Diabetic Ketoacidosis (DKA)

Description
Life-threatening acute Cx of DM characterised by dehydration, hyperglycaemia, glycosuria, ketonaemia, ketonuria & acidosis. [Biochem: BSL>11, pH <7.3, HCO₃⁻<15mmol/L, ketonuria/aemia].

Pathophysiology
- Inadequate insulin→progressive hyperglycaemia→‘cellular starvation’→↑release of glucagon, catecholamines, cortisol and GH → glycogenolysis & gluconeogenesis, ↑BSL
- The stress response →proteolysis and lipolysis, forming free fatty acids, which are then converted to the ketacids acetoacetate, beta-hydroxybutyrate and acetone.
- The high glucose levels cause a huge osmotic diuresis and gross dehydration which may reduce tissue perfusion and further derange metabolism by causing lactic acidosis

Epidemiology
1-5% T1DM (20% new). T2DM unusual (HONK more likely). 2F:1M. In children, risk of DKA at onset age related: 0-4y (~45%), 4-14 (~20%), 15-21 (~15%). Unusual in T2DM.

Precipitating conditions:
- Infection (19-56%) e.g. pneumonia, UTI
- Inadequate insulin/non-compliance (15-41%)
- Undiagnosed diabetes (10-22%)
- Other medical illness (10-12%) e.g. hypothyroidism, pancreatitis, inborn errors of metab
- Cardiovascular disease (3-6%) e.g. PE, stroke, MI
- Other physiological stress e.g. pregnancy, surgery
- Drugs e.g. corticosteroids, sympathomimetics, α- and β-blockers and diuretics
- Cause unknown (4-33%)

Presentation
History
- Insidious onset of ↑thirst (polydipsia), worsening polyuria, & weight loss. (Rarely ↑hunger)
- Nausea and vomiting are common ± non-specific abdominal pain
- Lassitude, weakness and fatiguability often occur
- Global cerebral symptoms such as confusion and disorientation may be present
- Note focal symptoms of infection, dyspnoea, chest pain, palpitations, abdominal pain, recent changes in medication, episodes of overdose/ingestion of poisons, and EtOH use
- If on insulin note regimen and compliance

Examination
- Check vitals (T,HR, BP, RR, SaO2, GCS)
- Signs of gross dehydration Check CVS for signs of cardiac failure or shock.
- Ketotic foetor (pear drops or nail-polish remover)
- Respiratory compensation of acidosis can lead to tachypnoea or Kussmaul’s respiration
- Assess mental status and orientation & neurology
- Examine the chest, abdomen, skin for signs of infective precipitant

Differential Diagnosis
- Alcoholic ketoacidosis
- HONK
- Lactic acidosis
- Causes of metabolic acidosis, e.g. OD
- Acute pancreatitis
- Septicaemia without ketoacidosis
- Acute abdomen
- Ketoacidosis due to starvation
Investigations

Urine: urinalysis for glycosuria and ketonuria. Send for M, C & S

Bloods: FBC, UEC, Glucose, ABG, anion gap, plasma osmolarity, Trop/CK, amylase, cultures. Note:
- Assay of blood ketones (N<0.6mmol/L) more sens & spec than urinary but not always avail
- GAD, IAA, IA-2 autoantibodies if new T1DM suspected
- WCC, Trop/CK, amylase may all be ↑ by DKA itself rather than by a precipitant
- Na' may ↑(dehydration), normal or ↓ ( pseudohypoNa: Corr.Na=Na + (glu-5.5) x 0.3 )
  K' may ↑(acidosis), normal or occ. ↓, but overall there is depletion of body K'; Cr & Ur rise with pre-renal RF; bicarbonate ↓.
- Plasma Osmolarity = 2([Na] + [K]) + [Ur] + [glucose]. >290mOsm/L in cases of DKA.
  Consider HONK if >320 mOsm/l and lack of ketonuria or glu>30mmol/L.
- Anion Gap = ([Na] + [K]) – ([Cl] + [HCO3]) >13 mEq/l in DKA

Radiology:
- CXR (?pneumonia or cardiac failure), CT/MRI (if LOC, ?CVA), LP (if ?meningitis)

