DIABETIC KETOACIDOSIS: MANAGEMENT

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- Diabetes ketoacidosis is a potentially life threatening disorder. Management requires intensive monitoring of clinical and biochemical parameters and careful replacement of fluid, electrolyte and insulin deficits.
- Resuscitation may be required, 1-2 boluses of 10mL/kg 0.9% Saline. Calculate initial fluid rate to give maintenance fluid volume and correct fluid and electrolyte deficits over 48 hours.
- Commence KCl replacement at a rate of 5mmol/kg/day when resuscitation has been completed.
- The starting insulin dose is **0.1 Units/kg/hour and this dose should continue to be used until acidosis improves, HCO_3 > 12-15mmol/L**. Sometimes a higher dose may be required or in special circumstances this dose may be lower eg. very young patients or known sensitivity to insulin. The aim is to produce a fall in blood glucose of 4 – 5 mmol/L per hour. Adjustments to the glucose concentration of replacement fluids will be required if plasma glucose is falling rapidly and/or when glucose <15mmol/L.
- When acidosis has improved, an insulin adjustment algorithm is provided to help maintain plasma **glucose within range 5 – 10mmol/L**.
- Hypoglycaemia, electrolyte imbalance and cerebral oedema are all potential complications of therapy that require close surveillance and management if present.

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

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Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) may:

- be the initial presentation of Type I Diabetes Mellitus
- recur if insulin is omitted (recurrent DKA in adolescence is almost always due to insulin omission)
- occur as a result of an intercurrent illness
- can also occur in Type 2 Diabetes

Clinical features

- moderate - severe dehydration
- decreased perfusion or shock (rapid pulse rate, low blood pressure, poor peripheral circulation, mottling and peripheral cyanosis)
- frequent vomiting
- continuing polyuria despite the dehydration
- weight loss due to fluid loss and loss of muscle and fat
- flushed cheeks due to the ketosis
- acetone detected on the breath
- hyperventilation of DKA (Kussmaul respiration), characterised by high respiratory rate and large tidal volume giving a sighing quality. This is due to acidosis.
- disordered sensorium (disoriented, drowsy, or, rarely, comatose)

Management of DKA

See also "Algorithm for the Management of Diabetic Ketoacidosis" (Appendix 1)

- When the diagnosis is confirmed outside a hospital, a 0.9% saline infusion (see below: 'Rehydration') should be started and insulin therapy initiated upon arrival at the hospital. Expert advice should be sought. Retrieval to an appropriate centre should be arranged
- Close clinical and biochemical monitoring and individualisation of therapy is essential.
- Management in PICU is essential for severe DKA or if hypernatraemic and preferable for milder DKA in young children or if there are associated problems.
- Consider a possible precipitant for DKA, e.g. occult infection
- Cerebral oedema is an ever-present risk of diabetic ketoacidosis and can occur despite careful attention to rate of rehydration, choice of fluids and attention to electrolyte management.

Criteria for PICU admission

(Note: these are not absolute criteria and can be individually negotiated)

- Severe DKA: pH <7.1
- Moderate DKA pH 7.15 – 7.25 with severe hypo - or hypernatremia (corrected plasma sodium <130 or >160mmol/L), or severe hypo - or hyperkalemia (plasma potassium <3.0 or >5.5mmol/L)
- Any patient with DKA and neurologic or hemodynamic compromise
- age <2years new onset diabetes with DKA

Resuscitation

- If **signs of shock** (i.e. hypotension, severe peripheral shut-down, oliguria) are present, resuscitate with boluses of 10mL/kg of 0.9% saline. It is rare that more than 1 or 2 boluses are required. Unless there is continuing shock/hypovolemia, repeated boluses should be avoided as this may increase the risk of cerebral oedema. Remember that decreased peripheral perfusion is contributed to by acidosis and will only correct gradually as the acidosis is reversed.
- **In shock:** oxygen by face mask should be given.

