What non-diabetes specialists need to know about diabetes

RESOURCES DOCUMENT
COVID-19 infection in people with or without previously recognised diabetes increases the risk of the EMERGENCY states of hyperglycaemia with ketones, Diabetic KetoAcidosis (DKA) and Hyperosmolar Hyperglycaemic State (HHS)

Being acutely unwell with suspected/confirmed COVID-19 requires adjustment to standard approaches to diabetes management (see table below).

The guidance in this document is based on experience from UK centres with the greatest experience of looking after patients with COVID-19 disease and will be updated as more evidence becomes available.

<table>
<thead>
<tr>
<th>WHERE CHANGE SEEN</th>
<th>KEY DIFFERENCE WITH COVID-19</th>
<th>SUGGESTED ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early in admission</td>
<td>People with COVID-19 infection appear to have a greater risk of hyperglycaemia with ketones including:   › People with type 2 diabetes (risk even greater if on a SGLT-2 inhibitor)   › People with newly diagnosed diabetes COVID-19 disease precipitates atypical presentations of diabetes emergencies (eg, mixed DKA and hyperosmolar states)</td>
<td>Check blood glucose in everybody on admission Check ketones in:   › everybody with diabetes being admitted   › everybody with an admission glucose over 12 mmol/l Stop SGLT-2 inhibitors in all people admitted to hospital Consider using 10-20% glucose where ketosis persists despite treatment in line with usual protocols</td>
</tr>
<tr>
<td>Severe illness on admission</td>
<td>Fluid requirements may differ in those with DKA/HHS and evidence of “lung leak” or myocarditis</td>
<td>After restoring the circulating volume the rate of fluid replacement regimen may need to be adjusted where evidence of “lung leak” or myocarditis Contact the diabetes specialist team early Early involvement of the critical care team</td>
</tr>
<tr>
<td>All inpatient areas</td>
<td>Infusion pumps may not be available to manage hyperglycaemia using intravenous insulin as these are required elsewhere (eg for sedation in ICU)</td>
<td>Use alternative s/c regimens to manage Hyperglycaemia Mild DKA Contact the diabetes specialist team for support</td>
</tr>
<tr>
<td>ICU</td>
<td>Significant insulin resistance seen in people with type 2 diabetes in ICU settings</td>
<td>IV insulin protocols may need amending (people seen requiring up to 20 units/hr) Patients often nursed prone so feeding may be accidentally interrupted – paradoxical risk of hypoglycaemia</td>
</tr>
</tbody>
</table>
CONCISE ADVICE ON INPATIENT DIABETES (COVID:Diabetes): GUIDANCE

COVID-19 infection in people with or without previously recognised diabetes increases the risk of the EMERGENCY states of hyperglycaemia with ketones, Diabetic KetoAcidosis (DKA) and Hyperosmolar Hyperglycaemic State (HHS)

Management of Acute Diabetes at the Front Door for Emergency Departments & Acute Medical Units

Patient Assessment: A B C D E

⚠️ NOTE: Shortness of Breath can also be due to METABOLIC Acidosis (e.g. DKA)

Ensure ALL newly admitted patients are evaluated for diabetes

GLUCOSE measurement in ALL patients and KETONE check if known diabetes or blood glucose level above 12mmol/L

⚠️ STOP SGLT-2 inhibitor (Cana-/Dapa-/Empa- or Ertu-gliflozin) and Metformin in ALL patients

REVIEW safety of continuing ACE-inhibitors, ARBs, NSAIDs

Glucose < 4mmol/L = HYPOGLYCAEMIA

FOLLOW LOCAL GUIDELINES

Glucose ≥ 12mmol/L or known diabetes

Blood GLUCOSE Level Advice (Known OR Unknown diabetes)

Primary diagnoses to URGENTLY consider:

› DKA (defined as glucose >11mmol/L or history of diabetes, blood ketones ≥ 3mmol/L or urine ketones ≥ +2 and pH <7.3 or bicarbonate <15). Note: glucose can be normal in SGLT-2 inhibitor associated DKA & pregnancy associated DKA

› HHS (defined as glucose ≥ 30mmol/L, Serum Osmolality [(2 x Na) + glucose + urea] > 320mOsm/kg and pH > 7.3)

Follow local guidelines if either of above is confirmed and involve diabetes team as soon as possible, as changes to usual fluid replacement regimen may be necessary

⚠️ NOTE: NEVER STOP BASAL INSULIN IN PERSON WITH KNOWN TYPE 1 DIABETES OR DKA MAY RESULT

Other URGENT causes of hyperglycaemia to consider:

› New presentation of diabetes (type 1 or 2 - age/weight irrelevant for either)

› SEPSIS (e.g. COVID-19 or foot infection)

› Missed/delayed usual diabetes treatment (e.g. insulin pen or personal insulin pump problem)

› Reflection of uncontrolled diabetes/inappropriate treatment regimen (recent HbA1c available?)