Other: ECG

Management

- Triage to resuscitation/acute area. Attach continuous monitoring, weigh if possible
- ABCD. Give O₂, consider intubation and ventilation if ↓LOC
- Lines: IVC + extra sampling line or insert central venous catheter. Consider IDC ± NG

Intravenous fluid and electrolyte replacement:
- Adult: may be sig. dehydrated (10%) can give: 1L NS stat, q1h, q2h unless concern of CCF.
- Child: 10-20mL/kg if shocked, beware cerebral oedema. Maintenance+deficit over 48hrs (longer if hypernatraemic & consider 0.45 NaCl). Only subtract resus fluid if >20ml/kg.
- Give potassium replacement when K’<5.5 and urine output established & chk UEC q2-4h

Insulin therapy:
- Initially 6U/hr (child: 0.05/kg/hr if<5y else 0.1U/kg/hr) short-acting soluble insulin
- In adults use a sliding scale for hourly insulin dose based. In children do not ↓ insulin.

<table>
<thead>
<tr>
<th>BSL (mmol/l)</th>
<th>Insulin infusion rate (U/hr=ml/hr for 50U fast-acting soluble insulin in 50ml 0.9%NaCl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥17</td>
<td>6</td>
</tr>
<tr>
<td>11-16.9</td>
<td>4</td>
</tr>
<tr>
<td>9-10.9</td>
<td>3</td>
</tr>
<tr>
<td>7-8.9</td>
<td>2</td>
</tr>
<tr>
<td>4-6.9</td>
<td>1</td>
</tr>
<tr>
<td>&lt;3.9</td>
<td>Discontinue and repeat glucose estimation in 30 mins.</td>
</tr>
</tbody>
</table>

- Hourly BSL. Aim is to reduce plasma glucose by 3-5 mmol/hr after initial fluid bolus.
- When BSL<15mmol/l add 5%D (child: NS+5%D or 0.45%NaCl if >6hs) so BSL 8-12 til pH/ketone norm

Further measures:
- HCO₃ in rare cases (pH≤6.9): 0.15 x wt x base deficit mmol (give over 1 hr & reassess)
- DKA leads to phosphate depletion but this rarely causes significant clinical problems.
- Any precipitating illness should be managed optimally as per current guidance

Progression:
- When eating dbl infusion rate while eating +1hr (meals) or +30min (snacks)
- If stable (pH≥7.3, BSL<12, HCO₃>15, no ketonuria) & eating – convert to an sc insulin regime and wean off infusion 90min after sc dose.
- Give this dose before breakfast, lunch, dinner & about half this dose at midnight
- Dietician, education, blood testing, and conversion to home insulin regime
Complications
- Cerebral oedema commoner in children (~1%). Mortality 20-90%. Presents in first 24h with headache, behavioural changes and urinary incontinence → abrupt neurological deterioration and coma. RF: Age<5y, sev dehydration/hyperosmolar, rapid drop in BSL or rapid rehydration/low Na, use of bicarb. Mx: 3-5ml/kg of 3% saline or 0.5-1g/kg mannitol IV over 20mins, reduce rate of fluid administration, elevate head of bed, CT, call ICU.
- Pulmonary oedema due to overzealous fluid replacement or as a spontaneous phenomenon
- Iatrogenic hypoglycaemia, hypokalaemia
- Cardiac dysrhythmia due to electrolyte disturbance (particularly K+) or acidosis
- Venous thromboembolism
- Diabetic retinopathic changes may be seen prior to or after therapy for DKA
- Hypophosphataemia
- Adult respiratory distress syndrome

Prognosis
- Tx to ICU - age<5, pH<7.2, Na'>150, BSL>50, CNS depression
- Prognosis worse with extremes of age and the severity of the underlying precip pathology
- Coma at presentation, hypothermia or persistent oliguria are poor prognostic indicators
- Overall mortality rates vary from 1-10% (less in children) depending expertise of Mx
- There has been a marked ↓mortality in expert centres over the last 20 years.