Laboratory measurements

- Baseline blood glucose, electrolytes, calcium, phosphate, venous pH status, full blood count, urea and creatinine, triglycerides.
- micro-urine for culture and sensitivity, urine test for ketones,
- investigation for infection if indicated
- Hourly blood glucose measurement
- 2 – 4 hourly electrolytes and venous pH, depending on severity and progress (Insert a sampling cannula if possible)

Clinical observations

- Hourly pulse rate, respiratory rate, blood pressure, neurological observations.
- Hourly blood glucose measurement while on an insulin infusion.
- Accurate fluid balance (an indwelling catheter may be required).
- 2 – 4 hourly temperature
- Test all urine for ketones until negative.
- Reassess fluid status every few hours. Continuing polyuria may worsen the dehydration if a positive fluid balance is not being achieved.

The patient initially should be "**Nil by Mouth**" except for ice to suck.

Rehydration

Dehydration is frequently in the order of 7.5 – 10% in significant ketoacidosis.

- Give maintenance fluid volumes plus calculated replacement volume minus fluid already given.
- **Initial rehydration** fluid should be 0.9% saline for up to 4 – 6hours.
  Potassium chloride (KCl) should be added at the commencement of rehydration *unless* the patient is known to have renal failure. In certain situations potassium phosphate may be warranted – consult with an Endocrinologist on-call or PICU Intensivist.
- Calculate initial fluid rate (formula below) to correct fluid and electrolyte deficits over 48 hours:

$$\textbf{Hourly rate} = \frac{(48 \times \text{hourly maintenance requirement}) + \text{deficit} - \text{all fluid already given}}{48}$$

Example:

A 20kg child is 10% dehydrated, has already received 20mL/kg saline

• 10% x 20kg	=	2000mL deficit
• **plus** 60mL x 20kg	=	1200mL maintenance each 24hr
	=	1200mL 4400mL
• **minus** 20kg x 20mL	=	400mL resus fluid 4000mL over 48 hrs
	=	83mL/hr

Note: If the corrected serum sodium value is in the hypernatremic range (>150mmol/L), even slower rehydration may be considered (i.e. replace calculated deficit over 72 hours)

- Regular reassessment of fluid balance is required.
  If there are ongoing urine losses due to osmotic diuresis and the metabolic status of the patient is not improving, it may be necessary to part replace these so that positive fluid balances are achieved.

Electrolyte replacement

Sodium

- Sodium (Na) replacement is individualised on the basis of biochemical monitoring. The measured serum sodium concentration is lowered by the dilutional effect of the coexistent hyperglycaemia. Coexistent hyperlipidaemia may also falsely lower the serum sodium measurements, depending on the method used. An approximate corrected sodium can be calculated as follows:

Calculate the corrected serum sodium and serum osmolality and anion gap

(all values in mmol/L)

1. **Corrected sodium** = measured sodium + 0.3 x (glucose – 5.5)
2. **Serum osmolality** = 1.85 x (Na + K) + glucose + urea (normal 270-295)
3. **Anion gap** = [(Na + K) – (HCO_3 + Cl)] (normal =16)

- If corrected sodium is greater than 150mmol/L, a hypernatraemic as well as an independent glucose hyper osmolar state exists and correction of the dehydration and electrolyte imbalance over 48-72 hours is advocated to minimise the risk of cerebral oedema. Consider using half normal saline after consultation with an Endocrinologist on-call if the corrected Na continues to rise.
- If corrected sodium remains <140mmol/L, continue rehydration with 0.9% saline and slow the rate of rehydration if the corrected Na continues to fall. Consider 3% saline therapy if signs of raised intracranial pressure after consultation with an Endocrinologist on-call.
- Hyponatraemia during treatment usually reflects over-zealous volume correction and insufficient electrolyte replacement.