› Oral steroid use

Persistently high glucose levels may need treatment with subcutaneous or intravenous insulin

If an infusion pump is not available for IV insulin then seek advice regarding an alternative subcutaneous regimen.

In all cases, if unsure please seek diabetes team guidance as early as possible or follow local protocols

FURTHER ADVICE ON NEXT PAGE:
FURTHER ADVICE ON INPATIENT DIABETES (COVID:Diabetes):

BLOOD KETONE LEVEL ADVICE:

| Blood ketones less than 0.6 mmol/L = SAFE level |
| Blood ketones 1.5 – 2.9 mmol/L = INCREASED DKA RISK |
| ▶ PO or IV fluids |
| ▶ Consider rapid acting insulin if glucose above 16 mmol/L - 1 unit rapid acting insulin ‘typically’ expected to lower glucose by anywhere between 1-3 mmol/L. Recheck in 2 hours. |

**Blood ketones 3mmol/L or greater then check pH and bicarbonate (venous blood gas). DKA confirmed if high ketones accompanied by:**

| ▶ Blood glucose > 11 mmol/L (or history of diabetes) and |
| ▶ pH < 7.3 or bicarbonate <15 |

⚠️ **NOTE:** Glucose can be <11 mmol/L if patients are on SGLT-2 inhibitor treatment, pregnant AND/OR severe COVID-19 infection

INSULIN ADVICE – ALWAYS ASK IF YOUR PATIENT IS ON INSULIN

▶ ALWAYS CONTINUE USUAL LONG ACTING BASAL INSULIN
▶ Patients who are very sick or not eating should have a Variable Rate Intravenous Insulin Infusion (VRIII/‘sliding scale’), with usual basal subcutaneous (SC) insulin continued alongside
▶ If an infusion pump is not available for IV insulin, contact diabetes team or follow local protocols for an alternative subcutaneous regimen

PATIENTS USING WEARABLE DIABETES TECHNOLOGY

▶ If patients are unable to manage their personal insulin pump and no specialist advice is immediately available, start a VRIII or S/C basal-bolus insulin regimen then remove the pump and store it safely. If S/C regime required and not able to find out total daily insulin dose from pump then the following would be safe: calculate total daily insulin dose using 0.5 units/kg and give half the total dose as basal/background insulin and half as bolus/mealtime rapid acting insulin.
Example, 0.5 units x 60 kg = total daily insulin dose of 30 units. Give half dose (15 units) as basal insulin and 15 units as bolus insulin (5 units at each meal-time). Ensure that pump is disconnected AFTER S/C basal insulin given.
▶ Continuous glucose monitors (CGM) and Freestyle Libre (FSL) devices can be left on the patient but conventional capillary glucose monitoring will still be necessary
▶ For imaging, insulin pumps, Continuous Glucose Monitors (CGM) and FreeStyle Libre (FSL) devices need to be removed for magnetic scans such as MRI

FOOTNOTES

▶ ALWAYS need to exclude acute foot infection (may be the source of sepsis) or critical limb ischaemia
▶ ALWAYS ensure foot intact and protected
⚠️ **TAKE ACTION ON ACUTE FOOT DISEASE AS PER LOCAL DIABETIC FOOT PROTOCOLS**
COncise adVice on Inpatient Diabetes (COVID:Diabetes):  
GUIDELINE FOR MANAGING DKA USING SUBCUTANEOUS INSULIN  
(where intravenous insulin infusion is not possible)

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

Acknowledgements: London Diabetes Inpatient Network – COVID-19 • Designed by: Leicester Diabetes Centre
**FLUID REPLACEMENT**

