recorded in the notes

- Review the 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
    - If blood ketone measurement is available and blood ketones are not falling by at least 0.5 mmol/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**)
    - If blood ketone measurement is not available, use venous bicarbonate. If the bicarbonate is not rising by at least 3.0 mmol/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**
    - Alternatively use plasma glucose. If the glucose is not falling by at least 3.0 mmol/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 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 (4.0 – 5.5 mmol/L), 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 p26)
- Continue the FRIII until the ketone measurement is less than 0.6 mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18 mmol/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 (15)
- If the glucose falls below 14.0 mmol/L, commence 10% glucose given at 125 ml/hour alongside the 0.9% sodium chloride solution. In addition **consider** reducing the rate of intravenous insulin infusion to 0.05 units/kg/hr.
- Monitor and replace potassium because it may fall rapidly

****The intravenous insulin and the dextrose infusions should be infused using a Y connector**

Action 3 – Identify and treat precipitating factors

Action 4 –

Those presenting with newly diagnosed type 1 diabetes should be given long acting basal insulin (e.g. glargine, detemir or degludec - 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 (62).

6 to 12 hours

Aim:

The aim within this time period is to:

- Ensure that clinical and biochemical parameters are improving at the correct rates
- 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
- Consider referral to a Level 2 (HDU) environment if criteria for severity are met despite adequate treatment, or if there is a deterioration in clinical status, or if facilities for intensive monitoring are unavailable

Action 1 – Re-assess the individual and monitor vital signs

- If the person is not improving as expected then seek early senior advice
- Regular assessment of Glasgow Coma Scale score, if this drops then urgent brain imaging should be considered
- Ensure a referral has been made to the specialist diabetes team
- Consider referral to a Level 2 (HDU) environment if criteria for severity are met or if facilities for intensive monitoring are unavailable

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 0.6 mmol/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 has resolved go to section E

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

12 to 24 hours

Expectation:

By 24 hours the ketonaemia and acidosis should have resolved in most people (45)

Aim:

- Ensure that the clinical and biochemical parameters are improving or have normalised
- Continue IV fluids if the person is not eating and drinking
- If the person is not eating and drinking and there is no ketonaemia move to a VRIII as per local guidelines or following the JBDS guideline (63)
- Re-assess for complications of treatment e.g. fluid overload
- Regular assessment of Glasgow Coma Scale score, if this drops then urgent brain imaging should be considered
- Continue to treat any precipitating factors as necessary
- Transfer to subcutaneous insulin if the individual 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 30-60 minutes later

Action 1 – Re-assess the individual and monitor vital signs

Action 2 – Review the 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 0.6 mmol/L, **and** venous pH over 7.3

If DKA resolved go to section E.

If DKA has 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 metabolic 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: People who have had DKA 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 – e.g. gastritis. **It is unusual for DKA not to have biochemically resolved by 24 hours with appropriate treatment** and requires senior and specialist input.

E. Conversion to subcutaneous insulin

The person with diabetes should be converted to an appropriate subcutaneous regime when biochemically stable (blood ketones less than 0.6 mmol/L, pH over 7.3) and they are ready and able to eat (63). Conversion to subcutaneous insulin is ideally managed by the diabetes specialist team. If the team is not available see Appendix 1. If the person with diabetes is newly diagnosed, it is essential they are seen by a member of the specialist team prior to discharge.

Specialist diabetes team input

If they are not already involved, the local diabetes team should be informed and the person with diabetes reviewed within 24 hours of admission. Diabetes team input is important to allow re-education, to reduce the chance of recurrence, and to facilitate appropriate follow up. Hospitals should enable diabetes teams to provide sufficient cover to allow anyone admitted with DKA to be reviewed within 24 hours of admission.

Pathophysiology of DKA

Diabetic ketoacidosis (DKA) is a complex disordered metabolic state characterised by hyperglycaemia, ketonaemia, and acidosis. DKA usually occurs as a consequence of absolute or relative insulin deficiency that is accompanied by an increase in counter regulatory hormones (i.e., glucagon, cortisol, growth hormone, catecholamines). This type of hormonal imbalance enhances hepatic gluconeogenesis and glycogenolysis resulting in severe hyperglycaemia. Enhanced lipolysis increases serum free fatty acids that are then metabolised as an alternative energy source in the process of ketogenesis (25). This results in accumulation of large quantities of ketone bodies and subsequent metabolic acidosis. Ketones include acetone, 3-beta-hydroxybutyrate, and acetoacetate. The predominant ketone in the blood is 3-beta-hydroxybutyrate (15). A more detailed description of the pathophysiology of DKA is available elsewhere (25).