Potassium

- Commence potassium (K) replacement as soon as resuscitation is completed and prior to commencing the insulin infusion.
- If renal failure in the severely dehydrated child is suspected, **withhold potassium** until electrolytes are available and an indwelling catheter is inserted.
- At presentation serum potassium may be normal, low or high.
  - **Even with normal or high serum potassium levels there is always a total body deficit of potassium**.
  - Beware of the patient with low or low-normal serum potassium. In the face of acidosis this indicates *severe* potassium depletion.
- Calculate required potassium replacement = 5mmol/kg/day (= 0.2mmol/kg/hour)

Example

20kg child with DKA

5mmol x 20kg = 100mmol over 24 hrs = 1mmol/hr

- Start by adding 20mmol potassium per 500mL bag.
- Check serum potassium two hours later and then 4 hourly. (Monitor hourly if persistent hypo- or hypernatremia)
- More potassium may be given (with continuous ECG monitoring) in the face of hypokalaemia. (may need to increase to 30 – 40mmol per 500mL bag if patient remains hypokalemic with treatment)
- Potassium phosphate *may* be used with potassium chloride (consider if using >30mmol per 500mL bag and after consultation with an Intensivist or Endocrinologist on-call). Give potassium replacement as:
  - ½ potassium dihydrogen phosphate and ½ potassium chloride
  - **Note**: If phosphate is used, check calcium 4th hourly

Bicarbonate

- Even with optimal therapy, serum bicarbonate only gradually normalizes over 12 to 24 hours (often lagging behind improvement in pH) and **in general bicarbonate therapy is not required**.
- Bicarbonate therapy may be considered after consultation in the severely shocked patient with severe acidosis (i.e. arterial pH <7.0 and/or HCO_3 <5mmol/L).
  - Dose 1-2 mmol/kg over 60 min - **always discuss with an Intensivist and Endocrinologist** if considering bicarbonate therapy.
  - Monitor venous pH hourly
  - Cardiac monitoring is required; hypokalaemia and exacerbation of hypernatraemia are risks.

Insulin infusion

- The starting insulin dose is **0.1 Units/kg/hour and this dose should continue to be used until acidosis improves; HCO_3 > 12-15mmol/L**. Sometimes a higher dose may be required or in special circumstances this dose may be lower e.g. very young patients or known sensitivity to insulin.
- Record the infusion rate on the Insulin Infusion Chart (Go to Forms > Endocrinology > Insulin Infusion Chart: http://intranet.kids/o/forms/endocrinology/insulin_infusion_chart.pdf)
- When acidosis has improved (bicarbonate 12 – 15mmol/L) **and** the child has been stabilised for 4 – 6 hours use the Insulin Infusion for Diabetic Ketoacidosis – Adjustment Algorithm (Table 2, page 13)
- If acidosis is not improving or getting worse after 2 hours, and in particular if the starting dose was less than 0.1units/kg, then the insulin dose needs to be increased.

Preparation of infusion

50 units of soluble insulin (Actrapid or Humulin R) are added to 500mL of normal saline to make an **insulin concentration of 0.1 unit per mL**. (10mL solution will contain 1 unit of insulin).

Starting insulin dose

- Usually 0.1 Units/kg/hour

Example: Using the above concentration for a 20kg child start at 0.1units/kg/hr = 20mL/hr

- In special circumstances the starting dose may be lower e.g. very young patients or known sensitivity to insulin.
- The starting rate will be specified by the Endocrinology team.

Intravenous fluids

- Patient will also be receiving IV replacement and maintenance fluids. Initially this will be normal saline (with added potassium).
- Once the blood glucose level (BGL) falls below 15mmol/L, glucose containing IV fluids need to be used. In the first 4 – 6hours use normal saline made up to 5% glucose. After 4 – 6hours of treatment this can be changed to N/2 & 2.5% made up to 5% Glucose (with added potassium). See Table 1 for how to increase the concentration of glucose in IV fluids.

