ENDOCRINOLOGY

1. INPATIENT MANAGEMENT OF DIABETES

INTRODUCTION

- Up to 30% of hospital in-patients may have diabetes

- Mortality, complications and length of stay are higher for those with diabetes
- Both hyperglycaemia and hypoglycaemia are associated with increased risks of adverse outcomes
- Wound infection and delayed wound healing are more likely, particularly if BGL > 11mmol/l.

- Glycaemic control is often disrupted due to
  - Stress of intercurrent illness or complications (e.g. infections, ischaemia)
  - Investigations/ treatment of intercurrent illness
  - Changes in carbohydrate intake
  - Fasting, absences from ward, vomiting or poor oral intake
  - Changes in rates of enteric feeds or TPN
  - Changes in medications, including glucocorticoids
  - Changes in activity

- Patients at greatest risk of dysglycaemia include
  - Type I Diabetes
  - Pre-existing suboptimal glycaemic control
  - Loss of hypoglycaemia awareness
  - Glucocorticoid therapy
  - Enteric Feeds

MANAGEMENT OF HYPER/HYPOGLYCAEMIA

MONITORING

- Regular Blood glucose (BGL) monitoring pre and 2 hr post meals for all known diabetics
- HbA1C on admission (unless measured in previous month) for any patient with BGL > 10mmol/l or with known diabetes.

NB:

- Notify the endocrinology team for:
  - All patients with Type I Diabetes
  - All patients on an insulin pump
  - All pregnant patients with diabetes (including gestational diabetes)
(NB: Contact the inpatient diabetes registrar for surgical patients, the endocrine registrar on call for medical patients)

**GENERAL ISSUES**

- Assess factors contributing to hyper- and hypoglycaemia
- Try to avoid or correct those factors or at least to allow for those factors in future treatment
  
  e.g.: Prednisolone dose adjustment:
- Increased prednisolone doses likely to require commencement or increases in insulin doses
- Decreased prednisolone doses likely to require decreases in insulin doses
- Prednisolone administration in the morning results in a predictable impact on BGL levels, thereby facilitating insulin dose adjustment.
- Omission of / not charting variable prednisolone doses till later than usual time could cause early hypoglycaemia (because insulin doses appropriate for the prednisolone at usual time may have already been given) or late hyperglycaemia,
- Consider intravenous variable dose insulin-glucose infusion if prolonged fasting, including for investigations
- Ensure alternative source of glucose or carbohydrates are given if patient is fasting/vomiting or enteric feeds ceased and if insulin or oral hypoglycaemic agents have already been given
- Adjust dose of insulin/ oral hypoglycaemic agents (or discuss with diabetes/endocrine registrar) **prior to** changes in doses of prednisolone, changes in rates of enteric feeds etc

**NB:**
- Smaller doses of insulin for initiation and titration should be given for patients likely to be insulin sensitive or at greater risk of/from hypoglycemia. These include: Type I Diabetes, renal failure, hepatic failure, elderly, loss of hypoglycaemia awareness, cognitive dysfunction or poor English, patients with severe hypoglycaemia requiring assistance/ recurrent hypoglycaemia
- Patients on high doses of steroids, morbid obesity may be insulin resistant

**HYPERGLYCAEMIA**

**INITIATION OF INSULIN THERAPY**

**Type I Diabetes**

- **Contact diabetes registrar for assistance**
- **Basal bolus regimen:**
  
  0.3-0.4 units/kg/day

  1/3 as basal insulin before bed (e.g. lantus (glargine) or levemir (detemir))
2/3 as rapid acting insulin divided equally before each meal (e.g. lispro (Humalog), aspart (Novorapid), glulisine (Apidra))
Give supplemental rapid acting insulin as required to correct hyperglycaemia
Review glycaemic control and adjust insulin doses daily

**Type II Diabetes**

**A Oral hypoglycaemic agents** (OHAs) may be able to be continued/titrated in some cases, but consider cessation/dose reduction under the following circumstances:

1. **Metformin:**
   - Cease if eGFR < 30 or if rapidly progressive renal failure or if lactic acidosis.
   - Reduce/withhold dose if eGFR 30-60 or if radio-contrast required.
   - Metformin can be resumed if renal function improves sufficiently.

2. **Sulphonylureas:**
   - Consider ceasing/omitting if poor oral intake/risk of hypoglycaemia

3. **Glitazones:**
   - Cease if cardiac failure present

4. **Incretins: DPP4 Inhibitors/GLP1 agonists**
   - Cease DPPIV inhibitors/GLP1 analogues if pancreatitis present

5. **SGLT2 Inhibitors:**
   - Cease if has renal failure or urogenital infections

**B Insulin:** often ultimately necessary to achieve satisfactory glycaemic control, especially with:

- Pre-existing poor glycaemic levels (HbA1C > 8% on maximal oral hypoglycaemic agents or > 9% in any case) OR with precipitants e.g. glucocorticoids OR if usual oral hypoglycaemic agents have to be ceased
- Continue metformin if no contraindications. Cease other oral hypoglycaemic agents.
- Commence insulin: Total daily dose =0.3-0.5 units/kg/day (0.3 units for insulin sensitive, 0.5 units for standard).
  - 50% of this to be given as once daily basal insulin (Lantus)
  - 50% of this to be given as prandial (bolus) insulin e.g. Novorapid, Humalog, Apidra- should be given with meals.
NB: If insulin is initiated in hospital, please ensure adequate time for discharge planning, either for a change to an appropriate discharge regimen (e.g. a bd premix or basal only regime) or to allow sufficient time for patient to be educated about insulin administration.

**CORRECTION OF HYPERGLYCEMIA WITH SUBCUTANEOUS INSULIN**

- Avoid use of sliding scale insulin as *sole* therapy as it tends to exacerbate metabolic instability
- A change to basal-bolus insulin could be considered in patients with:
  - a) Pre-existing poor glycaemic control (HbA1C > 8%)
  - b) Risk factors for hyperglycaemia or fluctuations in blood glucose levels (e.g. > 10mg daily prednisolone or equivalent doses of glucocorticoids; enteric feeds) in patients with known diabetes mellitus
  - c) Patients already on insulin or maximal doses of oral hypoglycaemic agents, particularly with other risk factors / high risk major surgery (e.g. coronary artery bypass surgery)
- Supplemental rapid acting insulin in addition to usual charted SC insulin at meal times may be advisable. Frequent need for supplemental insulin suggests that usual insulin needs may need to be increased. Supplemental insulin should not be given without concurrent regular review of charted insulin requirements.

_Suggested Starting Supplemental Insulin Algorithm:_

<table>
<thead>
<tr>
<th>BGL mmol/l (before meals only)</th>
<th>Insulin dose (at meal times only)</th>
<th>Insulin Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Standard</strong></td>
<td><strong>Insulin Sensitive</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>e.g. T1D, low BMI elderly, renal failure Frequent hypoglycemia</td>
</tr>
<tr>
<td>10.1-12</td>
<td>2</td>
<td>0-1 *</td>
</tr>
<tr>
<td>12.1-16</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>16.1-20</td>
<td>6</td>
<td>3-4</td>
</tr>
<tr>
<td>&gt; 20: Call RMO; Also Check Ketones for Type I Diabetes</td>
<td></td>
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</tbody>
</table>

- Review insulin requirements daily and adjust usual insulin doses, as insulin requirements are likely to change during admission. A lower threshold for giving supplemental insulin such as 8 mmol/L may be appropriate in some patients.

_Titration:_

- Basal Insulin e.g. Lantus, Levemir
  - If fasting and/or mean BGL > 10mmol/l and no hypoglycemia
    _Increase by 10-20% (not more than 5 units)_
  - If mild hypoglycaemia (BGL 3.1-4mmol/l) on single occasion
    _Decrease by 10-20%_
• if moderate-severe hypoglycaemia (BGL < 3mmol/l or decreased conscious state) or recurrent hypoglycaemia
  
  \textit{Decrease by 20-30\% + endocrine consult}

• Bolus (prandial) insulin e.g. Novorapid, Humalog, Apidra
  
  • If the 2hr post-meal BGL exceeds 10 mmol/L (or target range for patient), that individual mealtime bolus should be increased the next day by 2-4 units

• If additional corrective doses of insulin are required, avoid excessive and overlapping doses of insulin. For significant hyperglycaemia, e.g. > 20mmol/l, a corrective dose of 0.1 units/kg of rapid acting insulin analogue could be considered (minimise night time doses because of risk of hypoglycaemia- not more than 0.025-0.05units/kg). If significant hyperglycaemia persists, consider intravenous variable dose insulin-glucose infusion

• Re-check BGL 2 hr after administration of extra insulin in order to ensure it has not been over- or under- effective

• Avoid giving extra insulin too frequently
  
  Give rapid-acting insulin analogues rather than regular human short acting insulin (such as Actrapid) given the more rapid onset of action and the reduced potential for overlapping of doses

\textbf{HYPOGLYCAEMIA}

1. Acute Treatment:
   
   • 1 tube Glucose 15 gel orally or 75-150 ml lemonade or 60-120ml fruit juice
   
   • If unconscious or fasting: IV 50ml -100ml 50\% Dextrose

2. Recheck Blood glucose level (BGL) after 5-15 minutes (sooner if poor conscious state or other symptomatic concerns).

3. a. If BGL < 4mmol/l, re-treat / repeat BGL monitoring as above.
   
   b. If BGL > 4.0 mmol/l
      
      • Give sandwich or other meal with carbohydrate
      
      • If fasting or poor oral intake: 5\% Glucose at 80ml/hr or 10\% Glucose at 40ml/hr
      
      OR if already receiving IV glucose, may need increase in rate or concentration

4. Recheck BGL after another 2 hr

5. a. \textbf{Type I Diabetes: Do NOT OMIT insulin}, though the dose may need to be reduced by 20-40\% and/or a glucose infusion commenced.
   
   b. \textbf{Type II Diabetes:} Consider reduction/withholding insulin dose and/or oral hypoglycaemic agents depending on severity / precipitant / recurrent hypoglycaemia, but need to ensure the patient does not have type I Diabetes and ensure parent team review.
6. Recurrent hypoglycaemia or failure to improve: Contact endocrine team or medical registrar or MET call if clinically indicated

**INTRAVENTOUS VARIABLE DOSE INSULIN-GLUCOSE INFUSION**

**Indications:**
- Prolonged Fasting (bowel rest, surgery, investigations)
- Persistent vomiting (especially Type I Diabetes)
- Severe intercurrent illness (e.g. myocardial infarction, septicaemia)
- Metabolic Instability

**Principles of Intravenous Variable Dose Insulin-Glucose Infusion:**
- Provide fluids and calories and prevents ketogenesis with IV Glucose
- Keep glucose infusion rate constant and adjust IV insulin infusion rate to maintain euglycaemia
- Commence intravenous insulin-glucose infusion at least 2 hrs prior to planned procedure to allow sufficient steady state conditions to develop.

DO NOT OMIT usual doses of subcutaneous insulin, especially basal insulin, prior to commencing the infusion. If insulin omitted, then check blood ketones and if elevated, evaluate for possible DKA and manage accordingly

Commence infusion the night beforehand if procedure planned for early in the morning.

- Initiation and rate adjustment as per insulin-glucose infusion adjustment algorithm (WSHR-2733)
- If BGL > 15mmol/l, defer commencing glucose infusion until BGL < 15mmol/l.
- Measure capillary BGLs hourly to guide adjustment of insulin infusion rate.
- Adjust insulin infusion rate each hour according to insulin-glucose infusion adjustment algorithm
- Aim for BGL targets of 4.0-10.0mmol/l
- Recomence SC insulin or oral agents and cease IV infusion when patient capable of resuming full oral intake
- Continue IV insulin infusion until after SC Insulin has been given, with sufficient time for onset of action of SC insulin (e.g. 1 hr for rapid acting insulin's) - see below

If insulin infusion ceased prior to SC insulin injection, then check blood ketones to exclude development of DKA due to insulin deficiency.