There are several mechanisms responsible for fluid depletion in DKA. These include osmotic diuresis due to hyperglycaemia, vomiting - commonly associated with DKA - and eventually, inability to take in fluid due to a diminished level of consciousness. Electrolyte shifts and depletion are in part related to the osmotic diuresis. Hyperkalaemia and hypokalaemia need particular attention.

Epidemiology and cost

Whilst DKA occurs predominantly in people with type 1 diabetes, about a third of cases occur in people with type 2 diabetes (24; 64). However, the initial treatment is the same for both. The true incidence is difficult to establish. In the UK the incidence of DKA was highest in those aged 18 to 24 years old (24). Other data has suggested that the incidence of DKA ranges between 8.0 – 51.3 cases per 1000 patient years in people with type 1 diabetes (65). However, in China the incidence has been reported to be as high as 263 per 1000 patient years (66; 67). DKA is also an expensive condition to treat. Data from national surveys in the UK show that the cost of one episode is estimated to cost £2,064 in adults and £1,387 in those aged 11 to 18 years (68; 69). Treating DKA in the USA is significantly more expensive with a single episode estimated to cost ~$26,566 (70).

Mortality and morbidity

In the UK and other developed nations, whilst the mortality from DKA remains <1% (45; 71), it is the leading cause of death amongst people under 58 years old with T1DM (72). Unsurprisingly perhaps, mortality increases with age and with the presence of pre-existing comorbidities (73; 74).

The mortality rate is still high at over 40% in some low and middle income countries (25). This high mortality rate illustrates the necessity of early diagnosis and the implementation of effective prevention programmes.

Cerebral oedema remains the most common cause of mortality, particularly in young children and adolescents. The main causes of mortality in the adult population include severe hypokalaemia, adult respiratory distress syndrome, and co-morbid states which may have precipitated the DKA such as pneumonia, acute myocardial infarction and sepsis (25).

Implementation of the guidelines

Repeated audits by many diabetes units in all constituent UK countries have consistently demonstrated poor adherence to local (or national) guidelines in the management of DKA. There are two main problems to be addressed:

1) The guidelines must be implemented
2) The guidelines must be audited

The guidelines must be reviewed regularly. This is a 'live' document and feedback to the authors is welcomed and encouraged.

Commissioning of care

Diabetic ketoacidosis is a common medical emergency and must be treated appropriately. For this to occur, the Health Economies within the United Kingdom must address management of DKA in the context of provision of expert medical and nursing input within secondary care. In the majority of cases people with type 1 diabetes should be under specialist care. 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.

Audit

Quality indicators

Every Acute Trust should have a local management plan in place based upon these, or other authoritative guidelines. Guidelines must be current and valid and should not be used if the review date has expired. If there is no review date, they should not be used

Every Acute Trust should have nominated lead for implementing and auditing local diabetic ketoacidosis guidelines

Every Acute Trust should have a rolling education programme for nursing and medical staff caring for those with diabetic ketoacidosis

Every Acute Trust should have nominated care areas for people with diabetic ketoacidosis

Every Acute Trust should have trained Health Care Workers available to measure blood glucose concentrations 24 hours per day – ideally using point of care testing meters

Every Acute Trust should have trained Health Care Workers available to measure blood ketone concentrations 24 hours per day – ideally using point of care testing meters

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

People admitted to hospital with diabetic ketoacidosis receive educational and psychological support prior to discharge and are followed up by a diabetes specialist team (NICE CG15)

We recommend that every Acute Trust use performance indicators to assess the quality of care given (examples given in Appendix 2). A Treatment Pathway document may be beneficial, as adherence to guidelines for this condition is very poor and integrated pathway documents (an example of which is given online) would improve compliance

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Appendix 1

Restarting subcutaneous insulin for those already established on insulin (63)

The person's previous regimen should generally be re-started if their most recent HbA1c suggests acceptable level of control i.e. HbA1c 64 mmol/mmol (<8.0%)

With all regimens the intravenous insulin infusion should not be discontinued for at least 30 to 60 minutes after the administration of the subcutaneous dose given in association with a meal.