**FLUID SHOULD BE REPLACED INTRAVENOUSLY**

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

**Important 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)

<table>
<thead>
<tr>
<th>WEIGHT (KG)</th>
<th>RATE (ML/HR)</th>
<th>RATE OF 0.9% SODIUM CHLORIDE INFUSION (MLS/HR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 50</td>
<td>100</td>
<td>pH 7.1 OR LESS</td>
</tr>
<tr>
<td>50 – 60</td>
<td>115</td>
<td>greater than 7.1</td>
</tr>
<tr>
<td>61 – 70</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>71 – 80</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>81 – 90</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>91 – 100</td>
<td>165</td>
<td></td>
</tr>
<tr>
<td>Over 100</td>
<td>170</td>
<td></td>
</tr>
</tbody>
</table>

**FLUID REPLACEMENT**

If a more cautious approach is required in COVID-19 positive/suspected, after an initial 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:

<table>
<thead>
<tr>
<th>WEIGHT (KG)</th>
<th>RATE (ML/HR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st litre (given over 1 hr)</td>
<td>1000</td>
</tr>
<tr>
<td>2nd litre (given over 2 hr)</td>
<td>500</td>
</tr>
<tr>
<td>3rd litre (given over 2 hr)</td>
<td>500</td>
</tr>
<tr>
<td>4th litre (given over 4 hr)</td>
<td>250</td>
</tr>
<tr>
<td>5th litre (given over 4 hr)</td>
<td>250</td>
</tr>
</tbody>
</table>

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 euglycaemic 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

**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 initial 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 – 14 mmol/l)**

**BASEL 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
**Concise adVice on Inpatient Diabetes (COVID:Diabetes): GUIDANCE FOR MANAGING INPATIENT HYPERGLYCAEMIA**

**NATIONAL INPATIENT DIABETES COVID-19 RESPONSE GROUP***

**Use when:**

- Glucose above 12 mmol/l and a correction dose is appropriate for the individual patient
- DKA/HHS not present

*Can be used in place of variable rate intravenous insulin when infusion pumps not available

**DO NOT use for people with COVID-19 causing severe insulin resistance in the ICU. Contact your local diabetes team for advice in this circumstance.**

**After 9pm consider risk of hypoglycaemia overnight when thinking about the use of a corrective dose**

---

**IF GLUCOSE > 12 MMOL/L AND NO INSULIN ADMINISTERED IN PREVIOUS 4 HRS CONSIDER A CORRECTIVE DOSE OF RAPID-ACTING ANALOGUE INSULIN (NOVORAPID®/HUMALOG®/APIDRA®)**

- Re-check glucose after 4 hours OR before next meal – further action may be required
- Target glucose 6–10 mmol/l – aiming for higher end of range (up to 12 mmol/l acceptable)
- Dose decided using one of the following 3 factors and the table below. Factors are listed in order of importance:
  1. If person uses pre-existing correction ratio (CR) (e.g. 1 unit insulin lowers glucose by 3 mmol/l) this should be used
  2. If person using insulin but doesn’t have correction ratio, use their usual total daily insulin dose (TDD)
  3. If person not previously using insulin, or dose is unknown, use their weight
- If the person has rapid-acting insulin with each meal the corrective dose can be added to their mealtime dose if appropriate.

**GLUCOSE (MMOL/L) | CR* = 1 UNIT ↓ 4 MMOL/L OR TDD** LESS THAN 50 UNITS OR WEIGHT LESS THAN 50KG | CR* = 1 UNIT ↓ 3 MMOL/L OR TDD** = 50–100 UNITS OR WEIGHT BETWEEN 50–100 KG | CR* = 1 UNIT ↓ 2 MMOL/L OR TDD** OVER 100 UNITS OR WEIGHT OVER 100 KG
---|---|---|---
12.0–14.9 | 1 | 1 | 2
15.0–16.9 | 2 | 2 | 3
17.0–18.9 | 2 | 3 | 4
19.0–20.9 | 3 | 3 | 5
21.0–22.9 | 3 | 4 | 6
23.0–24.9 | 4 | 5 | 7
25.0–27.0 | 4 | 5 | 8
Over 27 | 5 | 6 | 9