**Practicalities:**

- GLUCOSE: 5% glucose 80ml/hr (or 10% glucose 40ml/hr if fluid restriction required)
- Add KCL when duration of insulin infusion > 24 hr
- Initiation:

<table>
<thead>
<tr>
<th>BGL</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4mmol/l</td>
<td>0 Units/hr</td>
</tr>
<tr>
<td>Glucose Range</td>
<td>Insulin Rate</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------</td>
</tr>
<tr>
<td>4-4.9</td>
<td>0.5</td>
</tr>
<tr>
<td>5-7.9</td>
<td>1.0</td>
</tr>
<tr>
<td>8-9.9</td>
<td>1.5</td>
</tr>
<tr>
<td>10.0-14.9</td>
<td>2.0</td>
</tr>
<tr>
<td>15-19.9</td>
<td>3.0</td>
</tr>
<tr>
<td>&gt;20</td>
<td>4.0</td>
</tr>
</tbody>
</table>

- Initial insulin infusion rates may need to be reduced in patients with Type 1 Diabetes who are insulin sensitive, e.g.
  a) dialysis dependent renal failure,
  b) total daily insulin dose ≤0.25 units/Kg/day,
  c) recurrent hypoglycaemia (consult Endocrine team).

Dose / infusion rate adjustments as per insulin-glucose infusion algorithm (WSHR-2733) and hourly BGL measures

- Commence SC insulin after patient capable of resuming full diet. Basal insulin (Lantus or Leveimir) can be resumed the night before ceasing the insulin infusion.
- Continue IV insulin-glucose infusion until patient has eaten AND
  - 1 hr after rapid acting SC Insulin (lispro [Humalog, Humalog Mix 25, 50], aspart [Novorapid, Novomix 30], glulisine [Apidra]) or
  - 2 hr after regular insulin (Actrapid, Humulin R) or
  - 4 hr after long acting insulins (e.g., Leveimir, Lantus) given in the morning without rapid/quick acting insulin (although this situation is unusual)

DO NOT CEASE THE INSULIN-GLUCOSE INFUSION UNTIL THE SC BASAL INSULIN DOSE FOR THAT DAY HAS BEEN GIVEN

- Modifications with respect to initiation dose or adjustment of doses may be required for some patients with Type I Diabetes (see above) - consult with endocrine team

NB: This rationale and regimen differs for patients with diabetic ketoacidosis, when higher levels of insulin are required to normalise ketosis and acidosis- see DKA protocol which utilises a fixed dose insulin infusion

**TYPE I DIABETES**

- Most patients with type I diabetes will be treated either with basal-bolus insulin, an insulin pump or an intravenous insulin–glucose infusion.
- Notify the diabetes/endocrine team for assistance in care with all patients with type I Diabetes
- **Do not omit** insulin as this may result in hyperglycaemia and ketoacidosis. (NB This can occur even with delays of a few hours.
  - If fasting: Variable dose insulin-glucose infusion intravenously for all patients with Type I Diabetes, unless previously discussed with endocrine team. If fasting commences soon after injection of day-time insulin, then commence IV Glucose infusion to prevent hypoglycaemia
NB: Do NOT omit Lantus or Levemir dose the night before surgery, unless specifically requested by endocrine team.

- If normoglycaemic - Give charted dose with meals. **Do NOT omit charted insulin.**
- If hypoglycaemic - Treat hypoglycaemia as per protocol until BGL > 4.0 mmol/l

Ensure carbohydrates are given to maintain normoglycaemia. Consider reduction in insulin dose by 20% and/or add IV Dextrose if poor oral intake but **do not omit insulin**

- Patients with Type I diabetes are often insulin sensitive - care with titrating insulin doses.
- If BGL > 20 mmol/l (or if > 15mmol/l in pregnancy or recent ketoacidosis ) check for ketones. If ketones > 1.0, exclude diabetic ketoacidosis - see DKA protocol for management and contact endocrine team. If DKA not present, then give corrective dose(s) of rapid acting insulin, but if BGL remains >20 mmol/L, then consider variable dose intravenous insulin-glucose infusion

**INSULIN PUMPS**

- Contact diabetes registrar/consultant on call and diabetes educator for ALL patients treated with an insulin pump
- IV variable dose insulin-glucose infusion if pump not functioning until endocrine review (see Pump Troubleshooting Guide in RMO’s Handbook)

**DIABETES IN PREGNANCY**

- Notify endocrine team
- Treatment goals are:
  - Fasting: BGL 4-5.5mmol/l
  - 2 hr post prandial: 4-7.0mmol/l
- Avoidance of hypoglycaemia

  - Oral hypoglycaemic agents should be ceased. (Metformin may be continued under some circumstances but should be discussed with endocrine team).
  - Insulin, most commonly basal-bolus insulin, may be required.
  - Basal insulin: Protaphane or Humulin NPH insulin (i.e. human insulins) used primarily
  - Prandial insulin: Novorapid, Humalog. (Actrapid and Apidra insulin can also be used).
  - During Labour: variable dose insulin-glucose infusion. This may not be necessary in those with gestational diabetes where the total daily insulin dose is less than 20 units per day.

**GLUCOCORTICOID INDUCED DIABETES**

- Hyperglycaemia is more likely in patients with pre-existing diabetes or receiving higher doses of glucocorticoids
- Does not always remit when glucocorticoids withdrawn
- Characterised by postprandial hyperglycaemia (especially after lunch when prednisolone is given in the morning) and insulin resistance
• The doses of insulin or of oral hypoglycaemic agents (OHA) may need to be increased or decreased depending on variations in the dose of glucocorticoids. It is critical that changes in doses of glucocorticoids are planned in conjunction with the endocrine team or the medical team managing the diabetes to allow sufficient time to alter doses of insulin/OHAs. Glucocorticoids such as prednisolone should always be given at the same time each day, preferably in the morning, to facilitate insulin dose adjustment, given its predictable effect on blood glucose levels.

• Check HbA1c

• Monitor ac/pc BGLS **including 2 hr post lunch, before dinner and 2 hr post dinner** when BGLS are most likely to be elevated (if prednisolone is given with breakfast)

In those not known to have diabetes, BGLS should be checked for at least 48 hr after commencement of glucocorticoids or if doses are increased.

• If BGLS are not elevated after 48 hr, BGLS should still continue to be monitored on an ongoing basis for patients with pre-existing diabetes (HbA1C > 7% or known diabetes) or with higher doses of glucocorticoids

• If hyperglycaemia mild, oral hypoglycaemic agents may be effective

• If hyperglycaemia more severe (e.g. BGL > 11.0mmol/l) or pre-existing diabetes, insulin will usually be required.

  • **tds rapid acting insulin with meals**, the largest dose usually required before lunch
  • **either mane only or bd Protaphane /Humulin NPH** may be required as well

• Test for diabetes after cessation of glucocorticoids

### DIABETES AND MYOCARDIAL INFARCTION

- Diabetes and hyperglycaemia are associated with increased mortality.
- Beta-blockers are not contra-indicated.
- May benefit from an insulin-glucose infusion (variable dose) for 24-48 hours, followed by the commencement of sc insulin in those not previously treated with insulin - see CCU protocol for details – especially if hyperglycaemic (BGL > 8 mmol/L).

  - Ideal blood glucose target in peri-infarct period is 4-10 mmol/L.
  - Glycaemic control will deteriorate in those with pre-existing diabetes.
  - Previously undiagnosed diabetes may be unmasked:

    - If FBGL > 7.0mmol/L or RBGL > 11.1mmol/L assume diabetes is present, check HbA1C, and manage accordingly.
    - If FBGL 6-7mmol/L, or RBGL 7.8-11mmol/L, then check HbA1C and re-assess glucose tolerance after discharge.

- Patients on metformin with normal renal function should have this temporarily ceased for 48 hours after an angiogram/angioplasty (because of potential for contrast-induced renal failure and subsequent risk of lactic acidosis). Resume Metformin if renal function has not deteriorated. Correct hyperglycaemia following metformin withdrawal with supplemental rapid-acting insulin – hyperglycaemia-induced dehydration may increase the risk of contrast-induced renal failure.
2. DIABETIC KETOACIDOSIS

I. KEY POINTS

- Rapid and adequate fluid replacement
- Insulin infusion 5 units/hr - don’t stop/reduce, may need to increase
- Manage in high-dependency ward after initial resuscitation and initiation of treatment
- Anticipate rapid fall in serum potassium and replace early.
- Monitor frequently
- IV glucose when blood glucose < 15 mmol/L
- Look for cause - infection/infarction
- This condition carries a significant mortality of up to 5-10%, often due to the underlying precipitating condition.

II. CLINICAL FEATURES:

- Type I diabetes (sometimes Type II insulin deficient diabetes)
- Gastrointestinal symptoms, usually vomiting and abdominal pain.
- Dehydration, occas. assoc. with hypotension and shock, ketoacidosis, lactic acidosis, electrolyte imbalance, disturbed intermediary metabolism.
- In more advanced stages the patient may be confused or obtunded.

Major features:

- Metabolic acidosis (pH < 7.30, HCO3 < 16).
- Hyperglycaemia
- Hyperketonaemia - Blood ketones > 1.5 mmol/L (or raised plasma anion gap acidosis, associated with significant ketonuria).

Underlying precipitant:

- A diligent search for a precipitant is essential. In the known diabetic, more than 80% of episodes will have an identifiable precipitant.
- The commonest are: infection, cessation of insulin, acute myocardial infarct (may be painless, partic. in elderly), trauma.

“Euglycaemic” Diabetic Ketoacidosis:

- Initial blood glucose level < 16 mmol/L, may occur in approx. 15% of patients with DKA. It may result from either impaired gluconeogenesis (liver disease, alcohol excess, or food deprivation), increased insulin independent glucose utilisation (eg
pregnancy), or failure to adequately increase insulin doses when requirements have increased (eg infection) whilst maintaining hydration.

III. INVESTIGATIONS

Immediate tests:

- Capillary blood glucose and blood ketone by ward meter, venous blood gases (check arterial blood gases if oxygen saturation is low), venous plasma glucose, sodium, potassium, bicarbonate, urea, creatinine, calcium, phosphate, osmolality, urine M/C/S,
- Blood cultures (NB: 1. the patient may be afebrile, yet septic, and 2. the WCC is usually raised in DKA and is not a reliable indicator of infection),
- ECG, chest x ray.

Consider:

- Amylase and lipase (if pancreatitis likely), CK and Troponin (silent myocardial infarction) (Amylase and lipase may be elevated up to 10 fold in 16-25% of patients with uncomplicated DKA in the absence of clinical pancreatitis – perform CT scan of pancreas if serum amylase/lipase >3xULN). (Elevated CK and Troponin levels may also be elevated in the absence of myocardial infarction in patients with DKA)
- Beta HCG: if possibility of pregnancy. DKA in pregnancy has a high foetal mortality rate (up to 50%).
- Cortisol if possibility of hypoadrenalism (and treat immediately – see below).

Measure or calculate:

- Serum osmolality: \(2 \times [Na+K] + \text{glucose (or glucose+urea+2xNa)}\).
- Anion gap: Na - [Cl+HCO_3^-]

IV. THERAPY

Principles:

- Resuscitation: ABC (Airway, Breathing, Circulation)
- Replace salt and fluid losses
- Restrain lipolysis and inhibit hepatic glucose production with insulin
- Identify and correct precipitant
- Re-establish normal physiology
- Greatest dangers to the patient are acidosis and electrolyte disturbances
especially hypokalaemia) not hyperglycaemia.
- Keep nil by mouth until ketoacidosis has cleared

1.) Intravenous fluids (for rehydration)

- If there is evidence of SHOCK, give 500 – 1000 ml 0.9% saline stat. Monitor clinical response and repeat if necessary.
- Where there is no evidence of shock, rapid IV rehydration is still required. The amount and rate of IV fluid depends on the severity of the DKA. 0.9% saline should be used initially for rehydration.