If they were on basal bolus insulin

- There should be an overlap between the insulin infusion and first injection of fast acting insulin. The fast acting insulin should be injected with the meal and the intravenous insulin and fluids discontinued 30 to 60 minutes later
- If the person was previously on a long acting insulin such as glargine, degludec, detemir or human isophane, this should have been continued and thus the only action should be to restart their normal short acting insulin at the next meal
- If the basal insulin had been stopped in error, the insulin infusion should not be stopped until some form of background insulin has been given. If the basal insulin was normally taken once daily in the evening and the intention is to convert to subcutaneous insulin in the morning, give half the usual daily dose of basal insulin as isophane (i.e. Insulatard®, Humulin I®, Insuman basal®) in the morning. This will provide essential background insulin until the long acting analogue can be recommenced. Check the blood ketone and glucose levels regularly

If they were on twice daily fixed-mix insulin

- Re-introduce the subcutaneous insulin before breakfast or before the evening meal. Do not change at any other time. Maintain the insulin infusion for 30 to 60 minutes after the subcutaneous insulin was given

If they were on CSII

- Ensure the availability of necessary supplies/ and or consumables
- Ensure that the individual has been assessed as being able to use the CSII
- If they are deemed as able to use the pump, recommence the CSII at the normal basal rate. Continue intravenous insulin infusion until the meal bolus has been given. Do not recommence CSII at bedtime

Calculating the subcutaneous insulin dose in those who are insulin-naïve

Estimate Total Daily Dose (TDD) of insulin

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

Example: a 72 kg 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. aspart (e.g. Novorapid®) / glulisine (e.g. Apidra®) / lispro (e.g. Humalog®)	6 units	6 units	6 units	
Long acting insulin, e.g. glargine (e.g. Lantus®), detemir (e.g. Levemir®) or degludec (e.g. Tresiba®)			18 units	

Administer the first dose of fast acting subcutaneous insulin preferably prior to breakfast or lunch. Only administer the first dose before the evening meal if appropriate monitoring can be guaranteed. Do not convert to a subcutaneous regimen at bed time.

In those new to insulin therapy, dose requirements may decrease within a few days because the insulin resistance associated with DKA resolves. Close supervision from the diabetes specialist team is required.

Calculating a twice daily (BD) regimen:

If a twice daily pre-mixed insulin regimen is to be used, give two thirds of the total daily dose at breakfast, with the remaining third given with the evening meal.

Appendix 2

Audit standards for the management of any person who has diabetic ketoacidosis admitted under an adult medical team

Purpose of these audit standards

- Maximise patient safety and quality of care
- Support professional best practice
- Deliver enhanced patient satisfaction
- Reduce Trust operating costs (litigation, complaint procedures)
- Contribute to improved financial performance (reduced length of stay)

Institutional Standards:	
Indicator	**Standard**
Access:	
Has the Trust either adopted these national guidelines or has their own alternative, evidence based and audited internal guidelines for the management of any person admitted with diabetic ketoacidosis under an adult medical team?	Yes
Does the Trust collect data about the outcomes for those admitted with diabetic ketoacidosis?	Yes
Does the Trust have the services of a dedicated Diabetes Inpatient Specialist Nurse (DISN) at staffing levels most recently recommended by the Diabetes UK?	Yes
Institutional Accountability and Integrity:	
Does the Trust have a 'clinical lead' for the management of those admitted with diabetic ketoacidosis under an adult team who has responsibility for implementation of the DKA guidelines?	Yes
NPSA Standards (75; 76)	
Indicator	**Standard**
All regular and single insulin (bolus) doses are measured and administered using an insulin syringe or commercial insulin pen device. Intravenous syringes must never be used for insulin administration	100%
The term 'units' is used in all contexts. Abbreviations, such as 'U' or 'IU', are never used	100%

