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## Guidance on the management of Diabetic Ketoacidosis in the exceptional circumstances of the COVID-19 pandemic

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During the early stages of the COVID-19 pandemic, hospitals in London, the UK epicentre, reported an unusually high number of people presenting with COVID-19 disease developing diabetic ketoacidosis, hyperosmolar hyperglycaemic state, or a combination of both. Very high doses of insulin were often needed to manage the hyperglycaemia. It has been proposed that these metabolic disturbances may result from severe insulin resistance combined with decreased insulin secretion due to beta cell dysfunction [1]. The increased demand for pumps to deliver inotropes has led to concerns of possible shortages of infusion pumps and/or 50 ml syringes being available for insulin infusions to manage these hyperglycaemic emergencies. Concerns were also raised about the potential risk of exacerbating 'lung leak' in COVID-19 positive patients using the traditional rates of fluid replacement for the management of DKA. Clinicians therefore requested that a subcutaneous insulin regimen be made available as a backup strategy for managing diabetic ketoacidosis and guidance on the fluid replacement regimen.

In response to these requests the National Diabetes Inpatient COVID-19 Response Group has developed guidance on the management of DKA using subcutaneous insulin based on a regimen developed by Umpierrez and colleagues in the US [2], accompanied by two alternative fluid replacement regimens. The first is that from the Joint British Diabetes Societies [3] guidance for managing typical DKA. The second is a more cautious regimen for COVID-19 positive/suspected patients with consideration of a higher rate of fluid replacement if there is significant hypovolaemia or acute kidney injury (Figure 1). Importantly, clinical judgement, frequent senior review, and regular monitoring of fluid balance and oxygen saturations are advised. The regimen recommends using rapid acting insulin analogues. Given the need to reduce the time the health professional is in direct contact with the patient a 4 hourly dosing schedule has been recommended with the dose calculated on body weight to equate to a similar quantity of insulin that would have been delivered by an insulin infusion. Finally, as with other guidance we recommend continuing or starting a basal insulin alongside.

We hope that most teams will not find it necessary to use the subcutaneous insulin route to manage DKA, but we understand that this regimen has been welcomed by some working in less well-resourced countries.

**G. Rayman[1], A. Lumb[2], B. Kennon[3], C. Cottrell[4], D. Nagi[5], E. Page[1], D. Voigt[6], H. Courtney[7], H. Atkins[8], J. Platts[9], K. Higgins[9], K. Dhatariya[10], M. Patel[11], P. Narendran[12], P. Kar[13,14], P. Newland-Jones[15], R. Stewart[16], O. Burr[17] and S. Thomas[18]**

*[1]The Ipswich Hospital and Ipswich Diabetes Centre and Research Unit, East Suffolk and North Essex NHS Foundation Trust, Colchester, [2]Oxford University Hospitals NHS Foundation Trust, OCDEM, Oxford, UK, [3]Department of Diabetes, Queen Elizabeth University Hospital, Glasgow, Scotland, [4]Diabetes, Swansea Bay University Health Board, Port Talbot, [5]Diabetes, Mid Yorkshire Hospitals NHS Trust, Wakefield, UK, [6]Tayside University Hospitals NHS Trust, Ninewells Hospital, Dundee, Scotland, [7]Diabetes, Belfast Health and Social Care Trust, Belfast, [8]Diabetes, University Hospitals of Leicester NHS Trust, Leicester, [9]College of Medicine, Cardiff and Vale University Local Health Board, Cardiff, [10]Elsie Bertram Diabetes Centre, Norfolk & Norwich University Hospital NHS Foundation Trust, Norwich, [11]Diabetes, University Hospital Southampton NHS Trust, Southampton, [12]Diabetes, Queen Elizabeth Hospital Birmingham, Birmingham, [13]Portsmouth Hospitals NHS trust, Portsmouth, [14]NHS Diabetes Programme, NHS England, London, [15]Diabetes and Endocrinology, University of Southampton Faculty of Medicine, Southampton, [16]Diabetes, Wrexham Maelor Hospital, Betsi Cadwaladr University Health Board, Wrexham, [17]Diabetes, Diabetes UK, and [18]Diabetes Centre, Guy's and Saint Thomas' NHS Foundation Trust, London, UK*

