South Australian Paediatric Clinical Practice Guidelines

Diabetic Ketoacidosis (DKA) in Children and Adolescents

Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:
The aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant women. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Cultural safety enhances clinical safety.

To secure the best health outcomes, clinicians must provide a culturally safe health care experience for Aboriginal children, young people and their families. Aboriginal children are born into strong kinship structures where roles and responsibilities are integral and woven into the social fabric of Aboriginal societies.

Australian Aboriginal culture is the oldest living culture in the world, yet Aboriginal people currently experience the poorest health outcomes when compared to non-Aboriginal Australians.

It remains a national disgrace that Australia has one of the highest youth suicide rates in the world. The over representation of Aboriginal children and young people in out of home care and juvenile detention and justice system is intolerable.

The cumulative effects of forced removal of Aboriginal children, poverty, exposure to violence, historical and transgenerational trauma, the ongoing effects of past and present systemic racism, culturally unsafe and discriminatory health services are all major contributors to the disparities in Aboriginal health outcomes.

Clinicians can secure positive long term health and wellbeing outcomes by making well informed clinical decisions based on cultural considerations.

The term 'Aboriginal' is used to refer to people who identify as Aboriginal, Torres Strait Islanders, or both Aboriginal and Torres Strait Islander. This is done because the people indigenous to South Australia are Aboriginal and we respect that many Aboriginal people prefer the term 'Aboriginal'. We also acknowledge and respect that many Aboriginal South Australians prefer to be known by their specific language group(s).

Purpose and Scope of PCPG

The Diabetic Ketoacidosis (DKA) Guideline is primarily aimed at medical staff working in any of primary care, local, regional, general or tertiary hospitals. It may however assist the care provided by other clinicians such as nurses. The information is current at the time of publication and provides a minimum standard for the assessment (including investigations) and management of Diabetic Ketoacidosis; it does not replace or remove clinical judgement or the professional care and duty necessary for each specific case.

The management of DKA in children is different to that in adults. Early consultation with MedSTAR or the Paediatric Endocrinologist on Call at WCH is recommended.

Retrieval/Emergency Management Flowchart

Contact MedSTAR (137 827) or the Paediatric Endocrinologist on Call

Recognition of DKA

DKA can occur in existing or new onset type 1 or type 2 diabetes

Diagnostic criteria: Glucose >11mmol/L, pH <7.3, bicarbonate <15mmol/L, ketones >3mmol/L or ketonuria

Clinical features: Polyuria, polydipsia, weight loss, dehydration, Kussmaul breathing, abdominal pain, vomiting, decreased level of consciousness

Initial management

- Assess ABCs, Vital signs: HR, RR, BP and Neurovitals: GCS and pupils
- Rapid blood glucose and ketones with point of care meter
- O_2 100% if signs of shock
- Establish IV access
- Send blood for glucose, electrolytes, venous acid/base, urea, creatinine
- Urinalysis for glucose, ketones
- Consider other investigations – if sepsis suspected
- ECG monitoring for potassium related changes

Evidence of Cerebral Oedema?
GCS <14 and/or irritability
and/or unexpected ↑BP+ ↓HR+ ↓RR

No → continue

Yes → Cerebral Oedema Management

Fluid Resuscitation

If <u>not</u> in shock: Begin rehydration with 10mL/kg 0.9% sodium chloride rehydration bolus over 60 minutes

<u>If shocked</u>: Give 20mL/kg 0.9% sodium chloride resuscitation bolus over 15 minutes and reassess

(Shock = ↑HR + prolonged capillary refill + poor peripheral pulses ± ↓BP; Shock is not just poor peripheral perfusion)

Not in shock

Calculate IV fluid requirement
Fluid deficit estimation is based on DKA severity and replaced evenly over 48hrs
Fluid requirement = Maintenance + [(Deficit – 10mL/kg rehydration bolus) / 48hrs]
Resuscitation boluses given for shock should NOT be subtracted from the deficit
For fluid calculation table see Appendix 3

Persistent signs of shock

Repeat 10mL/kg 0.9% sodium chloride resuscitation boluses until circulation restored

Do not exceed 40mL/kg without senior consultation

IV Fluids

- **Continue rehydration with 0.9% sodium chloride with 40mmol KCL per litre** (unless K >5mmol/L)
- **When blood glucose <15mmol/L** (or decreases > 5mmol/L/hr once glucose is <25mmol/L) **add 5 % glucose to rehydration fluid**

Insulin

- **Start insulin infusion at 0.05units/kg/hr after 1 hour of IV fluids**
- **DO NOT start insulin if K <2.5mmol/L <u>or</u> before KCL replacement has been started (unless hyperkalaemic)**

Dilute 50 units of regular insulin (Actrapid) in 50mls 0.9% sodium chloride for 1unit/1mL solution. Flush tubing with 5mLs of insulin solution