All clinical areas and community staff treating people with diabetes with insulin have adequate supplies of insulin syringes and subcutaneous needles which staff can obtain at all times	100%
An insulin syringe must always be used to measure and prepare insulin for an intravenous infusion	100%
A training programme should be put in place for all healthcare staff (including medical staff) expected to prescribe, prepare and administer insulin (e.g. the safe use of insulin and the safe use of intravenous insulin e-learning packages from NHS Improving Quality)	100%
Policies and procedures for the preparation and administration of insulin and insulin infusions in clinical areas are reviewed to ensure compliance with the above	100%
Department of Health 'Never Event' Standard (51)	
Indicator	**Standard**
Death or severe harm as a result of maladministration of insulin by a health professional	Never
Additional Best Practice Tariff Standards (22):	
Indicator	**Standard**
People admitted to hospital with diabetic ketoacidosis should be referred to the diabetes specialist team on admission	100%
People admitted to hospital with diabetic ketoacidosis should be seen by member of the diabetes specialist team within 1 working day of admission	100%
People with diabetes should have access to the specialist diabetes team	100%
Where clinically appropriate, people with diabetes should have the choice to self-monitor their condition	80%
People admitted to hospital with diabetic ketoacidosis receive educational support from a member of the diabetes specialist team prior to discharge. This education should include: • Review of usual glycaemic control • Review of injection technique/blood glucose monitoring/equipment/sites • Discussion of sick day rules • Assessment of the need for home ketone testing (blood or urinary) with education to enable this • Provision of contact telephone numbers for the diabetes specialist team including out of hours	100%

Indicator	Standard
Those admitted with DKA are seen by a diabetologist or DISN prior to discharge	100%
People admitted to hospital with diabetic ketoacidosis receive psychological support from a member of the diabetes specialist team prior to discharge	75%
People admitted to hospital with diabetic ketoacidosis receive follow up by a diabetes specialist team	100%
People admitted to hospital with diabetic ketoacidosis should be discharged with a written care plan: a process that allows the person with diabetes to have active involvement in deciding, agreeing and owning how their diabetes is managed. This should be copied to the GP	100%
Percentage of people admitted with DKA where discharge is delayed because of diabetes related problems	0%
Access to structured education offered within three months	100%
Institutional Accountability and Integrity:	
Percentage of people with diabetes identified as such on hospital patient administration system	95%
Percentage of clinical coding that identifies people with diabetes correctly	100%
Patient and Staff Satisfaction:	
Percentage of staff who feel that they have sufficient levels of appropriate and timely support from the Diabetes Inpatient Specialist Team	100%
Percentage of people with diabetes who express satisfaction with their inpatient journey, using validated tools such as the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and the Diabetes Treatment Satisfaction Questionnaire for Inpatients (DTSQ-IP)	80%

Appendix 3

JBDS IP Review Group

Dr Ahmed El-Sharefi, South Tees Hospital NHS Foundation Trust
Dr Belinda Allan, Hull and East Yorkshire Hospital NHS Trust
Dr Parizad Avari, Imperial College Healthcare NHS Trust
Elizabeth Camfield, Guy's and St Thomas' NHS Foundation Trust
Erwin Castro, (East Sussex), Chair, Diabetes Inpatient Specialist Nurse (DISN) UK Group
Dr Jason Cheung, Norfolk and Norwich University Hospitals NHS Foundation Trust
Dr Umesh Dashora, East Sussex Healthcare NHS Trust
Dr Parijat De, Sandwell and West Birmingham Hospitals NHS Trust
Professor Ketan Dhatariya, (Norwich), Chair, Joint British Diabetes Societies (JBDS) for Inpatient Care
Dr Daniel Flanagan, Plymouth Hospitals NHS Trust
Dr Stella George, East and North Hertfordshire NHS Trust
Dr Chris Harrold, University Hospitals Coventry and Warwickshire NHS Trust
Dr Masud Haq, Maidstone and Tunbridge Wells NHS Trust
Dr Kath Higgins, University Hospitals of Leicester NHS Trust
David Jones, Diabetes UK
Andrea Lake, Cambridge University Hospitals NHS Foundation Trust
Dr Anthony Lewis, Belfast Health and Social Care Trust, Northern Ireland
Dr Sue Manley, University Hospitals Birmingham NHS Foundation Trust
Flora Mates, Diabetes UK
Dr Omar Mustafa, King's College Hospital NHS Foundation Trust, London
Philip Newland-Jones, University Hospital Southampton NHS Foundation Trust
Dr Dipesh Patel, Royal Free London, NHS Foundation Trust
Professor Gerry Rayman, The Ipswich Hospitals NHS Trust
Dr Stuart Ritchie, NHS Lothian
Dr Aled Roberts, Cardiff and Vale University Health Board
Professor Mike Sampson, Norfolk and Norwich University Hospitals NHS Foundation Trust
Professor Alan Sinclair, Director Diabetes Frail Ltd
Esther Walden, Diabetes UK
Dr Peter Winocour, East and North Hertfordshire NHS Trust

Special thanks to Christine Jones for her administrative work and help with these guidelines and with JBDS-IP.