Correction of acidosis requires adequate insulin and glucose. In most cases glucose concentration should be increased to 7.5% or 10% if needed before reducing the rate of insulin infusion below 0.1units/kg/hour (or the otherwise specified starting rate). See Table 1 for how to increase the concentration of glucose in IV fluids. Call the Endocrinologist / Intensivist on-call if acidosis is not improving.

Blood Glucose Targets

- The aim is to have BGL fall at a rate of approximately 4mmol/L each hour. Greater fall than this is inevitable early in therapy (during first 2 hours) due to fluid resuscitation. In the later stages of treatment aim to maintain a **BGL of 5 – 10mmol/L** until subcutaneous insulin is commenced.
- During the initial hyperglycaemic phase (when BGL >15mmol/L), if BGL is falling at more than 4 – 5mmol/hr, the first step is to increase the glucose concentration of the fluids (rather than increasing the fluid rate or decreasing the insulin rate). See Table 1. This does **not** apply to the first 2 hours of treatment as the BGL may fall more quickly if fluid resuscitation has been given.

Cerebral Oedema

- This can be a sudden and unpredictable complication of the therapy of diabetic ketoacidosis which occurs in the first 24 hours of treatment.
- more common in patients:
  - < 5 years old
  - severely dehydrated
  - severe acidosis (with very low CO_2)
  - hyperosmolar state or hyponatraemia, especially if it fails to correct with treatment

Recognition

- headache, changes in mental status can be early signs of evolving cerebral oedema
- papilledema and Cushing's triad (hypertension, bradycardia, irregular respirations) **late signs consistent with impending herniation**
- beware of patients with hyper- or hyponatremia. ***Cerebral oedema is more likely to occur in those patients where corrected serum sodium falls as serum glucose decreases. (always calculate corrected sodium and osmolality)***
- **Cerebral oedema is also more likely if low arterial CO_2**
- If suspected, treat immediately with mannitol (see Management below) and *transfer* to an intensive care facility.

Management

- Airway, Breathing, Circulation
- Elevate head of bed
- Reduce fluid rate by ⅓, consider Hartmann's or Lactate Ringers, do not use hypotonic saline solutions

- Mannitol or hypertonic saline can be used
  - Mannitol 0.5 – 1g/kg by IV infusion over 20 min
  - 3% hypertonic saline 5mL/kg over 20 min
- Consider intubation if GCS <8, careful to monitor pCO_2 levels and adequately ventilate to avoid changes in cerebral blood flow due to increasing pCO_2.
- Urgent head CT once patient is stable, consider neurosurgical consultation. (All patients should be monitored for signs and symptoms of raised intracranial pressure.)

PICU Discharge Criteria

- pH > 7.2 with correction of acidosis
- No severe electrolyte disturbance
- No neurologic or hemodynamic compromise

IV Insulin Infusion for Diabetic Ketoacidosis

Purpose

This algorithm is a guide to adjustment of an insulin infusion in patients with diabetic ketoacidosis (DKA). (Refer to Table 1. and Table 2). It is to be used in conjunction with the DKA Management practice guidelines (above) which also detail other essential aspects of management. A separate protocol is to be used for patients requiring peri-operative insulin infusions or other maintenance insulin infusions.

The Adjustment Algorithm (Table 2) is **ONLY** to be used when acidosis is improved (**HCO_3 > 12-15mmol/L)** and **ONLY** after 4 – 6 hours of stabilisation

Insulin dose and adjustment

- The treating medical doctor will prescribe the insulin infusion on the Insulin Infusion Chart and **signs** "*to be adjusted by nursing staff according to insulin infusion algorithm*".
- When an adjustment is made to the rate of the insulin infusion it should be checked and signed for by *two* (2) nurses in the corresponding time slot on the Insulin Infusion Chart. In the Emergency Department this would be a doctor and a nurse.
- A working example is given on page 14.
- If no adjustment is required only one nurse's signature is required in the corresponding time slot on the Insulin Infusion Chart.