NEVER give IV insulin bolus

NEVER give IV sodium bicarbonate

Fluid Deficit based on DKA Severity

DKA	pH	HCO3	Fluid Deficit
Mild	7.2-7.3	10-15	5%
Moderate	7.1-7.2	5-10	7%
Severe	<7.1	<5	10%

Mild DKA may not require an insulin infusion - contact Paediatric Endocrinologist for advice

Consider Hyperosmolar Hyperglycaemic State (HHS) if:

- Glucose >33mmol/L,
- Mild acidosis/ketosis: bicarbonate >15, ketones <3
- Osmolality > 330mOsmo/L

For HHS management see Appendix 5

Cerebral Oedema Management

- **Contact MedSTAR/PICU**
- Assess and support ABCs
- Raise head of bed >30°
- If shocked give 10mL/kg 0.9% sodium chloride over 30mins, reassess and repeat x 1, if circulation not restored. Discuss with senior staff before further boluses
- Run IV fluids at 50% of rate outlined in Rehydration Table
- **Give 3% Sodium Chloride (3mL/kg) IV over 15 minutes** <u>OR</u> 20% Mannitol (0.5 - 1g/kg) IV over 15 minutes
- Start insulin infusion at 0.05units/kg/hr after 1 hour of IV fluids

Contact MedSTAR/PICU for:

- Difficult IV access
- Cerebral oedema management
- Airway management
- Ongoing fluid management

Intubation and ventilation are high risk procedures in DKA and should never be undertaken without senior consultation

Monitor and Record

Hourly: Blood glucose
Fluid input:output
HR and BP
Neuro vitals (GCS, pupils)

2-4 Hourly: Electrolytes, venous acid base

Dedicate 2nd IV line for blood sampling

Non-urgent bloods for new diagnosis: TSH, FT4, Coeliac Ab, total IgA, Islet autoantibodies: GAD and IA2

Ongoing Management Flowchart

Notify PICU and Paediatric Endocrinologist on Call

Monitoring

Hourly: Blood glucose (venous)
Fluid input:output
Vital signs
Neurological status at least hourly. If any fall in GCS - suspect cerebral oedema

2 hours after initiation of treatment, then 2 - 4 Hourly: Na, K, Cl, urea, creatinine, calcium, acid base and blood ketones (βOHB - using point of care meter)
Calculate and monitor: Corrected Na = Measured Na + [0.4 x (glucose -5.5)] mmol/L

If acidosis not improving after 2 hours of fluid and insulin therapy - re-evaluate:

- Need for further resuscitation
- Fluid balance/IV fluid calculations
- Insulin dose and delivery
- Consider sepsis

IV Fluid Therapy

Requirement = Maintenance + [(Deficit – 10mL/kg rehydration bolus)/48hrs]
Calculate fluid deficit according to degree of acidosis and correct evenly over 48hrs:
Assume a fluid deficit of 5% in mild DKA, 7% in moderate DKA and 10% in severe DKA
Resuscitation boluses given for shock, should NOT be subtracted from the deficit

Sodium chloride: Start with **0.9% sodium chloride** with added potassium
Consider changing to Plasma-Lyte 148 to reduce chloride load in severe DKA
Adjust IV fluids to promote an increase in corrected sodium

- A fall in Na_{corr} of >5mmol/L in 4-8hours suggests too much fluid replacement
- A rise in Na_{corr} of >5mmol/L in 4-8hrs suggests insufficient fluid replacement

Potassium: Add Potassium only when K < 5mmol/L
At least **40mmol/L potassium chloride** is typically required
Consider 50:50 mix of 20mmol/L potassium chloride and 20mmol/L potassium dihydrogen phosphate to reduce chloride load
Maximum recommended concentration of K in a peripheral IV is 60mmol/L
When blood glucose < 15mmol/L: Add 5% Glucose to IV fluids and continue/reduce insulin to 0.05units/kg/hr**.** If continuing insulin at 0.1units/kg/hr, add 10% glucose to IV fluids
DO NOT reduce insulin infusion below 0.05units/kg/hr, if blood ketones >1mmol/L
If blood glucose < 6mmol/L: Add more glucose to IV fluids
If blood glucose < 4mmol/L: Give 2mL/kg 10% glucose + add more glucose to IV fluids

Insulin Therapy

Start insulin infusion after 1hr of IV fluids
DO NOT start insulin if K < 2.5mmol/L or before KCL replacement has been started (unless hyperkalaemic)

IV insulin infusion dose: 0.05units/kg/hr – 0.1units/kg/hr
After the initial fall in glucose following fluid bolus, aim for gradual fall of 2-5mmol/L/hr
Do not reduce IV insulin below 0.05units/kg/hr until blood ketones <1mmol/L or pH >7.3 and bicarbonate >15
Patients with DKA are at risk of hyperchloraemic acidosis, βOHB and Anion Gap are better indicators of DKA correction than pH and bicarbonate alone*