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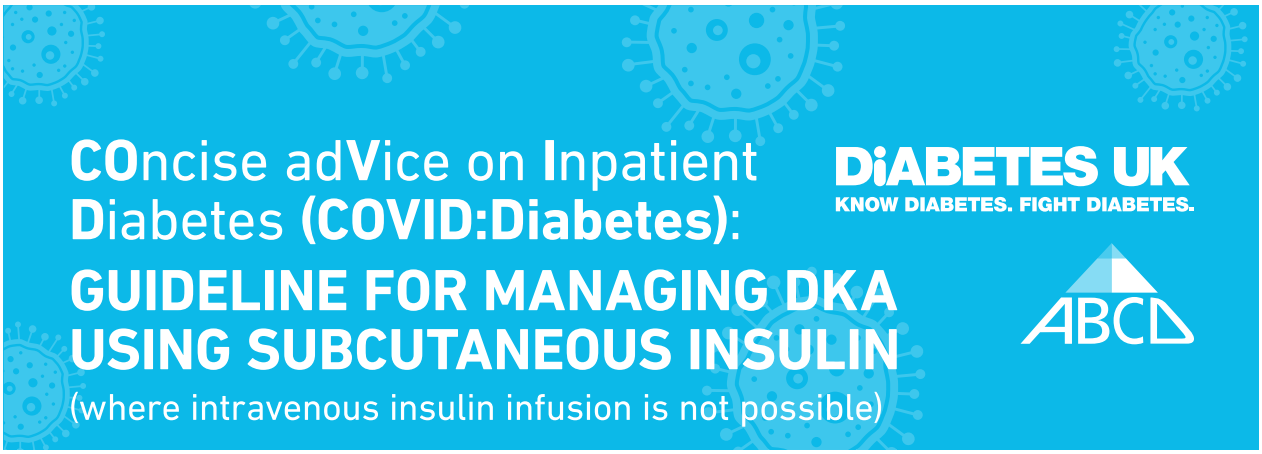


## NATIONAL INPATIENT DIABETES COVID-19 RESPONSE GROUP*

**For use in Covid-19 suspected/positive people and those without Covid-19 disease when diagnosis of DKA has been confirmed (see COVID: Diabetes Front Door Guidance)**

This approach is **NOT** recommended where:

- **Mixed DKA/Hyperosmolar state (osmolality greater than 320 - osmolality = [2 x Na] + Urea + Glucose)**
- **The person is pregnant**
- **Severe metabolic derangement (e.g. pH less than 7.0, OR bicarbonate less than 10 mmol/l, OR potassium less than 3.5 mmol/l)**
- **Significant other co-morbidity (e.g. acute coronary syndrome, CKD stage 4 or 5, end-stage liver disease)**
- **Conscious level impaired**

In these situations, help should be sought early from the specialist diabetes team and teams should refer to their local DKA protocol.

**Aims of treatment:**

- Fall in ketones of 0.5 mmol/l/hour while
- Maintaining glucose at a safe level without hypoglycaemia
  - Target glucose range is 6 - 14 mmol/l
  - Additional glucose is required (by IV infusion – see Fluid Replacement over) when glucose is lower than 14 mmol/l

**Remember, euglycaemic DKA – where glucose levels are normal – can occur in pregnancy or in those using SGLT2 inhibitors**

**Targets of treatment:**

- **Ketones less than 0.6 mmol/l**
- **pH greater than 7.3**

*NATIONAL INPATIENT DIABETES COVID-19 RESPONSE GROUP:

Professor Gerry Rayman (Chair), Dr Alistair Lumb, Dr Brian Kennon, Chris Cottrell, Dr Dinesh Nagi, Emma Page, Debbie Voigt, Dr Hamish Courtney, Helen Atkins, Dr Julia Platts, Dr Kath Higgins, Professor Ketan Dhatariya, Dr Mayank Patel, Dr Parth Narendran, Professor Partha Kar, Philip Newland-Jones, Dr Rose Stewart, Dr Stephen Thomas, Dr Stuart Ritchie

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**FIGURE 1** Guideline graphic

## FLUID REPLACEMENT

**FLUID SHOULD BE REPLACED INTRAVENOUSLY**

For general guidance regarding intravenous fluid replacement see local guidance or JBDS guidance available here.