<table>
<thead>
<tr>
<th>NSaline:</th>
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<tr>
<td><strong>1st litre:</strong></td>
<td>½-1 hour</td>
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<tr>
<td><strong>2nd litre:</strong></td>
<td>1-2 hours</td>
</tr>
<tr>
<td><strong>3rd litre:</strong></td>
<td>2-4 hours</td>
</tr>
</tbody>
</table>

- Commence prior to the availability of other results.
- Patients with peripheral shutdown or with pH < 7.2 may require a central line for haemodynamic monitoring. Also, consider this in the elderly where there may be greater concern about cardiac and renal function.

2.) Insulin

- Infuse 50 units of Actrapid insulin in 50mls normal saline by syringe pump (eg Injectomat).
- PRIME line - Flush line with the insulin/saline solution prior to commencing the infusion. (see nursing procedures manual).
- In ADULTS: Start insulin infusion at 5 units/hr (an initial IV bolus of 5-10 units of insulin may be given, but this does not usually influence the rate of reversal of acidosis and may worsen hypokalaemia).
- In CHILDREN: infuse insulin at 0.1 unit/kg/hr. There are specific guidelines for the management of DKA in children. All children with DKA should be transferred to an appropriate paediatric unit (such as The Childrens Hospital at Westmead or to Nepean Hospital)

- Commence fixed dose intravenous insulin infusion (5 units per hour) as soon as possible if there is clear clinical evidence of ketoacidosis.
- The insulin infusion rate should be doubled if the blood glucose does not fall or if the acidosis has not improved (see below). Approximately 10% of patients with DKA are
severely resistant to insulin. If, after 2-3 hours of insulin therapy, the blood glucose level does not decrease by ≥ 8-12 mmol/L, OR the capillary beta-hydroxybutyrate level does not fall by ≥1-2 mmol/L, then the insulin infusion rate should be increased up to 10 units/hour. (The insulin infusion rate may need to be increased further but this should ALWAYS be discussed with the consultant beforehand). If both the blood glucose and ketone levels are falling, but the pH fails to improve, consider other causes of acidosis.

- Before increasing the insulin infusion rate, ensure that the correct dose of insulin has been added to the infusion, that the correct priming procedure has been followed, and that the insulin is being infused at the correct rate.

- Maintain the insulin infusion at the above rate until there is biochemical evidence that the acidosis is reversed, i.e. normalisation of pH, bicarbonate and blood ketones. If higher infusion rates have been required in the initial period, but blood glucose and ketones subsequently fall rapidly, consider reducing the insulin infusion rate to 5 units per hour but monitor closely for subsequent deterioration.

- The most common mistake is to reduce the rate of insulin as the blood glucose falls before the acidosis is reversed. Instead, a glucose infusion is commenced when the BGL is approx. 15 mmol/L and adjusted to maintain the BGL within the desired range (see below). It takes longer to correct the acidosis (up to 24 hrs) than to correct the hyperglycaemia (4-8 hours). Never cease insulin completely: its purpose is to reverse the ketoacidotic state, not just the hyperglycaemia.

- When blood ketones are <0.5mmol/L, then progressively reduce the insulin (and glucose) infusion rate(s) and adjust in order to maintain the blood ketones level <0.5mmol/L and the BGL within the target range.

- Consider continuing the patients’ usual dose of basal insulin (glargine or detemir) subcutaneously whilst receiving the intravenous insulin infusion, as this will help maintain glycaemic control once the intravenous insulin infusion has been ceased.

3.) Potassium

<table>
<thead>
<tr>
<th>Measure serum potassium levels every 1-2 hours. Refer to Potassium Chloride Administration Protocol (Westmead Hospital Drug Committee):</th>
</tr>
</thead>
<tbody>
<tr>
<td>If: K⁺ &lt; 3.5 mmol/L, give 20mmol/hr</td>
</tr>
<tr>
<td>K⁺ 3.5- 5.5 mmol/L, give 10mmol/hr</td>
</tr>
<tr>
<td>K⁺ &gt;5.5 mmol/L, cease potassium infusion</td>
</tr>
</tbody>
</table>

- Beware development of life threatening hypokalaemia.

- All patients with DKA are potassium deficient. Serum potassium may often be initially elevated. Marked hyperkalaemia rarely occurs unless there is superimposed acute renal failure. Potassium levels fall with therapy since insulin moves the potassium into cells, as does correction of the acidosis. Anticipate that the serum potassium will fall rapidly and
commence potassium replacement as soon as urinary flow is established, even when serum potassium is normal.

- Potassium chloride infusion rates of 20mmol/hr (or higher) mandate monitoring in a high dependency ward (if not undertaken already).

4.) Glucose Infusion

- When blood glucose is ≤15mmol/L, commence an IV glucose infusion eg. 5% Glucose at 80-120 ml/hr, and adjust the rate in order to stabilise the blood glucose at between 10-15mmol/L for the next 6-8 hours.

- Then adjust IV glucose rate, whilst maintaining IV insulin rate, to maintain blood glucose between 5-10mmols/L until acidosis is reversed (see below).

- If glucose infusion rates of ≥200 ml/hr are required then change to 10% glucose infusion to limit fluid overload.

- If unable to maintain target blood glucose levels despite switching to 10% glucose in high flow rates, then reduce insulin infusion rate (e.g. to 3 units per hour), even if the acidosis is not completely reversed, and continue to adjust glucose infusion rate in order to maintain blood glucose within target range. Reducing the insulin infusion rate will delay the correction of the acidosis, but is necessary to prevent hypoglycaemia.

- Reduce normal saline infusion rate once blood glucose level is <10 mmol/L, unless either still clinically dehydrated or fluid deficit has not been corrected.

5.) Phosphate

- Hypophosphataemia is common, but rarely clinically significant. If serum phosphate level is low (even in the absence of clinical consequences), replace potassium as KH$_2$PO$_4$. Excessive phosphate replacement may cause hypocalcaemia. Rate of phosphate replacement is generally determined by the rate of potassium replacement required.

- Monitor serum phosphate every 4 hrs until normal (and then resume potassium replacement as KCl).

6.) Bicarbonate

- Bicarbonate should rarely be used in DKA as it may be lethal.

- Major indication is severe acidosis: (a) not corrected despite rehydration and adequate insulin therapy; and (b) associated with cardiovascular collapse.

- Persistent acidosis is usually due to inadequate fluid replacement, insulin and glucose therapy. Always discuss the indications for NaHCO$_3$ with the consultant on call.
• Consider use if PH<7.0 and HCO₃ <5mmol/L, with evidence of hypotension, arrhythmias or pulmonary oedema.

V. MONITORING THERAPY:

• Urine output, fluid balance and CVP (if required).
• One hour after commencement of therapy, check blood glucose, beta-hydroxybutyrate (blood ketones), Na, K, venous blood gases and thence hourly blood glucose levels (measure capillary blood glucose levels once blood glucose is 20mmol/L or lower), 2nd hourly beta-hydroxybutyrate (blood ketones), and 4th hourly Na, K, and venous blood gases.
• 4-8 hours after commencement of therapy check PO₄ and Mg and correct deficiencies. ECG monitoring and CXR as required.

VI. CHECK POINTS:

• Serum K+ may fall rapidly as the acidosis is corrected.
• If the blood glucose level falls to below target range, despite increasing the concentration and infusion rate of the IV glucose, and capillary beta-hydroxybutyrate (blood ketone) concentration is still elevated, then reduce IV insulin infusion rate to 3 units/hr. Once the capillary beta-hydroxybutyrate (blood ketone) level is <0.5mmol/L, then reduce IV insulin (and therefore IV glucose) infusion rate(s) in order to maintain the beta-hydroxybutyrate (blood ketone) and glucose levels within the target range.
• Remember IV insulin has a short half life (approximately 5 minutes) and therefore the insulin infusion should not be ceased. Otherwise the acidosis will quickly recur or increase.
• The capillary beta-hydroxybutyrate (blood ketone) level may normalise before the acidosis is completely reversed. Therefore, the insulin infusion should be continued until the pH and bicarbonate level are also normal.
• Causes of persistent acidosis are: inadequate insulin dosage, insufficient IV glucose, underlying infection or inadequate fluid replacement. Ensure that insulin is being infused in the correct rate, and that the correct priming procedure has been followed.

VII. THE DETERIORATING PATIENT

• Cerebral oedema. Headache, agitation and decreasing level of consciousness, accompanied by nausea, vomiting and signs of raised intracranial pressure – this is a medical emergency and the patient should be managed in ICU. Possible precipitants include rapid correction of hyperglycaemia and excessive fluid resuscitation. More common in children, but may also occur in young adults.
• **Persistent hypotension** despite adequate fluid resuscitation. Consider hypoadrenalism (and treat immediately if suspected) and treat with bicarbonate (if acidosis not improving) and/or inotropes.

• **Respiratory failure** may occur, due to either pulmonary oedema, fatigue resulting from prolonged hyperventilation or associated co-morbidities such as pneumonia or pulmonary embolism. Possible contributory factors include excessive fluid resuscitation, persistent acidosis and hypophosphataemia.

VIII. RESOLUTION PHASE:

**Ceasing the insulin infusion:**

• The insulin infusion can be ceased, the patient commenced on sc insulin and allowed to eat when:
  - Ketoacidosis reversed (normal pH, HCO3 and beta-hydroxybutyrate).
  - Plasma glucose level is stable and near normal.
  - Nausea is absent and the patient is tolerating oral fluids.

• Plan to cease the insulin infusion with a meal (preferably breakfast) and provide sufficient overlap between sc injection of insulin and ceasing IV insulin: 1 hour for Lispro (Humalog) Glulisine (Apidra) and Aspart (Novorapid) insulins or 2 hours for regular, soluble insulin (Actrapid or Humulin R). Give basal insulin at the same time (see below) if not given earlier.

• If ceasing the infusion at breakfast or lunch, **and the basal insulin has not been continued**, give half the usual dose of basal insulin (ie Glargine [Lantus] or Detemir [Levemir]) at that time, and the remaining half of the dose that night. Resume the usual full dose of Glargine or Detemir insulin the following night. Alternatively, give the usual dose of Glargine or Detemir insulin the night before the infusion is ceased.

• If the patient has previously been managed with an insulin pump, then resume the subcutaneous insulin infusion (if it has been ceased) once the acidosis has been reversed, at the rate appropriate for that time of day, and resume pre-programmed bolus doses of insulin as determined by the pump when the patient resumes eating. Cease the intravenous insulin infusion two (2) hours after the meal bolus dose of insulin has been given.

• **If patient known to have diabetes:**
  - Resume usual insulin regimen (as above), but may require higher doses if DKA associated with infection. Consider “basal-bolus” regimen if not previously receiving this and glycaemic control prior to admission was poor.
  - Give extra supplemental quick or rapid acting insulin if necessary, preferably before meals, according to capillary blood glucose level.
If not previously treated with insulin, commence “basal-bolus” insulin regimen (see below).

- **If NOT previously known to have diabetes:**
  - Calculate insulin dose according to body weight (see below).
  - Give quick or rapid acting insulin before each meal and intermediate acting insulin or long acting insulin analogue before bed (discuss with consultant or endocrinology registrar), plus extra supplemental quick acting insulin before meals, if necessary depending upon capillary blood glucose levels, in addition to usual insulin dose.

- **Approximate indication of the daily insulin requirements (Type 1 Diabetes):**
  - 0.5 - 0.7 units of insulin/kg body weight /day. Divide dose as follows:
    - ½-⅔ as short-acting insulin, eg Actrapid, Humulin R, or rapid acting eg Novorapid, Humalog, or Apidra divided equally between the three main meals
    - Remaining ⅓-½ as long acting analogue (eg Lantus or Levemir) insulin (or intermediate acting, eg Protaphane or Humulin NPH – although these are now less commonly used) before bed (2200 hrs).