Transfer to subcutaneous insulin when clinically well, tolerating oral fluids and blood ketones <1mmol/L
Discontinue IV insulin infusion 15-30 mins after SC rapid acting insulin injection given
Once DKA is corrected the IV insulin dose may need to be reduced to <0.05units/kg/hr

Cerebral Oedema

May be apparent at presentation or develop within the first 24 hours of treatment

Risk factors:

- Severe acidosis/ ↓pCO_2
- Severe dehydration/ ↑Urea
- Young age <5yrs
- New onset diabetes

WARNING SIGNS:

- Headache, irritability/agitation
- Onset or recurrence of vomiting
- Slowing HR, rise in BP not related to fluid resuscitation
- Decreased conscious level
- Neurological signs
- Fall in corrected sodium

If cerebral oedema suspected

↓

Exclude hypoglycaemia

↓

Cerebral Oedema Management:

- Contact Senior Staff
- Assess and support ABCs
- Initiate intensive monitoring
- **Give 3% Sodium Chloride (3mL/kg) IV over 15mins** OR 20% Mannitol (0.5 -1g/kg) IV over 15mins
- Raise head of bed > 30°
- Restrict IV fluids by 50%
- Consider cranial imaging **only** after patient stabilised

*** DKA vs Hyperchloraemic Acidosis**

	Anion Gap	βOHB
DKA	>12	>1mmol/L
Hyperchloraemic acidosis	≤12	<1mmol/L

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Abbreviations

DKA	Diabetic Ketoacidosis
HDU	High Dependency Unit
HHS	Hyperosmolar Hyperglycaemic State
MET	Medical Emergency Team
PICU	Paediatric Intensive Care Unit
SC	Subcutaneous
T1D	Type 1 diabetes
T2D	Type 2 diabetes
WCH	Women's and Children's Hospital
βOHB	β hydroxybutyrate

Introduction

DKA results from absolute or relative deficiency of insulin and the combined effects of increased levels of counter-regulatory hormones. This leads to both increased production and impaired utilisation of glucose, with resultant hyperglycaemia and hyperosmolality. Increased lipolysis and ketone body production causes ketonaemia and metabolic acidosis. Hyperglycaemia and acidosis result in an osmotic diuresis, dehydration and obligate loss of electrolytes. DKA can occur at the onset of clinical diabetes or in children with established diabetes who have either omitted insulin or had inadequate insulin therapy during illness. Children on insulin pump therapy are at increased risk of DKA, if monitoring and pump delivery failure management guidelines are not followed. As only rapid acting insulin is used in insulin pumps, interruption of insulin delivery for any reason (most commonly a blocked delivery set) rapidly leads to insulin deficiency and ketosis.

DKA can occur in existing or new onset type 1 or type 2 diabetes

The biochemical criteria for the diagnosis of DKA are:

- Hyperglycaemia - blood glucose >11mmol/L
- Metabolic acidosis - venous pH <7.3 and/or bicarbonate <15mmol/L
- Ketosis - blood ketones (βOHB)* >3.0mmo/L or moderate – large urine ketones

*Measurement of blood ketone levels with a bedside/point of care meter is a useful triage tool to rapidly confirm or exclude DKA

The severity of DKA is categorised by the degree of acidosis:

Mild:	pH 7.2 - 7.3	bicarbonate 10 -15 mmol/L
Moderate:	pH 7.1 - 7.2	bicarbonate 5 - 10 mmol/L
Severe:	pH < 7.1	bicarbonate < 5 mmol/L

IMPORTANT NOTES:

- **The management of DKA in children is different to that in adults.** Early consultation with MedSTAR or the Paediatric Endocrinologist on call at WCH is recommended.
- **Children with mild DKA**, who are alert, not clinically dehydrated and not vomiting, may tolerate oral rehydration and subcutaneous insulin therapy, even if ketones are high.
- **Blood glucose levels are generally high (>11mmol/L) in DKA, but children with known diabetes can develop DKA with normal blood glucose levels.**
- **Hyperosmolar Hyperglycaemic State (HHS)** is a hyperglycaemic emergency and is distinguished from DKA by marked hyperglycaemia (>33.3mmol/L), minimal acidosis, absent or mild ketosis and marked elevation of serum osmolality (effective osmolality >320mOsm/L). HHS occasionally occurs in paediatric patients, most often adolescents with T2D. HHS requires a different treatment approach and urgent PICU/Paediatric Endocrinology consultation (Appendix 5).