Example intravenous insulin prescription and fluid protocol

FOR DIABETIC KETO-ACIDOSIS (DKA)

For use for ALL ADULT patients with a diagnosis of DKA
NOT FOR USE IN CHILDREN
NEVER use an IV syringe to draw up insulin
ALWAYS draw up insulin using an insulin syringe
ALWAYS continue subcutaneous intermediate* or basal insulin**
*Intermediate: Insulatard®, Humulin I®, Insuman Basal®
**Basal: Lantus® (glargine), Levemir® (detemir), Tresiba® (degludec), Toujeo® (long acting glargine)
Doctor: All prescriptions for insulin and fluids must be signed
Nurse: All entries must be signed

Ward	Consultant	Admission Date:
		Discharge Date:
Surname		First Name
Hospital Number		Date of Birth / Age
NHS Number		
Address		

ENTRY (diagnostic) CRITERIA (ALL must be ticked to establish diagnosis)

- Established or new diagnosis of diabetes mellitus ☐
- Capillary blood ketonaemia on Trust approved ketone meter of ≥ 3 mmol/L or ketonuria ++ or more on standard urine sticks ☐
- Venous bicarbonate <15 mmol/L and/or venous pH <7.3 ☐

If patient satisfies all ENTRY CRITERIA, commence insulin therapy (see BOX 1); intravenous fluid management (see BOX 2, BOX 3 and BOX 4); and intravenous fluid prescription (see BOX 5)
If patient has ketonaemia WITHOUT acidosis (pH≥7.3 or HCO3≥15 mmol/L, intravenous insulin therapy may not be required BUT intravenous fluid hydration and subcutaneous insulin dose correction may be necessary

BOX 1: INTRAVENOUS INSULIN THERAPY AND PRESCRIPTION

A Fixed Rate Intravenous Insulin Infusion (FRIII) calculated on 0.1 units/kg body weight is recommended (see Weight/insulin dose Reference Guide)
It may be necessary to estimate the weight of the patient

Patient's Weight: _____ kg (Actual/Estimated)
Insulin dose per hour: _____ units Date: _____
Print Name: _____ Signature: _____

If blood ketones not falling by at least 0.5 mmol/L/hr **OR** venous bicarbonate not rising by at least 3 mmol/L/hr **OR** CBG not falling by at least 3 mmol/L/hr- increase insulin infusion rate by 1.0 unit/hr until falling at target rates

Weight/insulin dose reference Guide			
Weight (in kg)	Insulin dose/hr (Units)	Weight (in kg)	Insulin dose/hr (Units)
*50-59	5	100-109	10
60-69	6	110-119	11
70-79	7	120-129	12
80-89	8	130-139	13
90-99	9	>140	*

*<50 kg or >140 kg: seek advice from the Diabetes Specialist Team

Date	Time	Adjusted dose (units/hr)	Prescriber Name	Prescriber Signature	Bleep

Drug (approved name)	Dose	Volume	Route	Prescriber's Signature	Prescriber Print name	Date
Actrapid®	50 UNITS	Made up to 50ml with NaCl 0.9% (1 UNIT per mL)	IV			

BOX 2: INTRAVENOUS FLUID MANAGEMENT (Saline regime)

CAUTION: Slower in young people aged 18-25 years, elderly, pregnant, heart or renal failure

0.9% sodium chloride 1 litre (no KCl)	Over 1st hour
0.9% sodium chloride 1 litre (check K+)	Over next 2 hours
0.9% sodium chloride 1 litre (check K+)	Over next 2 hours
0.9% sodium chloride 1 litre (check K+)	Over next 4 hours
0.9% sodium chloride 1 litre (check K+)	Over next 4 hours
Anticipate a fall in potassium and replace (see BOX 4)	

BOX 3: INTRAVENOUS FLUID MANAGEMENT (Dextrose regime)

Once CBG<14 mmol/L, or in the event of non-hyperglycaemic DKA presenting with CBG <14 mmol/L:

Give 10% Dextrose to run at 125 mls/hr AND
Continue saline as per Saline regime (see BOX 2)
Run through Saline and Dextrose regime in 2 separate lines at the SAME time
Run Dextrose regime and insulin therapy in the same line via a three way non-return valve

Re-assessment of cardio-vascular status at 12 hours is mandatory, further fluid may be required

SYRINGE PREPARATION

Prepared and administered by	Date	Time started	Time stopped

BOX 4: POTASSIUM REPLACEMENT

Add potassium as per guidance below
EXCEPT for the first Saline (1 hour) bag
ONLY use pre-prepared bags