**IX. FLOW CHART**

See below
**Management of Diabetic Ketoacidosis (DKA)**

**Diagnostic Criteria:**
- Arterial pH < 7.3 (or HCO₃ <16) plus Ketones in blood or urine plus Hyperglycaemia
- Mortality 5 – 10%, Often due to inadequate treatment of underlying precipitating condition

### Diagnose, Treat and Monitor

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>ABG, Blood ketones, BGL, K⁺, Investigate (see below)</td>
</tr>
<tr>
<td>Every hour</td>
<td>Capillary BGL, Vital signs, GCS (until stable)</td>
</tr>
<tr>
<td>Every 2nd hour</td>
<td>Venous gases, K⁺, HCO₃, Blood ketones</td>
</tr>
</tbody>
</table>

### Fluid resuscitation with NSaline:
- Give 1L stat if in shock (eg. BP <100 or HR ≥120). Repeat as necessary.
- Litre of NSaline | Duration |
<table>
<thead>
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<tbody>
<tr>
<td>1st L</td>
<td>½/1 hour</td>
</tr>
<tr>
<td>2nd L</td>
<td>1 - 2 hours</td>
</tr>
</tbody>
</table>
- Subsequent Fluids | Dependent on volume status |

### Insulin Infusion Therapy:
- 50 units Actrapid in 50mls NSaline
- PRIME THE INFUSION LINE
- Infusion rate: Strictly 5 units/hr
  - Do not stop
  - Do not decrease rate until ketonaemia is resolved or advised by endocrine team
  - Rate may need to increase if DKA fails to improve after 2 - 3 hours

### Potassium replacement:
- Adjust as per K⁺ on venous gas every 2 hrs. (Use K⁺H₂PO₄ if PO₄ is low)

### Commence Glucose (Dextrose) when BSL <15mmol/L and DON'T STOP INSULIN
- 5% glucose at 80 – 120mls/hr
- Continue NSaline if fluid status required
- Adjust glide rate per hour to achieve targets:
  - First 12 hours: 10 – 15 mmol/L
  - Thereafter: 5 – 10 mmol/L
- 10% glucose may be needed

### Consider & Treat Underlying Cause
- Baseline arterial ABG (hypoxia, lactic acidosis)
- Ca, Mg, PO₄, UEC
- LFTs, Amylase, Lipase
- ECG and troponins
- Septic screen (blood cultures, FBC, CRP, MSU, CXR)
- βHCG in women
- Check serum Cortisol if suspect adrenal insufficiency. Give iv hydrocortisone immediately after venesection. Do not delay treatment
  - (Alcohol & drug screen if drug use is suspected /Acidosis does not resolve)

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### Switching to S/C Insulin
- Cease Insulin/Glucose infusion 1- 2 hours (depending on type of insulin) after S/C insulin

### Red Flags & Pitfalls
- **RED FLAGS**
  - Review management + increase insulin infusion rate if after 2 - 3 hours:
    - Blood ketones have not fallen by 1mmol/L
    - BGL has not fallen by >4 mmol/L (Is line primed?)
    - pH or HCO₃ has not improved
  - Alert consultant (and or consider ICU) if:
    - Resistant hypotension, Hypoxia,
    - Decline in GCS, Increasing agitation,
    - Anuria despite fluids, Acute abdomen,
    - Hypoadrenalism
- **PITFALLS**
  - Reducing insulin inappropriately
  - Inadequate K⁺ replacement
  - Failing to start glucose when BSL<15 mmol/L
  - Delay in identify or treating precipitant
  - Too rapid fall in glucose causing cerebral oedema

### Things to remember:
- Circulatory shock- Inotrope support + hydrocortisone
- Rarely is NaHCO₃ needed (consider & discuss if pH<7.0 & HCO₃<5 & hypotension/arrhythmias/pulmonary oedema)

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**SWAHS Dept of Diabetes & Endocrinology. Version 1.6 November 2009**
3. HYPERGLYCAEMIC HYPEROSMOLAR STATE

Key Points

- The main priority of treatment is gradual correction of the hyperosmolality, rather than correction of hyperglycaemia.
- Avoid over vigorous rehydration – consider CVP monitoring and admission to HDU / ICU.
- Rehydrate with 0.9% (Normal) Saline. Hypotonic Saline (N/2) may be required if serum osmolality is not declining despite adequate fluid replacement.
- Aim to reduce serum sodium by <10 mmol/L in first 24hrs and osmolality by 3-8 mOsmol/Kg/hr.
- Insulin infusion in low dose (0.05 units/Kg/hr) if blood glucose is not falling or if there is coexistent significant ketonaemia. Aim to reduce the blood glucose level by <5 mmol/L/hr
- Subcutaneous Heparin
- Look for precipitating cause, especially sepsis
- Calculate “corrected” serum Sodium and total body water deficit.

Hallmark:

- Significant hyperglycaemia and hyperosmolarity with or without significant ketonaemia. A mixed picture of DKA and HHS may co-exist.
- Hypovolaemia (marked)

Diagnostic Criteria

- Serum osmolality ≥ 320 mOsm/Kg – measure directly or calculate (serum osmolality= 2xNa⁺ + BGL + Urea)
- Plasma glucose ≥ 30 mmol/L
- Anion gap <12
- Blood ketones may be normal or mildly elevated (<3 mmol/L)

Predisposing / Precipitating Factors

- Infection (30-60%) may be occult; exclude foot sepsis
- Myocardial infarction
- Dehydration
- Pancreatitis
- Stroke
- Parenteral feeding
- Drugs: especially glucocorticoids, sympathomimetics, antipsychotics
Previously undiagnosed diabetes in ~30%

Clinical Features
- Occurs mainly with Type II diabetes
- High morbidity and mortality (~15%) rate, largely due to patient age, co-morbidities, the precipitating illness and thrombo-embolic complications.
- Ketonaemia +/- acidosis may be present, particularly with sepsis or tissue hypoperfusion (resulting in lactic acidosis, possibly compounded by renal failure and Metformin therapy).
- Coma occurs in ~30%, and altered sensorium correlates with the severity of the hyperosmolarity (>330 mOsm/Kg).
- Dehydration usually significant.
- Cautious rehydration is essential to prevent rapid correction of hyperosmolality.
  Consider CVP monitoring for elderly patients, or those with underlying renal or cardiac disease.
- Hypernatraemia is common, and may rise after initial rehydration, due to fall in plasma glucose
  Measured serum Na may be spuriously low because of hyperglycaemia
  “Corrected” sodium = measured Na + 0.3(BGL-5.5) or Na + (BGL/4)

Goals of Treatment
- Normalise the osmolality gradually
- Replace fluid and electrolytes
- Restore euglycaemia
- Prevent complications
- Treat precipitants

Management
- Manage in High Dependency Unit or ICU
- The main initial priority is gradual correction of hyperosmolality, rather than correction of hyperglycaemia, together with identification and treatment of precipitants.

1. Correction of hyperosmolality.
   - REHYDRATE initially with 1-2L isotonic (0.9%) saline over 1-2hrs, and then 0.5-1 L/hr depending on severity of dehydration / risk of heart failure. Aim to achieve positive fluid balance of 2-3 litres by 6hrs. Only commence hypotonic saline (i.e. N/2) if (calculated) serum osmolality not declining despite adequate
positive fluid balance.

- Consider CVP monitoring after initial rehydration, +/- an arterial line to facilitate vascular access for frequent biochemical monitoring.
- Accurate fluid balance monitoring, including urine output, is essential.
- Monitor venous plasma glucose, urea and electrolytes hourly and calculate osmolality. **NB:** Blood glucose levels greater than 30 mmol/L are above the upper limit of the ward capillary blood glucose meters and any changes in the blood glucose level when greater than 30 mmol/L will therefore not be detected by the ward meters.

**AVOID RAPID CORRECTION OF HYPEROSMOLALITY**

- **Aim for rate of fall of serum Na <10 mmol/L in 24 hrs and of serum osmolality of 3-8mosmol/Kg/hr.** If rate of fall of osmolality >8 mosmol/Kg/hr, consider reducing infusion rate of IV fluids and/or insulin. (Serum Na may rise initially with rehydration as plasma glucose decreases)
- **Aim to replace half of predicted fluid deficit in first twenty four hours and the remainder over the next 12-36 hrs.**

  \[
  \text{TBW deficit} = 0.6 \times \text{Wt} \times (1-140/\text{serum sodium})
  \]

  *(use correction factor of 0.5 for women and elderly men and 0.45 for elderly women)*

2. **Correction of hyperglycaemia.**

- Hyperglycaemia will usually improve with rehydration and an insulin infusion may not be necessary initially.
- Commence a fixed dose insulin infusion at 0.05 units/Kg/hr once BGL is no longer falling after initial rehydration, or immediately if significant hyperketonaemia (blood ketones >1 mmol/L). Aim to reduce BGL by <5mmol/L/hr
- Reduce insulin infusion rate to 2-3 units/hr if BGL decreasing by >4 mmol/L per hour or when BGL reaches 15 mmol/L.
- Commence 5% Glucose IV when BGL reaches 15 mmol/L and adjust rate in order to maintain BGL 10-15 mmol/L until hyperosmolality improves. **Continue 0.9% (normal) saline infusion**
- Cease insulin and glucose infusions when serum osmolality <300, BGL <10, and patient awake and able to eat and drink normally. Patient should remain NBM until then (change to variable dose insulin infusion with glucose if necessary).
- Commence sc insulin (oral hypoglycaemic agents usually ineffective), initially with rapid acting analogue insulin (0.1 units/Kg) with each meal and slow acting
analogue insulin (0.3 units/Kg) in the evening, combined with Metformin if serum creatinine <150 umol/L.

3. **Prevention of complications / treatment of precipitants**

- Give low dose subcutaneous heparin to prevent thrombosis.
- Replace serum K+ (30-60mmol/L) if serum K+ <5mmol/L. Hypokalaemia is usually less significant than with DKA.
- Infection is common and often occult. Perform full septic workup, including measurement of CRP. Consider cholecystitis, peri-nephric abscess and septic foot, as well as UTI, and pneumonia, as well as more atypical sites (e.g. epidural abscess, meningitis)
- Exclude myocardial infarction
- Monitor closely / frequently for complications such as thrombosis, pulmonary embolus, myocardial infarction, cerebral oedema and fluid overload. Regular monitoring of clinical and volume status (including BP, JVP, HR, urine output), conscious state, electrolytes is essential to guide therapy.
- Cerebral oedema and/or central pontine myelinolysis may occur if correction of hyperosmolality occurs too rapidly.
- Contact consultant if conscious state deteriorates, over-rapid correction of serum osmolality or sodium occurs, or pulmonary oedema or oliguria develops.
Management of the Hyperosmolar Hyperglycaemic State (HHS)

**Diagnostic Criteria:**

CAN CO-EXIST with Diabetic Ketoacidosis (DKA)

Hypovolaemia with serum osmolality ≥ 320 mOsm/kg, measured or calculated (2 x Na+ + BGL + urea), anion gap < 12, plasma glucose ≥ 30 mmol/L without significant acidosis (pH > 7.3, HCO3 > 15 mmol/L), ketones may be normal or mildly elevated (< 3 mmol/L). High morbidity and mortality (15%)

**Clinical Assessment:**

Consider Precipitating Features
- Infection (30-60%) may be occult, exclude foot sepsis
- Myocardial infarction
- Pancreatitis
- Stroke
- Drugs (glucocorticoids, sympathomimetics, antipsychotics)
- Previously undiagnosed diabetes in 30%

Clinical Features
- Dehydration usually significant
- Coma in 30%, altered mental state with severe hyperosmolality (> 330 mOsm/kg)
- Lactic acidosis with sepsis or tissue hypoperfusion (check metformin use)

**Treatment Goals:**

- Normalise osmolarity
- Restore Euglycaemia
- Prevent Complications
- Treat Precipitants