**Initial resuscitation – if systolic BP less than 90 mmHg infuse 500mls 0.9% saline bolus over 15 minutes. Repeat if systolic BP remains below 90 mmHg. Seek senior support if requiring more than 1 bolus of this sort.**

**Standard rate of fluid replacement with 0.9% saline** (note slower rate should be considered in those aged 18-25 and over 70, and who are pregnant or who have cardiac or renal failure)

| | RATE (ML/HR) |
|---|---|
| 1st litre (given over 1 hr) | 1000 |
| 2nd litre (given over 2 hr) | 500 |
| 3rd litre (given over 2 hr) | 500 |
| 4th litre (given over 4 hr) | 250 |
| 5th litre (given over 4 hr) | 250 |

**If a more cautious approach is required in COVID-19 positive/suspected,** after an initial fluid bolus of 250ml in 15 minutes, the table below is a starting point only, and aims to avoid excessive fluid replacement. Use clinical judgment, frequent senior review and consider a higher rate of fluid replacement if significantly hypovolaemic/AKI:

| WEIGHT (KG) | RATE OF 0.9% SODIUM CHLORIDE INFUSION (MLS/HR) | |
|---|---|---|
| | pH 7.1 OR LESS | GREATER THAN 7.1 |
| Less than 50 | 100 | 90 |
| 50-60 | 115 | 100 |
| 61-70 | 130 | 115 |
| 71-80 | 140 | 125 |
| 81-90 | 150 | 135 |
| 91-100 | 165 | 145 |
| Over 100 | 170 | 155 |

**Remember:** Glucose-containing fluid (e.g. 10% glucose at 125 ml/hour) should be infused when the glucose is less than 14 mmol/l **and reviewed with insulin prescription when** ketones less than 0.6 mmol/l. The 10% glucose usually runs alongside the 0.9% sodium chloride solution.

**For euglygaemic DKA** 10% glucose should be used as the resuscitation fluid.

## RAPID-ACTING INSULIN

**4 HOURLY SUBCUTANEOUS DOSES OF RAPID-ACTING INSULIN ANALOGUE (NOVORAPID® /HUMALOG® /APIDRA®)**

Aiming for a reduction in ketones of at least 0.5 mmol/l/hour (2 mmol/l over 4 hours)

- **Initial dose of 0.4 units/kg every 4 hours.** This dose may appear large however is equivalent to the IV dose used in standard DKA management
- **Reduce to 0.2 units/kg every 4 hours** once glucose less than 14 mmol/l
- Continue until **ketones** less than 0.6 mmol/l

If ketones not falling as expected:

- Increase rapid acting insulin dose to 0.5 units/kg every 4 hours
- Contact the diabetes specialist team
- Consider switching to iv insulin if infusion pump available

## POTASSIUM

**The effect of Covid-19 disease on potassium regulation remains unknown, and so potassium replacement should follow standard protocols and be guided by 2 hourly monitoring**

## MONITORING IMPACT OF TREATMENT

- **Glucose and ketones** - check at least 2 hrly
- **Fluid balance** - record hrly, regular review and adjustment according to clinical condition
- **Oxygen saturations** - regular assessment as a potential marker of fluid overload

## BASAL INSULIN

**ALWAYS START/CONTINUE LONG-ACTING INSULIN WHEN TREATING DKA**

- **If using regular injectable long-acting insulin** this should be continued
- **If not previously using basal insulin** initiate a dose of 0.15* units/kg/day **(involve the local diabetes team at the earliest opportunity)**

**If using a personal insulin pump either:**

1. Continue basal insulin rate via pump if person can safely manage this themselves. The pump infusion set should be changed by the patient (it may be an infusion set problem that caused DKA)

   **OR**

2. Switch to sc basal insulin regime if the person is not able to safely manage their own pump:
   - Find the usual total **daily** basal insulin dose and use the same dose of injectable basal insulin (the patient will be able to find this dose from the pump)
   - If unable to find total basal insulin dose from pump then give a total daily basal insulin dose of 0.25* units/kg
   - Options are twice daily Levemir® or once daily Lantus® / Abasaglar® / Semglee®

* Different basal dose depending on insulin naive or previous insulin use

## ONCE TREATMENT TARGETS ARE ACHIEVED:

**If the person is already treated with insulin**

- Transfer back onto usual regimen
  - If on subcutaneous insulin injections
    - Long-acting insulin should have been continued – ensure this is the case
    - Add rapid-acting insulin according to the usual regimen before meals
    - Correction doses can be used according to the "Guidance for managing inpatient hyperglycaemia" document
  - If using a personal insulin pump
    - The person will need to be well enough to reinstate their pump and manage their insulin regimen themselves
    - Ensure pump started within 3 hrs of subcutaneous rapid acting insulin dose

**If the person was not previously on insulin**

- Administer long-acting insulin as above (Basal Insulin section) and use the "Guidance for managing inpatient hyperglycaemia" document for correction doses

**Involve your local diabetes team**

**ALWAYS monitor glucose and ketones initially 4 hourly following transfer to 'usual' insulin regimen to ensure ketones remain lower than 1.5 mmol/l and blood glucose is within target range (6 – 14mmol/l)**

**FIGURE 2** Continued