>5.5 mmol/L	None
3.5 – 5.5 mmol/L	40 mmol KCl per litre (see rate in Box 2)
<3.5 mmol/L	40 mmol KCl per litre (senior review if additional potassium needs to be given- See rate in Box 2)

BOX 5: INTRAVENOUS FLUID PRESCRIPTION

For information on dilutions, infusion rates, compatibilities and monitoring parameters, consult the:
Injectable Medicines Guide or contact Medicines Information
CAUTION: Slower in young people aged 18-25 years, elderly, pregnant, heart or renal failure

Date	Solution	Volume	Additives and dose Check potassium Refer to BOX 4		Rate	Duration	Route	Prescriber Signature & Bleep	Batch No.	Given by / 2nd check	Time started	Time stopped	Pharm and supply notes
	0.9% NaCl	1 litre	KCl	None	1000 mls/hr	1 hr	IV						
	0.9% NaCl	1 litre	KCl		500 mls/hr	2 hrs	IV						
	0.9% NaCl	1 litre	KCl		500 mls/hr	2 hrs	IV						
	0.9% NaCl	1 litre	KCl		250 mls/hr	4 hrs	IV						
	0.9% NaCl	1 litre	KCl		250 mls/hr	4 hrs	IV						
	0.9% NaCl	1 litre	KCl		166 mls/hr	6 hrs	IV						
	10% Dextrose	1 litre			125 mls/hr	8 hours	IV						

SWITCH FROM FIXED RATE INTRAVENOUS INSULIN INFUSION TO VARIABLE RATE INTRAVENOUS INSULIN INFUSION (VRIII) with 10% Dextrose with 0.15% KCl at 50 mls/hr IF:
DKA: CAPILLARY BLOOD KETONES < 0.6 mmol/L and HCO3 > 15 mmol/L and STILL not eating and drinking
HHS: Biochemical markers have normalised and STILL not eating and drinking

PRESCRIPTION

CBG mmol/L	Insulin units/hr	Insulin units/hr	Insulin units/hr
> 14	6		
12.1 – 14	4		
10.1 - 12	3		
7.1 – 10	2		
4 - 7	1		
< 4	0.5		
Signature			
Bleep No.			
Date			
Time			

Point of Care and laboratory results
Check creatinine, electrolyte and venous bicarbonate and pH at 2 hours then 2 to 4 hourly until venous bicarbonate >15 mmol/L

Date	Time	Ketones	Na+	K+	Creatinine	HCO3	pH	Osmolality	Signature

EXIT CRITERIA (ALL must be ticked)

DKA:
Blood ketones <0.6 mmol/L **and** ☐
Venous bicarbonate >15 mmol/L **and** ☐
Eating and drinking ☐

HHS:
Osmolality normalised **and** ☐
Eating and drinking ☐

Transfer to subcutaneous insulin regime

Notes:

Maintain IV insulin infusion for 30 minutes after re-starting original insulin regime- IV insulin has a 5 minute half-life

ALWAYS continue subcutaneous basal insulin

Refer to the Diabetes Specialist Team

Seek and treat precipitating factors

Consider prophylactic or full anticoagulation

Other issues:

INTRAVENOUS INSULIN, CBG AND KETONES MONITORING RECORD SHEET

Guide:

Only use for patients on intravenous insulin regimen (use different chart for patients on subcutaneous insulin)
Make sure the patient's hands are clean
Check CBG hourly
Check capillary blood ketone hourly until DKA resolved

ADDRESSOGRAPH LABEL

DATE	Time	Blood glucose	Blood ketones	Hourly infusion rate (units/hr)	Volume left in syringe (ml)	Volume infused in one hour (ml)	Total volume infused (ml)	Signatures		KEY EVENTS / NOTES

Example management chart for the management of DKA - Page 1

ADULT DIABETIC KETOACIDOSIS (DKA) – MONITORING CHART

Surname | Reg no
Forename | Sex | Date of birth
Address | Cons
Ward/Dept
Hosp

TREATMENT AIMS:
1. Blood ketones to fall by at least 0.5mmol/L/hour
2. Venous bicarbonate to rise by at least 3mmol/L/hour
3. Blood glucose to fall by at least 3mmol/L/hour