**Resuscitation Phase**

Rehydration with NSaline:
- Manage in HDU or ICU
- CVP monitoring- elderly, cardiac/renal disease
- Replace half of predicted fluid deficit in first 24hrs and remainder over next 12-36hrs
- Aim to achieve 2-3L positive fluid balance by 6hrs
- Hypotonic saline (0.45%) only if (calculated) serum osmolality not declining despite adequate positive fluid balance

Duration | Litre of NSaline
--- | ---
1st 1-2 hours | 1-2L isotonic (0.9%) saline
Followed by 0.5-1L/hr depending on severity of dehydration/comorbidities

**Restore Euglycaemia:**

- BGL will improve with rehydration
- Commence insulin infusion (50 units of Actrapid in 50mL N/S) at 0.05 units/kg/hr if:
  - Blood ketones > 1 mmol/L or
  - BGL no longer falling after initial rehydration
- Aim to reduce BGL by < 5mmol/L/hr
- Reduce insulin rate to 2-3units/hr if:
  - BGL falls by > 4 mmol/L/hr
  - BGL reaches 15
- When BGL < 15 start 5% dextrose but continue 0.9% N/S infusion
- Adjust glucose rate per hour to maintain BGL 10-15 until hyperosmolality improves

**Stabilisation Phase**

- Monitor glucose, urea, electrolytes hourly and calculate osmolality
- Aim for fall of serum Na < 10 mmol/L in 24 hours + osmolality 3-5mOsm/kg/hr
- If rate of fall of osmolality >8 mOsm/kg/hr consider reducing IVF/insulin rate

**Resolution Phase**

- Cease insulin and glucose infusions when serum osmolality < 300 mOsm/kg
- BGL < 10 mmol/L, and patient awake and able to eat and drink normally.
  - Commence subcutaneous insulin (oral hypoglycaemic agents usually ineffective)
  - Rapid acting analogue insulin (novorapid) 0.1 units/kg with meals
  - Slow acting analogue insulin (lantus) 0.3 units/kg in the evening

**Calculate total body water deficit = 0.6 x weight x (1-140/serum sodium) (use correction factor of 0.5 for women and 0.45 for elderly women)

Measure "corrected" sodium = measured Na + (BGL/4) or measured Na + 0.3 (BGL – 5.5)

**Identify and Treat Precipitants**

- Sepsis- infection common and often occult. Perform full septic workup. Consider cholecystitis, perinephric abscess, UTI, septic foot, pneumonia
- Myocardial infarction- 12-lead ECG, troponin, CK
- Stroke- clinical history, examination and imaging if clinically indicated

**Potassium Replacement**

- Hypokalaemia is usually less significant than with DKA
- Replace serum K+ (30 – 60 mmol) if serum K+ < 5 mmol/L

**RED FLAGS**

- High risk of arterial and venous thromboembolism. Remember anticoagulation- ALL patients should receive prophylactic low molecular weight heparin (LMWH) for duration of admission
- Monitor for complications -Thrombosis and pulmonary embolism
- Myocardial infarction
- Cerebral Oedema
- Fluid Overload
4. HYPOGLYCAEMIA

Definition
Venous plasma or capillary blood glucose level <4.0 mmol/l.

Causes
Commonest cause is the use of oral hypoglycaemic agents or insulin. Profound & prolonged hypoglycaemia may occur and patients may need to be monitored for at least 24 hours. Renal failure may impaire the excretion of the active drug and its metabolites (eg glibenclamide) or reduce the clearance of insulin, thereby potentiating its effect. Hypoadrenalism may also contribute to hypoglycaemia due to impaired ability to mount a counter-regulatory response.

In people with diabetes:
- Hypoglycaemia results from an excess of glucose utilisation compared to absorption/production. This may be due to-
  - Inappropriate doses of oral hypoglycaemic agents, incretin mimetics or insulin. Sulphonylureas (eg Gliclazide, Glibenclamide) are the most likely oral agents to cause hypoglycaemia. However, other oral agents may also contribute to hypoglycaemia, particularly if used in combination with sulphonylureas or insulin.
  - Deliberate or accidental insulin or sulphonylurea overdose
  - Inappropriate timing of drug administration in relation to food intake
  - Erratic absorption of insulin due to incorrect injection technique
  - Impaired elimination of insulin or other drugs in renal failure, or in the elderly.
  - Inadequate or delayed carbohydrate intake, vomiting, diarrhoea, inadvertent cessation of nasogastric feeds, short-term fasting for investigations/procedures
  - Increased physical activity levels
  - In patients on concomitant steroid therapy – recent dose reduction or cessation.
  - Alcohol or other drugs
  - Early pregnancy or breastfeeding

In people without diabetes:
Inadvertent or deliberate intake of oral hypoglycaemic agents or insulin should be considered. Most endocrine causes are uncommon or rare. Think of hypoadrenalism / hypopituitarism (cortisol and growth hormone deficiency) or insulinoma (autonomous excess production of insulin). Non-endocrine causes include alcohol excess, sepsis, liver failure, renal failure, cachexia and malignancy.

**Presenting features**

Hypoglycemic symptoms are related to:

- Activation of the sympathetic nervous system and appetite centre
  - sweating, tachycardia, tremulousness, anxiety, hunger
- Brain dysfunction secondary to decreased levels of glucose (neuroglycopaenia)
  - confusion, impaired concentration, altered level of consciousness
  - focal impairments (e.g. hemiplegia)
  - seizures, coma and death.
- Generalized glycopaenia to metabolising tissues
  - weakness and fatigue

Adrenergic symptoms usually precede the neuroglycopaenic symptoms and provide an early warning of hypoglycemia to the patient. Occasionally, symptoms of sympathetic autonomic stimulation may be absent, particularly in the elderly, and neuroglycopaenic symptoms may be the presenting feature. The blood glucose threshold for onset of hypoglycaemic symptoms is variable but most people experience symptoms at < 3.0mmol/L. This threshold decreases with repeated episodes of hypoglycaemia and some patients with repeated events can have almost no symptoms until unconsciousness ensues (hypoglycaemic unawareness). Hypoglycaemic unawareness is associated with increased mortality, especially in the setting of cardiovascular disease.

**Investigations**

Capillary BGL by reflectance meter, Venous BGL and insulin/c-peptide (if not diabetic), Blood gases and electrolytes, urea and creatinine, LFTs. In a patient without known diabetes, always confirm the diagnosis of hypoglycaemia with a venous plasma glucose level, together with a serum insulin and c-peptide level, prior to initiating treatment.

**Therapy:**

**STEP 1**
If fully conscious: give an oral sugar load, eg half a glass of non-diet soft-drink or juice, 6-7 jellybeans, or 1 tube of Glutose 15 glucose gel orally (equivalent to 15g carbohydrate), (see “hypo-kit”) and repeat as necessary

If not fully conscious: Appropriate resuscitation measures (ABCDE). 25-50mls 50% Glucose IVI stat. (can dilute 50:50 in sterile water to prevent extravasation injury and enable easier injection if venous access is problematic) followed by IV 5% Glucose infusion to maintain euglycaemia until fully conscious and until 30 minutes after a meal. Glucagon should not be given if IV glucose is available. (Note glucagon may be ineffective if hypoglycaemia is prolonged and in those with coexistent morbidities such as renal failure or liver failure). Glucagon 1mg IM can be given if intravenous access is not attainable (but requires re-suspension and may not be readily available in ward).

Remember to stop insulin infusion if it is running.

**STEP 2**

Repeat capillary blood glucose measurement 10-15 minutes later. If it is still less than 4.0mmol/L, repeat STEP 1 up to 3 times

**STEP 3**

When the patient is fully conscious and BGL>4 mmol/L: give oral slow acting carbohydrates – 2 biscuits OR a slice of bread OR a glass of milk OR the next carbohydrate containing meal if it is due.

If the next dose of insulin is due, DO NOT withhold it, although dose reduction of 10-20% may be considered in some circumstances.

If the patient does not recover quickly or is unable to resume oral intake:

- **Type 1 Diabetes**: Continue I.V. 5% Glucose at 125 ml/hr and commence insulin infusion when BGL > 8 mmol/l and manage according to variable dose intravenous insulin-glucose infusion protocol (WSHR-2733).

- **Type 2 Diabetes**: Continue I.V. 5% Glucose at 125 ml/hr (unless fluid restriction is necessary) and monitor BGLs every 2 hrs until able to resume oral intake. Ensure
carbohydrate intake is adequate, especially in the elderly and in those recovering from gastrointestinal disturbances. Commence variable dose intravenous insulin-glucose infusion if oral intake remains inadequate and BGL > 10 mmol/l.

If the patient remains unconscious despite restoration of normoglycaemia, then consider:

- Glucocorticoid administration;
- Possibility of other causes of coma (in addition to hypoglycaemia).

Beware of delayed recurrent hypoglycaemia in the elderly patient receiving a sulphonylurea. If hypoglycaemia has been recurrent then a more prolonged period of observation is necessary, with frequent monitoring of BGLs (especially overnight). Indeed, any elderly patient receiving sulphonylurea therapy who has developed hypoglycaemia resulting in unconsciousness requires admission to hospital for monitoring for at least 24hrs

If hypoglycaemia due to sulphonylurea therapy persists or recurs despite I.V. Glucose, then consider treatment with Octreotide. Discuss with endocrinologist on-call.

Ensure that all Type I Diabetic patients subsequently receive their usual insulin therapy. Resume oral therapy in Type 2 Diabetics at the next meal. Reduce dose of insulin or tablets if necessary, particularly if there is no obvious cause for the hypoglycaemia, if the insulin dose appears to be excessive, or if episodes have been recurrent.

5. OBESITY IN THE HOSPITAL SETTING

Introduction

- The prevalence of obesity is approximately 25% in Western Sydney, resulting in a corresponding increase in obesity related medical problems.
- Obesity is defined by the BMI: weight/height$^2$. BMI >30 = obese; >40 = morbidly obese; and >50 = super obese.

Obesity related medical problems

- A number of medical conditions are caused or significantly exacerbated by obesity, including:
- Diabetes, hypertension, ischaemic heart disease, heart failure, asthma, sleep apnoea, renal impairment, arthritis in lower back and knees, calf cellulitis, GORD, NASH and varicose veins.
• Weight loss of only 5-10% body weight can be very helpful in management of these problems.

**Obesity created medical problems.**

• Some quite severe medical and surgical problems are directly caused by obesity.

• Dyspnoea and oedema are very common in obesity, without necessarily any other cause.

• Lymphoedema in obese patients may simply be obesity related oedema. However, these are diagnoses of exclusion, after consideration of other more serious causes.

• Abdominal hernias are common, due to raised intra-abdominal pressure. Unfortunately recurrences are common after surgery.

• Obesity related peripheral venous hypertension frequently leads to calf oedema, dermal sclerosis, pigmentation, ulceration and cellulitis. Sometimes the cellulitis is chronic and requires prolonged treatment with bed rest and antibiotics. Stockings or pressure bandages can be used when acute cellulitis has subsided.

• The very obese may also develop a pendulous lower abdomen or large skin folds in the thighs or groins. These are often very oedematous, with peau d’orange appearance and again chronically inflamed. Bed rest and weight loss are very effective treatments for these debilitating problems.

• **Obesity hypoventilation syndrome is the most serious complication of severe obesity.** It usually presents with marked fluid retention (the patient may notice rapid weight gain) cyanosis and CO₂ retention. Decompensation from a stable state can always occur with intercurrent illness, a sedating medication or for no apparent reason. Onset of drowsiness requires the measurement of arterial blood gases. Artificial ventilation may be needed acutely and mild to moderate weight loss usually prevents recurrences.

• **Supportive care in hospital:** should include use of specific bariatric equipment to assist with patient care, transfers, and mobilisation, and attention to pressure areas and bowel and bladder function.

**Weight Loss in Obesity**

• Mild to moderate weight loss, maintained over a prolonged period is often very helpful for the conditions described above. Many people can achieve this by themselves, with commercial programs or obesity clinics. Medical/nursing staff should not assume weight loss programs are useless or bound to fail.