Prevention
- Education programs for diabetic patients & carers
- Improved awareness of the management of diabetes and intercurrent illness, and the presentation and early management of DKA, in the medical/allied healthcare professions

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**Alcoholic Ketoacidosis**

Pathophysiology

Epidemiology
Usually acute high use of EtOH in heavy alcohol abuser

Presentation
**History:** Nausea & vomiting. Anorexia. Mild abdominal pain.
**Exam:** ↑HR, ↑RR, signs of dehydration or chronic EtOH abuse, mildly tender abdo

Investigations
**Bloods:** FBC, UEC, BSL (↓, normal), ABG (met.acidosis±met.alkalosis [vom]), AG (↑), amylase, LFT, cultures. Nitroprusside assay of bld ketones may be -ve as doesn’t detect hydroxybutyrate.
**Urine:** urinalysis for glycosuria and ketonuria. Send for M, C & S
**Radiology:** CXR (pneumonia or cardiac failure), CT/MRI (if LOC, ?CVA), LP (if meningitis)
**Other:** ECG

Management
**General:** ABCD as necessary. Obtain IV access
**Fluids:** 5% dextrose in 0.9% saline.
**Other:** Thiamine. Correction of other metabolic/electrolyte/vitamin derangements. Treat underlying conditions. Manage alcohol withdrawal or other complications.
Appendix 1: Algorithm for the Management of DKA in Kids

**IMMEDIATE ASSESSMENT**

- **Clinical History**
  - Polyuria, polydipsia
  - Weight loss
  - Abdominal pain
  - Tiredness
  - Vomiting
  - Confusion

- **Clinical Assessment**
  - Assess hydration, perfusion, BP, GCS
  - Deep sighing respiration (Kussmaul)
  - Smell of ketones
  - Lethargy/drowsiness ± vomiting

- **Investigations**
  - Venous blood gas, FBC, electrolytes, urea, creatinine, other investigations as indicated
  - Biochemical signs of DKA include:
    - Ketonuria/ketonaemia
    - Blood glucose level >11mol/L
    - pH <7.25, Bicarb <15mmol/L

**CONFIRMED DIAGNOSIS OF DIABETIC KETOACIDOSIS**

- Contact Endocrinology Team on-call

**Shock (reduced peripheral pulses)**

- Reduced conscious level
- Coma

**Dehydration >5% but not in shock**

- Clinically acidic (hyperventilation)
- Vomiting

**Mild DKA (pH 7.25 to 7.3)**

- Clinically well
- Tolerating fluids orally

**Resuscitation**

- Airway ± insert NG tube
- Breathing (100% O₂)
- Circulation (Saline 0.9% 10mL/kg as a bolus (max of 2 boluses))

**IV Therapy**

- Calculate hourly fluid requirements:
  - (48 × hourly maintenance) + deficit
  - Use Saline 0.9% as initial fluid for 4–8 hrs, then change depending on corrected Na level
  - Monitor ECG for elevated T-waves
  - Use KCl 40mmol per 1000mL fluid

**Low-dose continuous INSULIN INFUSION**

- 0.05-0.1unit/kg/hour

**Critical Observations**

- Hourly blood glucose level, RR, HR, BP
- Hourly accurate fluid input & output (insert urinary catheter if conscious state impaired)
- Neurological status at least hourly
- Electrolytes and blood gas 2-4 hourly after start of IV therapy
- Monitor ECG for T-wave changes

**Acidosis NOT Improving**

**When blood glucose < 15mmol/L or blood glucose falls > 5mmol/hour**

**Re-evaluate**

- IV fluid calculations
- Insulin delivery systems & dose
- Need for additional resuscitation
- Consider sepsis

**IV Therapy**

- Change to Saline with added glucose (or change to 0.45% with added glucose) and increase glucose concentration if required

**Signs of neurological deterioration**

- Headache, slowing of heart rate, irritability, decreased conscious level, incontinence, specific neurological signs

**Exclude Hypoglycaemia**

- Is it Cerebral Oedema?

**Management**

- Airway Breathing Circulation
- Give Mannitol or 3% hypertonic saline
- Restrict IV fluids
- Call Intensive Care Team for admission
- Consider intubation if GCS<8
- Urgent head CT - only after patient stabilised

**Transition to SC Insulin**

- Start SC Insulin then Stop IV insulin 90 mins later