IF THIS IS NOT BEING ACHIEVED, CHECK LINES, THEN INCREASE RATE OF INSULIN BY 1-2mL/hour

MONITORING HOURLY CBG, CAPILLARY KETONES, Urinary Output
pH – 2, 4, 6, 12, 18, 24 HOURS (or until resolved)
U+Es – 4, 6, 12, 24 HOURS
EWS – hourly

RESOLUTION OF DKA: Blood ketones<0.3/L AND/OR pH>7.3

Hours from start of treatment (h)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Actual Time																									
Capillary Blood Glucose (mmol/L)	>20																								
	20																								
	19																								
	18																								
	17																								
	16																								
Start 10% Glucose at 100ml/hour when CBG<14	15																								
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	9																								
	8																								
	7																								
	6																								
	5																								
	4																								
	3																								
	2																								
	1																								
Blood ketones (mmol/L)																									
Insulin rate (mL/h)																									
0.9% NaCl (mL/h)																									
10% Glucose rate (mL/h)																									
Urine output (mL/h)																									
Venous pH																									
Venous K^+																									
Venous HCO_3^-																									

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ADULT DIABETIC KETOACIDOSIS (DKA) – MANAGEMENT CHART

Surname | Reg no
Forename | Sex | Date of birth
Address | Cons
Ward/Dept
Hosp

DATE: TIME: CONS:

CLERKING DR: GRADE: BLEEP:

IMMEDIATE MANAGEMENT 0-60 MINUTES

ACTION 1 — **CONFIRM DIAGNOSIS**

ALL 3 OF THE FOLLOWING MUST BE PRESENT TO CONFIRM DKA
1. Capillary blood glucose (CBG) 11.0mmol/L or known diabetes
2. Capillary blood ketones>3.0mmol/L or 2+ ketonuria
3. Venous pH<7.3 and/or venous bicarbonate<15mmol/L

CBG mmol/L
Ketones mmol/L
pH
HCO_3^- mmol/L

ACTION 2 — **BASELINE ASSESSMENT**

Na^+ K^+ Urea Creatinine Chloride eGFR HCO_3^- Lactate Lab glucose GCS EWS

E
M
V

ACTION 3 — **INVESTIGATIONS**

ECG CXR MSU βHCG STOOL MC&S BLOOD CULTURES CT HEAD VTE PROPHYLAXIS GIVEN?
CHECK ANION GAP

ACTION 4 — **PRECIPITATING FACTORS**

INFECTION/SEPSIS STRESS NON-COMPLIANCE IDIOPATHIC OTHERS (STEROIDS, ALCOHOL, PREGNANCY, PUMP FAILURE)

ACTION 5 — **IS THE PATIENT SHOCKED?**

Patient shocked (SBP<90 mmHg) or severe DKA*

YES ☐ Give 500ml 0.9% Sodium Chloride (NaCl) over 15 mins and give another 500ml bolus over 15mins if SBP still<100mmHg (Hypotension is likely to be due to low circulating volume but consider other causes such as sepsis/heart failure etc.)

NO ☐ Give 1L 0.9% Sodium Chloride over an hour

SpR/Consultant informed?
Time:

Severe DKA*
Ketones>6, pH<7.1, HCO_3^-<5, K^+<3.5, GCS<12, SpO_2<92% SBP<90, Pulse>100/<60
CALL ITU

ACTION 6 — **INSULIN**

Prescribe 50 units of Actrapid in 49.5ml 0.9%NaCl (1unit/ml)
Commence a fixed rate insulin infusion at 0.1unit/kg/hour
Maximum 15ml/hour (starting dose)

Done? ☐ Initial Time

Weight: kg Initial Insulin rate: ml(units)/hour

If patient takes long acting insulin e.g. Insuman Basal or Humulin I or Glargine or Levemir or Degludec or Toujeo continue as normal (circle which applies) ☐ **Dose: Units**

ACTION 7 — **POTASSIUM REPLACEMENT**

Venous potassium level	**Potassium Chloride (KCl) replacement**
>5.5mmol/L	NONE
3.5-5.5 mmol/L	40mmol/L
<3.5 mmol/L	SENIOR ADVICE, additional K^+ required

☐ Life threatening hypokalemia can occur with insulin infusion. If K^+ infusion is greater than 20mmol/hour cardiac monitoring is needed

DO NOT GIVE KCl IF ANURIC

ACTION 8 — **REASSESS PATIENT**

Poor urine output (<0.5ml/kg/hour)	**Persistent vomiting or reduced GCS**	**SpO_2<94% On Air**	**Persistent acidosis?**	**GCS<13**	**Senior review?**
Catheterise	Consider NGT	ABG/CXR	Consider other causes	Consider CT head	Name Time