**Very Low Calorie Diets**
• Obese patients sometimes undergo rapid weight loss treatment in hospital with a very low calorie diet. This is usually given for a serious obesity related problem i.e. respiratory failure or heart failure in a very unwell patient.

• The patient has each normal meal replaced by a liquid 250 calorie meal, made by mixing a sachet of powder with 400-500 ml water. This is usually accompanied by a salad or green vegetables, but no calorie containing foods. The patient is also given free access to water, tea and coffee (with artificial sweetener) and diet soft drinks.

• There is not only rapid weight loss, but marked fluid loss, drop in blood pressure and reduction in glucose levels. It is usual to halve doses of insulin and sulphonylureas when starting.

• Blood pressure medication often has to be reduced after 3-4 days and diuretics also halved, unless the patient has severe heart failure. If the patient has renal impairment, ACE inhibitors and ARBs should be ceased temporarily as combination with fluid loss and lower blood pressure can cause renal failure.

• Blood pressure and weight should be measured daily on this treatment.

6. THYROID CRISIS

Definition:
Severe thyrotoxicosis usually precipitated or exacerbated by an intercurrent event. Also known as “thyroid storm” Characterised by fever and extreme cardiovascular, GIT and neurological features of thyrotoxicosis. Mortality rate 20-30%.

Aetiology:
In most cases, hyperthyroidism is known to exist and the condition suddenly worsens. The commonest cause of hyperthyroidism is Graves Disease.

Precipitating factors for thyroid storm include:
- Thyroidectomy or radioactive iodine in inadequately prepared patient with hyperthyroidism.
- Non-thyroidal surgery,
- Parturition,
- Severe illness, eg. infections, myocardial infarction, pulmonary embolism, diabetic ketoacidosis
- Thyroxine overdose
- Large iodine load (eg radiocontrast, amiodarone)
Clinical features:

- Fever
- Severe thyrotoxicosis
- Arrhythmia (atrial fibrillation), congestive cardiac failure (especially in the elderly with underlying cardiac disease), shock
- Agitation, progressing to delirium, seizures and coma
- Abdominal pain mimicking an acute abdomen. Caution: an acute abdomen may also be the precipitant.
- Tachypnoea and dyspnoea. Caution: pulmonary thromboemboli may occur because of hypercoagulability.

Diagnosis:

The diagnosis of thyroid crisis (or storm) is clinical. There is no diagnostic test – if the diagnosis is suspected, treat thyrotoxicosis aggressively.

Investigations:

- Thyroid function - FT4, TSH, FT3 – the degree of elevation of the FT4 does not necessarily correlate with the severity of the thyrotoxicosis. The FT3 may not be elevated with co-existent systemic illness. These tests need to be performed urgently.
- Electrolytes, Urea, Creatinine, LFTs, Ca, FBC, BGL, Cortisol
- Blood gases, CXR, ECG
- CVP if indicated, urine output, fluid balance
- Blood culture or other cultures as indicated.
- Thyroid Gland imaging is not usually necessary at this stage.

THERAPY

Notify the Endocrinologist on call early if the diagnosis is suspected.

Transfer the patient to a HDU / ICU with specialist endocrine services after treatment initiated.

Principles of therapy:

- Inhibit new hormone synthesis
- Inhibit release of stored thyroid hormone
- Control the adrenergic effects of thyroid hormone excess
- Supportive

SPECIFIC THERAPY

Thyroid crisis requires urgent treatment, and multiple agents are used to achieve these effects.

- **Propranolol** 40-80mg, orally 4 to 6 hourly. (Small IV doses may be indicated - caution
should be taken to avoid cardiovascular complications, especially those with CCF).

- **Propylthiouracil** 500-1000mg orally stat., then 250mg q4h (or Carbimazole 50-100mg orally stat., 25mg q6h if PTU unavailable). PTU has the additional benefit of inhibiting the peripheral conversion of T4 to T3 and is preferred in this situation. Neither available as parenteral formulations. Given orally or per nasogastric tube in the stuporous or unco-operative patient.
  
  Rectal administration has also been used

- **Lugol's Iodine** 4-8 drops every 6-8hrs – **commence 1 hr after starting PTU, but not earlier**. Lithium carbonate is an alternative if there is an iodine allergy.

- **Hydrocortisone** IVI 100mg q6h

- **Plasmapheresis** can be considered where the patient is unresponsive to the above measures

### SUPPORTIVE THERAPY

- Treat cardiac failure with digoxin, diuretics and O₂. (Larger than normal doses of digoxin may be needed)
- Treat the precipitating factor
- Active cooling and paracetamol
- Fluid and calorie replacement.
- Cardiac monitoring
- Anticoagulation, especially if atrial fibrillation with CCF present.

Should proceed to total thyroidectomy once euthyroid, especially if Lugol’s Iodine used.

### 7. MYXODEMA COMA

#### Clinical features

- Usually long standing undiagnosed hypothyroidism but
- May occur several weeks after cessation of thyroid medication (especially in elderly and forgetful patients).
- More likely to occur in cold weather!
- High mortality rate: 50-60%

The main manifestations include:

- hypothermia, hypotension, bradycardia, hypoventilation with hypercapnia/hypoxia
- myxoedema (clinical features of hypothyroidism), hyponatraemia, hypoglycaemia,
- coma and
- subacute bowel obstruction usually in the elderly.

#### Precipitants

- Intercurrent infection, especially pneumonia
- Sedative drugs
- Cerebrovascular accident

**Investigations:**
- Thyroid function - FT4, TSH, (urgent)
- EUC, BGL (hypoglycaemia, hyponatraemia), FBC
- Blood gases (Respiratory Acidosis)
- Blood cultures, MSU
- CXR, ECG
- CVP as indicated, urine output, fluid balance
- (LDH, CK and cholesterol may also be elevated).

**Therapy**
The key to successful management of Myxoedema Coma is:
- early recognition and
- rapid institution of supportive and therapeutic measures

Once the diagnosis is ascertained, therapeutic measures should be commenced immediately even in the absence of confirmatory laboratory data: *when in doubt treat*.

Transfer to HDU/ICU with endocrinology service after initial treatment commenced.

**SUPPORTIVE MEASURES**
The cornerstone of initial therapy is to institute prompt supportive measures with the emphasis on the maintenance of cardiopulmonary status.
- Aggressive pursuit of the source of the precipitating event/illness and appropriate therapy.
- Treat any precipitating factors such as infection, CNS depressants, trauma, hypothermia.

**Bacterial infection**
- the most common precipitating event,
- Assume in all cases until proven otherwise.
- Note: Hypothyroid patients are frequently unable to generate a fever in response to infections.
- Commence broad spectrum antibiotics until the source of infection is identified.

**Respiratory assistance**
- Intubation and ventilate at the first sign of respiratory failure (rising CO₂).

**Cardiovascular assistance.**
Hypertension may occur with hypothyroidism, therefore:
- Hypotensive or even normotensive patient should be considered with some alarm – suggests volume depletion, may be exacerbated by warming.
• Additional causes of hypotension should be sought, particularly sepsis, silent GIT blood loss or a silent myocardial infarction.
• Central monitoring of venous pressure should be considered.

**Temperature Control**
• Aggressive warming may cause peripheral vasodilation and precipitate hypotension and shock.
• Therefore do **not** actively warm but prevent heat loss with blankets

**Fluid replacement.**
• The hypothyroid patient is volume depleted
• Blood pressure support requires the judicious use of intravenous fluids.
• Hyponatraemia may warrant hypertonic saline infusion – fluid restriction may exacerbate hypotension.

**SPECIFIC THERAPY**

**Thyroid hormone therapy.**
• In severe hypothyroidism, oral replacement therapy may be poorly absorbed. If possible, give Thyroxine 200mcg orally or via nasogastric tube followed by 100-150mcg/day thereafter.
• If patient not capable of taking/absorbing Thyroxine orally, give Tri-iodothyronine (T3) 10mcg q8h IV (has additional benefit of more rapid onset of action and shorter half-life). Oral thyroxine (T4) is substituted later, once patient is capable of oral absorption.
• Consider Beta Blockers if thyroxine therapy causes tachycardia or if there is a history of ischaemic heart disease.

**Hydrocortisone**
• Give 100mg hydrocortisone every 6 hours, because of possible co-existence of hypoadrenalism and accelerated metabolism of cortisol once thyroid hormone therapy is commenced. Adrenal insufficiency may also cause hypoglycaemia which should be treated by iv glucose. Monitor the response with capillary BGL.

8 **HYPOCALCAEMIA FOLLOWING THYROID OR PARATHYROID SURGERY**

**Clinical features**
May develop within hours of excision or surgical injury to the parathyroid glands, include:
• paraesthesia
• cramps
• tetany
• seizures
Post Parathyroidectomy

Check serum calcium level

- 4-6 hours post-op, and then
- Daily for at least 3 days.

May be some predictive value in an early post-op PTH level.

The best clinical sign is Trousseau's test:

- Inflate a BP cuff to 10mmHg above systolic pressure
- Maintain this pressure for 2 minutes.
  - Positive test is characterized by spasm of the muscles of the hand and forearm with flexion at the MCP joints and extension at the IP joints. ("main d’accoucheur").

Management

**Mild symptoms or corrected serum calcium > 2.0mmol/L:**
- Oral calcium (eg. Caltrate or Citracal)
  1g - 2g (elemental calcium equivalent) every 8 hrs

**Severe symptoms or corrected serum calcium < 2.0mmol/L:**
- Calcium by infusion:
  - 10% calcium gluconate solution 10 - 30 mls
    - (1 amp = 1g = 10mls) diluted in 5% dextrose over 30 mins.
  - May be repeated after re-measurement of serum calcium, or given as a continuous infusion 4g/day until normalised.
  - Ideally administered through a central vein, with cardiac monitoring.

**In persistent, severe hypocalcaemia:**
- Oral calcitriol (Rocaltral)
  - 0.25 micrograms, 2 - 4 tablets daily.

Check serum magnesium in all hypocalcaemic patients

- if low, give Mg replacement eg
  - iv Magnesium sulphate 4 - 5 grams (2 ampoules = 40 mEq) in 5% dextrose over 4 hours, or
  - Oral magnesium aspartate tablets (Magmin) 2 - 4 daily.

CLOSE MONITORING OF CALCIUM, MAGNESIUM, PHOSPHATE AND OTHER ELECTROLYTES IS ESSENTIAL ONCE TREATMENT IS INSTITUTED.
9. ADRENAL INSUFFICIENCY

Aetiology

Primary adrenal insufficiency:
- Polyglandular autoimmunity
  (approximately 60-75% have anti-adrenal antibodies; approx. 50% have another autoimmune disease)
  - Infections: tuberculosis, histoplasmosis, HIV associated, CMV, cryptococcus
  - Adrenal Haemorrhage:
    - Septicaemia, anticoagulation, ITP, Lupus anticoagulant, Heparin induced thrombocytopenia,
  - Metastatic disease
  - Drugs - Ketoconazole, Metyrapone
  - Familial (e.g. adrenal leukodystrophy, congenital adrenal hyperplasia)

Secondary Adrenal Insufficiency:
- Exogenous glucocorticoid administration and hypothalamic-pituitary-adrenal axis (HPA) suppression.
  NB: Patients who have been treated with glucocorticoids for prolonged periods, including inhalers (e.g. fluticasone) or topical steroids are at risk of adrenal suppression, and hence of adrenal insufficiency during an intercurrent illness, when there is increased need for glucocorticoid secretion.
- Pituitary/hypothalamic disease
  - Pituitary adenomas
  - Hypophysectomy
  - Pituitary irradiation
  - Sheehan’s syndrome (post-partum pituitary infarction)
  - Head trauma
  - Immune-checkpoint therapy for malignancies

Presentation
May vary from gradual course in non-acutely stressed individual to sudden fall in blood pressure associated with acute major events.