Monitoring

- Hourly BGLs required initially.
- Change to every 30 minutes as directed in the algorithm (Table 2) for BGL <4mmol/L or BGL falling rapidly with BGL 5 – 10mmol/L
- BGL can be done on blood gas analysis if a blood gas is due, or using the blood glucose meter.

Management of Hypoglycaemia

Hypoglycaemia becomes a possibility in the later stages of correction.

Mild hypoglycaemia

- BGL 3 – 4mmol/L
- requires cessation of insulin infusion
- Confirm that glucose containing IV fluids are running.
- Recheck BGL after 30 minutes.

Moderate or severe hypoglycaemia

- BGL < 3mmol/L, or symptomatic (Refer to Hypoglycaemia protocol)
- requires cessation of insulin infusion and an IV bolus of 2mL/kg of 10% glucose as directed by the algorithm. The Endocrinology Registrar must then be informed.
- Recheck BGL after 15 minutes.

Once BGL > 5mmol/L, resume insulin infusion at previous rate LESS 40%

Other situations

- For any situations not covered by the algorithm below, if the response to the infusion is unusual or unexpected, or if there is persistent hypo- or hyperglycaemia, call the Endocrinology Registrar.

Management of the ketoacidosis recovery phase

When to start oral fluid:

- The patient is kept Nil by Mouth, except for ice to suck, until metabolically stable (i.e. blood glucose <12mmol/L, pH >7.30 and HCO_3 >15mmol/L). Low joule or low calorie fluids can then be given by mouth to see if they are tolerated.

Use of insulin infusion to cover meals and snacks:

- It is useful to maintain the insulin infusion until the child has had at least one meal.
- For snacks the basal infusion rate is doubled at the start of the snack and continued for 30 minutes afterwards, before returning to the basal rate.
- For main meals the basal infusion rate should be doubled at the start of the meal and continued for 60 minutes after the meal, before returning to the basal rate.

When to stop the infusion:

- It is most convenient to change to subcutaneous insulin just before meal time.
- Subcutaneous insulin is given before the meal and insulin infusion continued throughout the meal for a total of 90 minutes at current rate (not doubled) after the subcutaneous insulin injection; then ceased.
- The half-life of intravenous insulin is only 4.5 minutes, so it is important that the subcutaneous insulin is given before stopping the infusion.

Subcutaneous insulin regimen:

- Total daily dose required is usually around 1 unit/kg body weight/day but this may need to be adjusted on the basis of previous insulin dosages and serial blood glucose levels. Patients should resume a combination of short and long-acting insulin based on their previous regimen or, for newly diagnosed patients, the regimen determined by the Diabetes Consultant.

Table 1

How to increase the concentration of glucose in commonly used intravenous fluids

N = Normal Saline (0.9%) **N/2** = half Normal Saline (0.45%) **N/4** = quarter Normal Saline (0.225%)

Fluid Type (500mL bag)	How much 50% Glucose to add	Total Glucose Concentration
N	50mL	5%
N	75mL	7.5%
N	100mL	10%
N	125mL	12.5%
N/2 + 2.5% Glucose	25mL	5%
N/2 + 2.5% Glucose	50mL	7.5%
N/2 + 2.5% Glucose	75mL	10%
N/2 + 2.5% Glucose	100mL	12.5%
N/4 + 3.75% Glucose	12.5mL	5%
N/4 + 3.75% Glucose	37.5mL	7.5%
N/4 + 3.75% Glucose	62.5mL	10%
N/4 + 3.75% Glucose	87.5mL	12.5%

Table 2: IV Insulin infusion for Diabetic Ketoacidosis - Adjustment Algorithm

Only to be used when acidosis improved (bicarbonate 12 – 15mmol/L) and ONLY after 4 – 6 hours of stabilisation

(E.g. for a 20kg child start at 0.1unit/kg/hr = 20mL/hr)

The table indicates the change in insulin infusion rate from the current hourly rate according to the current BGL and rate of change of BGL in the previous hour.