Example management chart for the management of DKA - Page 2

60 MINUTES TO 6 HOURS – ADMIT TO Monitored Bay

ACTION 1	CBG/BLOOD KETONES	VBG	U&Es	FLUID BALANCE	EWS
MONITORING	HOURLY	2, 4, 6, 12, 18hrs	6, 12, 24hrs	HOURLY	HOURLY

PLEASE CHART THESE VALUES ON THE MONITORING CHART

ACTION 2

IV FLUIDS

1L 0.9% sodium chloride +/- KCl over 2hrs (500ml/hour)
1L 0.9% sodium chloride +/- KCl over 2hrs (500ml/hour)
1L 0.9% sodium chloride +/- KCl over 4hrs (250ml/hour)

☐ NOTE – Caution in elderly, CCF, ESRF adolescence, pregnancy (risk of cerebral and pulmonary oedema)

When CBG<14.0mmol/L add 125ml/hour of 10% glucose to run alongside 0.9% Sodium Chloride
(consider reducing rate of 0.9% sodium chloride to reduce risk of fluid overload)

ACTION 3

Continue 0.9% sodium chloride (+KCl) as required to restore circulating volume

IV FLUID ADJUSTMENTS

Reassess patients volume status frequently (HR, BP, Urine Output, JVP, chest auscultation) and adjust fluid appropriately

When CBG<14.0mmol/L start 10% Glucose IV at 125ml/hour alongside 0.9% sodium chloride + potassium chloride

ACTION 4 **Ensure treatment targets are being met**

TREATMENT TARGETS

1. Fall in CBG of >3mmol/L (until CBG<14.0mmol/L)
2. Fall in capillary blood ketones of >0.5mmol/L/hour
3. Rise in venous bicarbonate of >3.0mmol/L

If the patient is not improving as expected, check the patency of the lines, check infusion pumps BEFORE increasing insulin by 1-2unit (ml)/hour

6 -12 HOURS

ACTIONS

1L 0.9% sodium chloride + /- potassium chloride over 4hours (250ml/hour)
1L 0.9% sodium chloride +/- potassium chloride over 6hours (125ml/hour)
If CBG<14.0mmol/L add 10% glucose 125 ml/hour, **using a separate port**
Reassess CV status
Check CBG, blood ketones, VBG, chloride,U&Es as above and signs of DKA resolution
Ensure early referral to ThinkGlucose (TG) Team

BEYOND 12 HOURS

RESOLUTION OF DKA

Resolution of DKA is defined as pH>7.3 and/or blood ketones<0.3 mmoll/L

1. If DKA has resolved and the patient is eating and drinking – switch to SC insulin (refer to TG team or DKA guideline on intranet)
2. If DKA has resolved but the patient cannot eat OR has another indication for IV insulin (severe sepsis/MI)- use a VRI infusion (see Medical guidelines)
3. Inform DSN/ThinkGlucose Team

By 24 hours ketonaemia and acidosis should have been resolved. Seek senior review or Diabetes Team support if not improving

ADULT DIABETIC KETOACIDOSIS (DKA) – MONITORING CHART

Surname Reg no
Forename Sex Date of birth
Address Cons
Ward/Dept
Hosp

TREATMENT AIMS:
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3. Blood glucose to fall by at least 3mmol/L/hour

IF THIS IS NOT BEING ACHIEVED, CHECK LINES, THEN INCREASE RATE OF INSULIN BY 1-2mL/hour

MONITORING
HOURLY CBG, CAPILLARY KETONES, Urinary Output
pH – 2, 4, 6, 12, 18, 24 HOURS (or until resolved)
U+Es – 4, 6, 12, 24 HOURS
EWS – hourly

RESOLUTION OF DKA: Blood ketones<0.3/L AND/OR pH>7.3

Hours from start of treatment (h)		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Actual Time																										
Capillary Blood Glucose (mmol/L)	>20																									
	20																									
	19																									
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	4																									
	3																									
	2																									
	1																									
Blood ketones (mmol/L)																										
Insulin rate (mL/h)																										
0.9% NaCl (ml/h)																										
10% Glucose rate (mL/h)																										
Urine output (mL/h)																										
Venous pH																										
Venous K^+																										
Venous HCO_3																										