Features vary but may include:
- Weight loss
- Fatigue
- Muscle weakness
- Abdominal pain
- Nausea, vomiting, diarrhoea
- Hypotension, shock, dehydration (“adrenal crisis”) particularly with acute illness
• Hyperpigmentation (in chronic primary adrenal insufficiency)
• Electrolyte disturbance
  • Hyponatraemia, hyperkalaemia (primary adrenal failure)
  • Hyponatraemia (secondary adrenal failure)
• Hypoglycaemia
• Features associated with underlying cause
e.g. Addison's disease: Other associated autoimmune disease e.g. autoimmune thyroid disease, Type I Diabetes, vitiligo, premature menopause
  Hypopituitarism: secondary hypothyroidism, secondary hypogonadism, growth failure, diabetes insipidus, previous pituitary surgery or radiotherapy.
  HPA suppression due to long term glucocorticoid therapy: History of underlying illness

Assessment
• History and exam- including usual medications (including oral or inhaled/topical glucocorticoid therapy)
• Volume status- JVP, clinical assessment, Urine output, fluid balance chart, (CVP if indicated)
• Electrolytes (Na, K Renal function) and Glucose; ABGs
  Hyponatraemia and hyperkalaemia, particularly with hypovolaemia suggest primary adrenal failure; isolated hyponatraemia and/or hypoglycaemia are more typical of secondary adrenal failure; however vomiting may mask hyperkalaemia. There can be other causes for these electrolyte abnormalities
• Plasma cortisol and ACTH levels

_A random cortisol >500 nmol/L usually excludes adrenal insufficiency in an otherwise well patient_,
_A morning serum cortisol level <150 nmol/L in a sick patient is highly suggestive of cortisol deficiency._
_Intermediate results often require a stimulation test for clarification, although interpretation of the result is often difficult._
_Interpretation of results may be confounded by treatment with exogenous glucocorticoids, oral contraceptive pills and pregnancy_

• Hb, WBC
• Blood cultures, urine culture and other appropriate cultures as indicated
• Other pituitary function tests if secondary adrenal failure is present/suspected (free T4, TSH, prolactin, FSH, LH, oestradiol/testosterone; +/- serum and urine osmolality)
• Synacthen stimulation test may be necessary (but should not delay therapy). A peak cortisol response of 500-550 nmol/L at 30-60 min. after 250mcg Synacthen IV excludes the diagnosis of primary adrenal insufficiency and most cases of secondary adrenal insufficiency (where present for more than 6 months)
• Secondary adrenal insufficiency: May require an insulin tolerance (hypoglycaemia) test to confirm diagnosis (arrange endocrinologist review).

TREATMENT
**Maintenance**

- Physiological glucocorticoid requirements are approximately 10-20 mg/day of hydrocortisone (equivalent to a prednisone dose of 2.5-5 mg/day), partly determined by the individual's weight. Twice daily (or even tds) dosing may be required, particularly for hydrocortisone. Requirements are increased 2-3 fold in moderate illness and up to 10-fold in acute severe stress.

**Acute**

- Adrenal crisis is a life-threatening situation. Treatment should not wait for the confirmation of the diagnosis in someone not previously known to have hypoadrenalism.

If Adrenal crisis is suspected:

1. Collect blood for serum cortisol and ACTH, then commence treatment immediately. (Treatment can be started without waiting for the results)
2. 200mg hydrocortisone IV stat then 100mg IV 6 hourly for 24-48, change to oral therapy, and then taper the dose over the next 4-5 days, towards maintenance doses, if the patient is well/has recovered
3. Rapid rehydration with normal saline or glucose saline.

NB: IF hypoglycaemic, treat hypoglycaemia as per standard care (see Hypoglycaemia management)

4. Exclude and treat the precipitant(s) and/or other associated endocrine deficiencies.
5. Monitor electrolytes, renal function, glucose, urine output/fluid balance and volume status in order to modify treatment if required.
6. Addition of mineralocorticoid therapy is not usually required in patients receiving the high doses of hydrocortisone, but should be commenced in patients with primary adrenal insufficiency once the dose of hydrocortisone is reduced to <100mg/day.
7. Contact endocrine team for advice

**Prevention of Adrenal Crisis** *(in patients known or suspected to have hypoadrenalism)*

- Adrenal crisis can be prevented by adequate glucocorticoid therapy for at risk patients.
- Potential precipitants of adrenal crisis include surgery / anaesthesia, invasive investigations, insulin hypoglycaemia, myocardial infarction and severe intercurrent illness (including infections).

**Steroid (glucocorticoid) cover:**

- Major Surgery (e.g. CABG): IV hydrocortisone 100mg with premedication, then 6th hourly for 2-3 days (or during period of major stress). Weaning dose depending on clinical progress.
- Intermediate surgery (e.g. appendicectomy) 100mg IV with premed then 6-8th hourly for 24 hr then 50-100mg 8th hourly for 1-3 days before further weaning depending on progress.
- Minor surgery (e.g gastroscopy): IV hydrocortisone 50-100mg with premedication, then double usual oral dose for 24-48 hr.
- Fasting, vomiting or malabsorption - IV or IM hydrocortisone required. Stress doses may be required (hydrocortisone 50-100mg 8th hourly) whilst unable to eat, then
change to oral hydrocortisone and gradually reduce towards physiological replacement 
doses.

• Intercurrent illness (e.g. infections): Normal doses of glucocorticoids may need to 
be doubled or increased further depending on severity of illness. Doses of 50-100mg IV 
hydrocortisone 6-8th hourly may be required depending on severity of illness but will need to 
be balanced against risk of sepsis – discuss with endocrine team if unsure.

• Do not taper the dose of hydrocortisone too quickly as the patient recovers - 
reduce the dose by ~50% every 24 hrs if the patient is well. Many patients will still 
need to take increased doses of hydrocortisone for another 48-72 hrs post-
discharge.

**Long Term Glucocorticoid Therapy:**

Patients who have been prescribed glucocorticoid therapy for non-endocrine disorders for a 
prolonged period of time are at risk of HPA suppression. This may occur with even low 
doses of glucocorticoids (including inhaled or topical steroids) with longer durations of use; 
or shorter durations of use if higher doses of glucocorticoids. They may therefore be at risk 
of an adrenal crisis if additional glucocorticoids are not given during significant intercurrent 
illnesses.

Adrenal insufficiency may present either with an acute adrenal crisis (hypotension, vomiting, 
hyponatraemia, hyperkalaemia) or with a less clear cut presentation (e.g. fatigue, nausea, 
abdominal pain, isolated hyponatraemia, hypoglycaemia or only one of the above)

• Inpatient admissions:
  • In patients with long term glucocorticoid use, Do NOT reduce dose of 
glucocorticoids during the acute hospital admission. This may precipitate an adrenal crisis 
OR May exacerbate the underlying condition for which the glucocorticoids were prescribed.
  • Glucocorticoid dose may need to be increased and/or given IV depending on reason 
for admission
  • Discuss management of glucocorticoids with the unit/doctor who prescribed the 
glucocorticoids (for underlying problem) +/- with endocrine team (for prevention of adrenal 
  supression/crisis)
  • Monitor glucose levels (particularly if steroid dose being altered) - see Inpatient 
Diabetes section
  • Weaning of glucocorticoid dose may be appropriate but this should occur in the 
longer term after recovery from the hospital admission, and under supervision of/discussion 
with the doctor/team appropriate for the underlying primary condition for which the 
glucocorticoids have been prescribed. Even if long-term glucocorticoid therapy may no 
longer be required for disease control, HPA axis suppression may persist and the patient 
may require maintenance glucocorticoid replacement therapy indefinitely.

**Check points**
• If in doubt give steroid (glucocorticoid) cover, but caution required with co-existent diabetes
• If known/suspected pituitary lesion (and adrenal insufficiency has not been excluded) or long term glucocorticoid therapy: Give steroid cover for intercurrent illnesses, labour or surgery/procedures

10 DIABETES INSIPIDUS
Deficiency of anti-diuretic hormone, (ADH) either partial or complete.

Clinical features
- Acute onset usually occurs after head injuries or after cranial surgery, particularly hypophysectomy (see Practice Points below)
- Occasionally occurs with hypothalamic - pituitary tumours and inflammatory/infiltratory disorders.
- Polyuria with dilute urine (and polydipsia if the patient is conscious)
  - in the absence of impaired renal concentrating ability e.g. diuretics, chronic pyelonephritis, hypercalcaemia, hyperglycaemia, hypokalaemia, multiple myeloma.

Most patients have an intact thirst response and, given adequate access to water, can usually maintain their hydration. Severe complications ensue when oral intake is limited. Dehydration and hypernatraemia may develop rapidly, followed by hypotension and then convulsions and coma.

Investigations
- Electrolytes and osmolality of both serum and urine
- BSL, creatinine, calcium, protein, albumin
- Pituitary function assessment if not known.

Therapy
- Rehydration, usually intravenously with hypotonic saline or glucose/saline
- Avoid overhydration as this will exacerbate polyuria.
- Once rehydrated, replace fluid losses (e.g. urine output less 20%) with glucose/saline intravenously, but be careful to avoid overhydration.
- If severe polyuria persists, e.g. ≥400mls/hr, ring the Consultant Endocrinologist to discuss use of vasopressin or DDAVP treatment

Practice Points
- Diabetes Insipidus is often over-diagnosed in patients who have other reasons for polyuria.
- The essential diagnostic criterion is polyuria and a dilute urine in the presence of elevated plasma osmolality.
- After head injury or intracranial surgery, there is often an initial outpouring of ADH with
water retention and therefore fluids should be restricted initially. When this ADH wears off (after approx 24 hours), the resultant polyuria (excretion of previously retained water) may be confused with the polyuria of ADH deficiency.

- Therefore, if serum osmolality is low or normal at this time, then initial management should be to restrict fluid input and observe the response in urine output.
- Diabetes insipidus should only be considered if the patient remains polyuric in the presence of a serum osmolality greater than 300 mOsm/kg.
- Remember that most cases of diabetes insipidus are transient and can usually be managed with fluid replacement only. Vasopressin is rarely needed.
- Use Vasopressin when fluid balance is difficult to achieve because of very high output, or if DI is prolonged

- **If Vasopressin is considered necessary**
  - Use DDAVP (Minirin) (1 mcg) by subcut. or IM route, (or Aqueous Pitressin [5 units])
  - Use a single dose initially, waiting to see if polyuria recurs before giving repeat doses. Give DDAVP 12th hourly if required and initial response has been satisfactory
  - Reduce fluid input after administration of DDAVP in anticipation of response (reduction in urine output).
  - Monitor serum electrolytes and osmolality closely as sensitivity to DDAVP varies, and some patients may develop hyponatraemia after only one dose.
  - If long term treatment is needed use oral or intranasal DDAVP.

### 11 PITUITARY APOPLEXY

An uncommon clinical syndrome:

**Aetiology**

- Sudden haemorrhage/infarction of the pituitary gland
- Most often:
  - Pre-existing pituitary adenoma involved (but might be previously undiagnosed) or
  - Post partum state
  - An apparently normal gland may be afflicted

**Clinical Presentation**

- acute and dramatic with rapidly developing neurological deficits, coma and death or
- subacute with symptoms evolving over days to weeks
- headache, most common, approx 75% visual deficits,
- ophthalmoplegia and
- altered mental status
Diagnosis:
Can mimic a number of other intracranial processes. The two most critical alternative diagnoses to consider are:
- Subarachnoid haemorrhage
- Bacterial meningitis

Established by MRI or CT imaging of the pituitary gland:
- Exclusion of haemorrhage or
- Demonstration of the sellar mass/infarct

Management
Includes both medical and surgical management.

Medical:
- Immediate administration of corticosteroids (hydrocortisone 100mg IV every 6 hours).
- Electrolytes and hydration status must be monitored closely for evidence of diabetes insipidus.
- Replacement of other hormones is not usually required in the acute setting, but hypopituitarism often develops later.

Neurosurgical:
- Decompression via a transphenoidal approach is the definitive therapy, but is not always required.