Current BGL (mmol/L)	Change in BGL from last hour	No change (within 0.5mmol/L of last hour)	Falling slowly Fall of 0.6-2mmol//L/hr	Falling moderately Fall of 2-4mmol/hr	Falling quickly Fall of > 4mmol/L/hr	Rising slowly Rise of 0.6-2mmol/L/hr	Rising moderately Rise of 2-4mmol/L/hr	Rising quickly Rise of > 4mmol/L/hr
> 15mmol/L		Increase by 10%	Increase by 10%	No change	Decrease by 20%	Increase by 20%	Increase by 20%	Increase by 20%
10.1 –15mmol/L (when BGL first falls to <15 mmol/L, first step is to add glucose to IV fluids before adjusting insulin infusion)		Increase by 10%	No change	No change	Decrease by 20%	Increase by 20%	Increase by 20%	Increase by 20%
5.1 – 10mmol/L		No change	Decrease by 10%	Decrease by 20%*	Decrease by 20%*	No change	No change	Increase by 20%
4.1 – 5mmol/L		Decrease by 10%	Decrease by 20%	Decrease by 20% *	Decrease by 50%*	No change	No change	Increase by 10%
3.1 – 4mmol/L		Cease temporarily. Recheck BGL in 30 mins & recommence infusion when BGL >5mmol/L at 40%lower basal rate				Cease temporarily. Give IV glucose bolus of 2mL/kg of 10% Glucose. Recheck BGL in 30 mins & when BGL >5mmol/L recommence infusion at 40% lower rate than previous infusion rate.	Recheck BGL in 30 minutes	
< 3mmol/L or symptomatic hypoglycemia		Cease temporarily Give IV glucose bolus 2mL/kg of 10% Glucose. Recheck BGL in 15 mins & when BGL >5mmol/L recommence infusion at 40% lower rate than previous infusion rate						