*CR = Correction ratio, **TDD = total daily insulin dose

**It is recommended that glucose is checked at least 4 times per day in people treated with insulin**

---

**LONG-ACTING INSULIN (LEVEMIR®/ ABASAGLAR®/LANTUS®/SEMGLEE®/ HUMULIN I®/ INSULATARD®/INSUMAN BASAL®)**

- Already using long-acting insulin: Continue and titrate dose (see tables below)
- NOT already using long-acting insulin: If 2 or more glucose readings in 24 hrs are > 12 mmol/l (eg, 2 or more corrective doses in previous 24 hrs)
  - ADD long-acting insulin – total dose 0.25 units/kg/day (eg, 0.25 x 80kg = 20 units OD OR 10 units BD depending on the choice of basal insulin – see below).
  - NOTE if:
    - Older (>70 yrs) or frail
    - Serum creatinine >175 umol/l
    - Use a reduced long-acting insulin dose of 0.15 units/kg (eg 0.15 x 80kg = 12 units OD OR 6 units BD)

**Recommended options (all acceptable – refer to local protocols):**

- **Levemir®**
  - Insulin detemir
  - 100 units/ml (U100)
  - Two equal doses of 0.125 units/kg, 12 hrs apart
  - Not available in vials so insulin pen needles must be available to use with a pen device*
  - Can adjust either dose

- **Abasaglar®/Lantus®/Semglee®**
  - Insulin glargine
  - 100 units/ml (U100)
  - Single dose of 0.25 units/kg/24 hrs (minimises patient contact) or
  - Split above into 2 equal doses, 12 hrs apart
  - Abasaglar®/Semglee® not available in vials so insulin pen needles must be available to use with an insulin pen device**

- **Humulin I®/Insulatard®/Insuman Basal®**
  - Isophane insulin
  - 100 units/ml (U100)
  - Two equal doses of 0.125 units/kg/10–14 hrs apart
  - Particularly suited to steroid treatment – dose given as ½ total long-acting insulin dose am ±½ total long-acting insulin dose pm

* Only specific insulin syringes/needles should be used to administer insulin from vials
** DO NOT WITHDRAW INSULIN FROM A 3ML INSULIN PEN CARTRIDGE OR 3ML PREFILLED
DOSE ADJUSTMENT FOR LONG-ACTING INSULIN

Doses can be titrated daily, although longer-acting insulins may take 48-72 hours to reach steady state. Dose adjustments will affect blood glucose throughout the day.

ONCE daily long-acting insulin

<table>
<thead>
<tr>
<th>GLUCOSE LEVEL JUST BEFORE INSULIN DOSE</th>
<th>JUST BEFORE MORNING INSULIN DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4mmol/L</td>
<td>Reduce insulin by 20%</td>
</tr>
<tr>
<td>4.1-6mmol/L</td>
<td>Reduce insulin by 10%</td>
</tr>
<tr>
<td>6.1-12mmol/L</td>
<td>No change</td>
</tr>
<tr>
<td>12.1-18mmol/L</td>
<td>Increase insulin by 10%</td>
</tr>
<tr>
<td>&gt;18mmol/L</td>
<td>Increase insulin by 20%</td>
</tr>
</tbody>
</table>

TWICE daily long-acting insulin

<table>
<thead>
<tr>
<th>GLUCOSE LEVEL</th>
<th>JUST BEFORE MORNING INSULIN DOSE</th>
<th>JUST BEFORE EVENING INSULIN DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4mmol/L</td>
<td>Reduce evening insulin by 20%</td>
<td>Reduce morning insulin by 20%</td>
</tr>
<tr>
<td>4.1-6mmol/L</td>
<td>Reduce evening insulin by 10%</td>
<td>Reduce morning insulin by 10%</td>
</tr>
<tr>
<td>6.1-12mmol/L</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td>12.1-18mmol/L</td>
<td>Increase evening insulin 10%</td>
<td>Increase morning insulin 10%</td>
</tr>
<tr>
<td>&gt;18mmol/L</td>
<td>Increase evening insulin 20%</td>
<td>Increase morning insulin 20%</td>
</tr>
</tbody>
</table>

Dose reduction should also be considered in the following circumstances:

- Improving infection (as measured by falling CRP)
- Enteral feed reducing or stopping
- Corticosteroid treatment reducing or stopping
- End of life care

⚠️ In people recovering from COVID-19-related insulin resistance, doses may need to be reduced RAPIDLY to avoid hypoglycaemia.

As noted above, severe insulin resistance has been noted in some people with COVID-19 in the ICU. In this circumstance, suggested alternative treatment strategies include four times daily doses of Levemir® or twice daily doses of Lantus®.

Contact your local diabetes team for advice.

*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

Acknowledgements: London Diabetes Inpatient Network – COVID-19 • Designed by: Leicester Diabetes Centre