12. THE VOMITING PATIENT WITH TYPE 1 DIABETES

1. Exclude Diabetic Ketoacidosis – if present then manage according to DKA protocol.

   When vomiting occurs in a patient with type 1 diabetes, it should always be considered a sign of insulin deficiency until proven otherwise. Blood or urine ketones must be tested.

2. Identify cause and treat

3. Rehydrate, give anti-emetics, consider insulin-glucose infusion

4. Manage glycaemia: a) correct hyperglycaemia either by subcutaneous (rapid-acting
insulin (see Sick Day Management Guidelines below for insulin doses) or by insulin-glucose infusion if significant hyperglycaemia (e.g. >20 mmol/L); b) continue usual basal insulin

5. If vomiting persists for >4 hrs, then commence variable dose intravenous insulin-glucose infusion (intravenous insulin adjustment algorithm – WSHR-2733) and admit.

6. If well enough for discharge: Ensure patient has Sick Day Management Plan (see below), and follow-up with GP and/or endocrinologist

Sick Day management and Type 1 diabetes (from Health Pathways)

The goal of sick day management is to prevent development of ketoacidosis. Ketoacidosis develops with insulin deficiency as a consequence of one or more of the following:

- Insulin omission
- A concurrent illness where insulin requirements are increased above normal
- Insulin pump line occlusion preventing normal insulin delivery
- Following glucagon administration particularly with subsequent insulin omission due to hypoglycemia

1. Check for signs and symptoms of ketosis and dehydration.

2. Make sure the patient has:
   - a current sick day plan, and they understand it
   - a blood ketone monitor or access to in-date ketone strips, and
   - someone at home to assist with monitoring if needed

Practice Point!

When vomiting occurs in a patient with diabetes, it should always be considered a sign of insulin deficiency until proven otherwise. Blood or urine ketones must be tested.

If the patient is stable and can be managed as an outpatient:

1. Treat the illness:
- Check for urinary tract infection, respiratory tract infection, and gastroenteritis.
- Recommend use of Hydralyte or other rehydration solution if there is gastroenteritis. If infrequent vomiting episodes, give Maxolon intramuscular injection (IMI).

2. Treat diabetes:

- Patient needs to take glucose to maintain glycaemia while additional insulin is given. When sick, it can be taken in any form tolerated e.g., lemonade, rehydration solutions, cordials.
- **Insulin must never be omitted in a patient with Type 1 diabetes, particularly when sick.** Additional insulin is required over normal daily requirements.
- Patients should have access to a written sick day management plan detailing adjustment of insulin dosage as per blood glucose level (BGL) and ketone level.
- Two hourly BGL, and ketone monitoring if one or both of the following until blood ketones <1.5

- Fluid intake:
  - If BGL < 15, 125 to 250 mL/hour of sweetened fluid.
  - If BGL > 15, 125 to 250 mL/hour of sugar-free fluid.

3. Insulin management:
   - Insulin doses may need to be increased or decreased, depending on the illness.
   - If the BG level is above 15 mmol/L and ketones are increased, additional rapid or short-acting insulin is needed. The dose and frequency of injection will depend on the level and duration of hyperglycaemia, and the severity of ketosis.
   - If there is hyperglycaemia with negative or small amounts of ketones, an additional 5–10% of total daily dose (TDD) (or 0.05–0.1 U/kg) should be given as rapid or short-acting insulin. This may be repeated every 2–4 hours based on results of BG level monitoring;
- If there is hyperglycaemia and more marked ketonaemia or ketonuria (moderate to high), an additional 10–20% of TDD (usually not more than 0.1 U/kg) may need to be given as rapid or short-acting insulin. This dose should be repeated every 2–4 hours; based on frequent BG levels and ketone results.

- People on continuous subcutaneous insulin infusion (CSII) use only rapid-acting insulin; therefore, DKA can develop rapidly. Episodes of hyperglycaemia must be taken seriously, especially if associated with positive urine or blood ketones (or both). Correction doses should be given through the pump if there are no ketones or with a syringe or pen injection if ketones are present.

- **Maintain hydration:**
  
  - Hyperglycaemia, fever, excessive glycosuria and ketonuria increase fluid losses.
  
  - Elevated levels of ketones, whether associated with low BG (starvation) or high BG (insulin deficiency), contribute to nausea and vomiting, leading to decreased food and fluid intake, further elevated levels of ketones, and dehydration and ketoacidosis.
  
  - Liquids for hydration should contain salt and water and not just plain water if there are ongoing losses due to vomiting or diarrhoea.
  
  - In young children with diabetes, intravenous (IV) fluids may be required if nausea, vomiting or diarrhoea are persistent.
  
  - When vomiting occurs in a person with diabetes, it should always be considered a sign of insulin deficiency until proven otherwise.

- **Treat the underlying illness:**
  
  - The underlying illness should be treated as it would be for a person without diabetes.
<table>
<thead>
<tr>
<th>Blood glucose level (mmol/L)</th>
<th>Ketones – blood (mmol/L)* or urine</th>
<th>Supplemental insulin dose (can be given up to 2 hourly)</th>
<th>Timing of review</th>
<th>Fluid intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4.0</td>
<td>&lt;1.0 Negative</td>
<td>Insulin dose reduction may be required. Consider mini dose glucagon to prevent hypoglycaemia if vomiting, diarrhoea or reduced carbohydrate intake.</td>
<td>Check every 20–30 minutes until BGL &gt;4. Supervised medical care required if ketones remain positive and BGL remains low</td>
<td>Take sweetened fluids or quick-acting carbohydrate (or both); hospital admission for IV fluids may be needed if BGL cannot be raised</td>
</tr>
<tr>
<td></td>
<td>≥1.0 Positive</td>
<td>Priority is to increase BGL with fluid and carbohydrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–8</td>
<td>&lt;1.0 Negative/trace</td>
<td>No change to insulin</td>
<td>Two hourly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0–1.4 Small</td>
<td>No change to insulin. Ketones indicate carbohydrate and insulin deficiency.</td>
<td>Two hourly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;1.5 Moderate/Large</td>
<td>5% supplemental insulin may be required</td>
<td>Two hourly</td>
<td></td>
</tr>
<tr>
<td>8–15</td>
<td>&lt;1.0 Negative/trace</td>
<td>May fall without extra insulin. If persistently elevated, consider 5% supplemental insulin.</td>
<td>Two hourly</td>
<td>Sweetened fluids recommended</td>
</tr>
<tr>
<td></td>
<td>1.0–1.4 Small</td>
<td>If persistently elevated ketones, consider 5–10% supplemental insulin</td>
<td>Two hourly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;1.5 Moderate/large</td>
<td>10% supplemental insulin dose</td>
<td>Hourly</td>
<td></td>
</tr>
<tr>
<td>&gt;15</td>
<td>&lt;1.0 Negative/trace</td>
<td>5–10% supplemental insulin dose</td>
<td>Hourly</td>
<td>Unsweetened fluids recommended</td>
</tr>
<tr>
<td></td>
<td>1.0–1.4 Small</td>
<td>10–15% supplemental insulin dose</td>
<td>Hourly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;1.5 Moderate/large</td>
<td>15–20% supplemental insulin dose</td>
<td>Hourly</td>
<td></td>
</tr>
</tbody>
</table>

BGL, blood glucose level; IV, intravenous

* blood 3β-hydroxybutyrate

* Refers to percentage of total daily insulin dosage given as rapid or fast-acting supplemental insulin dose. Exercise caution with supplemental insulin doses in the presence of BGL <8 mmol/L – advise increasing sweetened fluid intake first.

From National Evidence based Clinical Care Guidelines for Type I diabetes for children, adolescents and Adults, 2011


Ketone monitoring
13 INSULIN PUMPS – troubleshooting guidelines.

Insulin pump therapy (also known as CSII – continuous subcutaneous insulin infusion)

Insulin pumps are commonly prescribed for people with type I diabetes with 20% aged between 15 and 40 on IPT. Insulin pumps contain only rapid acting insulin (insulin-aspart [Novorapid], insulin - lispro [Humalog] or insulin- glulisine [Apidra]). Insulin is constantly infused at pre-programmed rates according to time of day and delivered automatically via a cannula placed in the subcutaneous tissue. The cannula should be routinely changed every three days to prevent line occlusion, or if line occlusion is suspected (see below). In addition the pump delivers bolus insulin based on blood sugar level and carbohydrate intake and this is manually delivered by the user. With continuous use there is a small reservoir of rapid acting insulin in the subcutaneous tissue. If line occlusion or pump disconnection or failure occurs this reservoir is exhausted in 2 – 4 hours and hyperglycemia and ketosis develop quickly as there is no long acting insulin on board. Ketosis which occurs with pump line occlusion rapidly responds to restoration of insulin delivery. The following steps should be followed.

Insulin pump line occlusion

Should be suspected:

- if a pump user has administered a correction bolus of insulin in response to a high blood glucose reading and the blood glucose does not fall in response
- at any time if ketones are >1.5 (blood testing) or moderate to large ketones on urine testing.

Line occlusion results in development of hyperglycemia with or without ketones depending on duration of line occlusion.

If suspected line occlusion and hyperglycemia with or without ketones the recommended procedure is to:

1) test blood sugar level and test for presence of ketones
2) use pump to determine recommended correction bolus dose and administer this as rapid acting insulin using either a syringe or insulin pen.
3) Replace cannula site and set up a temporary basal delivery of 150% for minimum of 4 hours depending on suspected duration of line occlusion (usually set for number of hours of suspected line occlusion to “catch up” missed insulin). At 2 hours after re-siting cannula use pump to deliver a correction bolus based on blood sugar level. If ketones are resolving and blood sugar level is falling the pump is fully operational.
4) Commence intravenous insulin dextrose infusion if
• dehydration and/or vomiting at presentation
• hyperglycemia and/or ketosis not responding within 4 hours

Insulin pump breakdown

Management of hyperglycemia with ketosis but without acidosis

Give rapid acting insulin correction dose equivalent to the patients’ usual correction. Patients who have been well educated on insulin pump therapy will have a good knowledge of what dose they require to manage high blood glucose.

The patient will also need to be given a long acting insulin dose at the same time to cover the loss of basal insulin delivery from the pump.

• Guidelines to prescription of long acting insulin to replace insulin pump basal when pump breakdown is suspected
  The long acting dose can safely be prescribed to be equivalent to the total daily basal insulin delivery on the patients pump. This may be able to be obtained from the pump even if delivery is faulty. If not, ask the patient if they know their total daily basal delivery or their total daily insulin delivery. Note: If total daily insulin dose is used then give 50% of total daily insulin as the long acting insulin dose as Lantus or Levemir.
  Lantus or levemir can be given once daily or split 50:50 into a twice daily regimen until the insulin pump can be replaced. Ensure the patient has supplies of long acting insulin at home before discharge. If not arrange script or supply of either Levemir or Lantus. The patient will have rapid acting insulin to use for meals as this is normally used in the insulin pump.

• Rapid acting insulin should be set to the patients existing bolus ratios for food and correction of high sugars.

• Patients are to contact
  o their usual treating endocrinologist or diabetes educator in usual business hours
  o The insulin pump supplier to organise a replacement if pump still under warranty (< 4 years from purchase)

Management of hyperglycemia with ketoacidosis due to insulin pump breakdown or line occlusion

Commence insulin infusion as per RMO handbook DKA protocol.

• Commence long acting insulin Levemir or Lantus in a twice daily regimen, concurrently with insulin infusion. Prescribe as per Guidelines to prescription of long acting insulin to replace insulin pump basal when pump breakdown is suspected (above). This will allow rapid return to basal bolus insulin therapy on correction of acidosis and facilitate early discharge from hospital.
• **Teaching point:** Ketoacidosis resulting from pump failure or line occlusion, *in the absence of intercurrent illness*, corrects rapidly on restoration of insulin delivery. Insulin dextrose infusion can be ceased once ketosis resolved and patient has been given a meal bolus of rapid acting insulin with two hour overlap of insulin dextrose infusion.