*Recheck BGL in 30 mins

NB: Call the Endocrinologist/Intensivist on call if acidosis is not improving

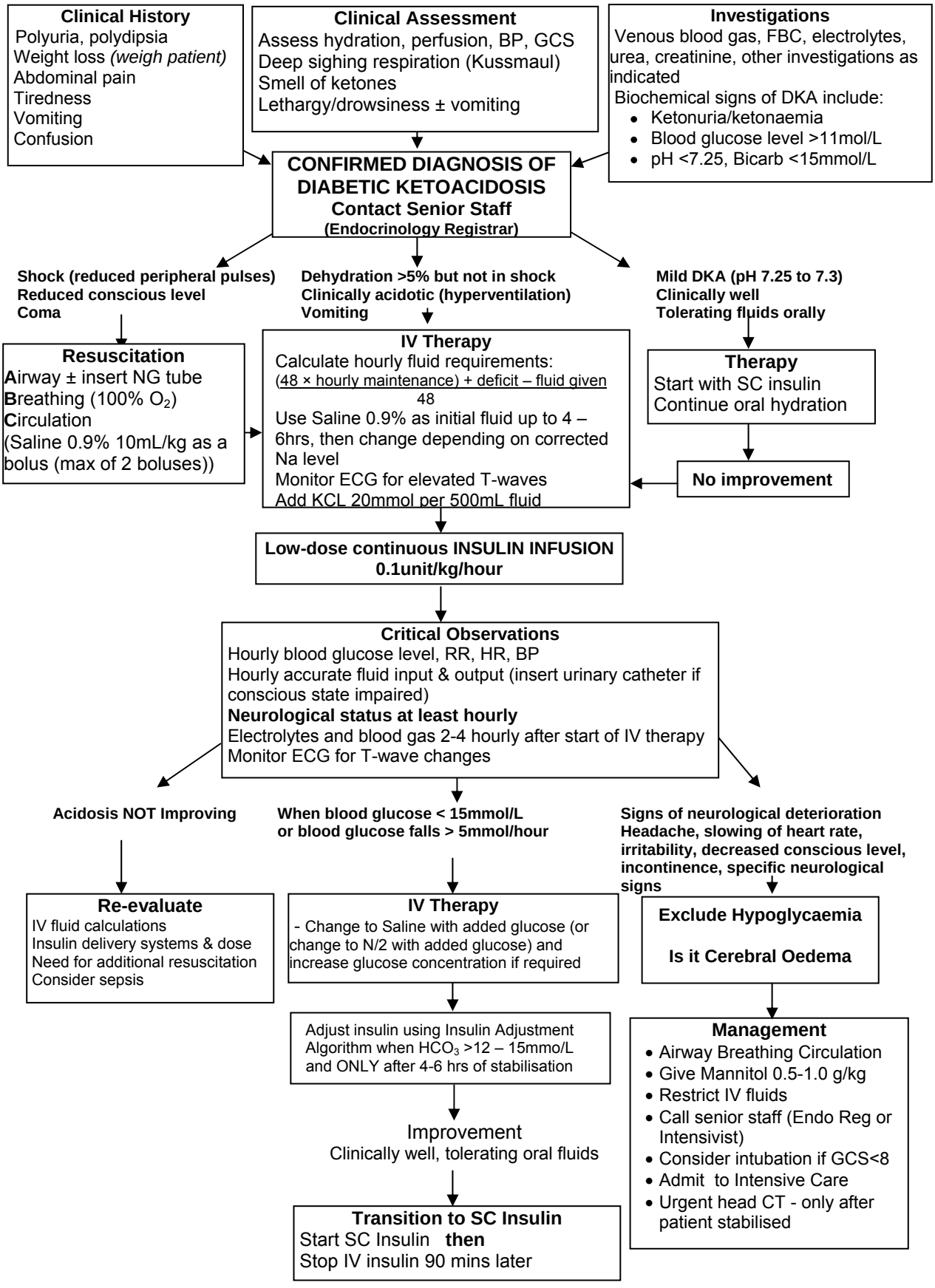
Working Example

The following table is an example of the type of insulin infusion adjustment which should be made using the DKA or Peri-operative insulin infusion adjustment algorithms. For each adjustment please refer to the algorithm.

Time	Rate of insulin infusion (mL/hour) (0.1unit insulin per 1mL)	BGL mmol/L	Urine Ketones	Comments/Rationale (Round up or down to the nearest whole number)
12MN	20mL/hour	20.6	moderate	Infusion commenced
1am	↑ to 22mL/hour	18.9	moderate	BGL falling slowly (by <2mmol/hr) therefore ↑infusion by 10% (10% of 20mL = 2mL)
2am	22mL/hour	15.2	small	BGL falling moderately (by 2-4 mmol/hr). Leave at same rate.
3am	22mL/hour	13.4	trace	BGL falling slowly. Leave at same rate. (Remember to change IV fluids from N.Saline to N/2 + 5% glucose when BGL drops below 15mmol/L.)
4am	22mL/hour	11.4	trace	Same rate
5am	↓ to 20mL/hour	9.8	negative	BGL falling slowly. Decrease by 10% (10% of 22mL= 2mL)
6am	20mL/hour	9.5		Same rate
7am	↓ to 18mL/hour	8.2		BGL falling slowly. Decrease by 10% (10% of 20mL = 2mL)
8am	↓ to 14mL/hour	6.1		BGL falling moderately. Decrease by 20% (20% of 18mL = 4mL)
9am	Cease temporarily	4.0		Cease temporarily and recheck BGL after 30 minutes. Only restart infusion when BGL >5mmol/L at 40% lower basal rate
9.30am	Restart infusion at 8mL/hour	6.9		Restart infusion when BGL >5mmol/L at 40% lower basal rate
10.30am	8mL/hour	6.8		Same rate
11.30am	8mL/hour	7.3		Same rate
12.30pm	8mL/hour	8.1		Same rate
1.30pm	8mL/hour	7.8		Same rate

Appendix 1: Algorithm for the Management of DKA

IMMEDIATE ASSESSMENT



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