Morbidity and Mortality of Paediatric DKA

- DKA is the most common cause of diabetes related deaths in children and adolescents and **most deaths in DKA occur as a result of cerebral oedema.**
- **Cerebral oedema** typically occurs 3-12 hours after treatment is started, but can occur prior to initiation treatment or anytime during treatment. Although the aetiology of cerebral oedema is poorly understood, it is more likely to occur in patients with severe DKA and severe dehydration, therefore more often in younger children with new onset type 1 diabetes where the diagnosis has been delayed. Independent risk factors for cerebral oedema include: high serum urea and low pCO2 at presentation, a fall in serum sodium during therapy and the use of bicarbonate therapy.
- Other causes of death include hypokalaemia, aspiration pneumonia, inadequate resuscitation, unrecognised sepsis.

DKA Management Goals

> Restoration of circulating blood volume if shocked.
> Replacement of fluid and electrolyte deficit evenly over 48 hours.
> Correction of acidosis and hyperglycaemia with low dose IV insulin infusion.
> Avoidance of the complications of DKA by frequent monitoring for:
  - Cerebral oedema
  - Hypoglycaemia
  - Electrolyte abnormalities (e.g. hypokalaemia and hyperchloraemic acidosis).

Emergency Assessment

> **Assess ABCs, Vital signs (HR, RR, BP)**
  - Signs of shock?

The Advanced Paediatric Life Support definition of shock: tachycardia + prolonged central capillary refill + poor peripheral pulses ± hypotension. Note: Shock is not just poor peripheral perfusion

> **Assess Level of Consciousness -** Glasgow Coma Scale (Appendix 1).
  - Signs of cerebral oedema?

> **Confirm Diagnosis of DKA**
  - Rapid bedside blood glucose and ketone (β-hydroxybutyrate) levels with point of care meter
  - IV access
  - Obtain a venous blood sample for laboratory measurement of glucose, electrolytes, urea, creatinine, acid/base and CBE (add non-urgent tests if sufficient sample*)

> **Assess Severity of Dehydration**
  - Weigh if possible
  - Estimation of fluid deficit should be based on the degree of metabolic acidosis as clinical assessment of dehydration is unreliable in DKA.
    - Assume 5% dehydration in mild DKA
    - Assume 7% dehydration in moderate DKA
    - Assume 10% dehydration in severe DKA

> **Determine the cause (new onset diabetes, inadequate or omitted insulin, blocked insulin pump delivery set?) and exclude predisposing infection**
  - History and examination
  - Full blood count and haematocrit (Note: elevated WBC count is common in DKA and does not necessarily indicate sepsis, but fever is not part of DKA)
  - Urine microscopy and culture
  - Throat swab, blood cultures and CXR if indicated

***Non-urgent blood tests for patients with newly diagnosed diabetes**

  - TSH/FT4
  - Coeliac screen and total IgA
  - Islet autoantibodies (GAD/IA2)

Emergency Management of DKA

General Resuscitation

> **Airway:** Ensure airway patent and if child comatose, insert airway. Insert a nasogastric tube in children with reduced consciousness and vomiting

> **Breathing:** Give 100% oxygen by face mask*

> **Circulation:**

- Insert IV cannula and take blood samples
- ECG monitoring for T wave changes
- Monitor blood pressure and heart rate

**Intubation and ventilation are high risk procedures in DKA and should never be undertaken without consultation; a sudden increase in pCO2 during or following intubation may cause CSF pH to decrease and contribute to worsening of cerebral oedema.*

Initial Fluid Bolus

> **All children with mild, moderate and severe DKA who are not shocked and are felt to require IV fluids** should receive **10mL/kg of 0.9% sodium chloride** over 60 minutes as an initial rehydration bolus

> **Shocked patients should receive a 20mL/kg resuscitation bolus of 0.9% sodium chloride over 15 minutes**

- **Call for help: MedSTAR (137827) or PED, PICU or Paediatric Endocrinologist at the earliest opportunity if aggressive resuscitation required**
- Following the initial 20mL/kg bolus, the patient should be reassessed and further 10mL/kg boluses may be given until circulation restored. Do not exceed 40mL/kg of resuscitation boluses without specialist consultation.
- Whilst excessive fluid should be avoided because of the risk of cerebral oedema, in those with shock, it is important to restore circulation, as hypotension will exacerbate the risk of brain injury

Where should the patient be managed?

All children with DKA are high-dependency patients and require a high level of nursing care. All patients requiring an insulin infusion should be managed in a unit that has experienced nursing staff trained in monitoring and management, clear written DKA management guidelines and access to laboratories for frequent evaluation of biochemical variables.

In health units without these facilities, such as regional and remote health services, early consultation with MedSTAR or the Paediatric Endocrinologist on call at WCH to arrange transfer is recommended.

PICU admission is recommended for:

> Severe DKA (pH <7.10, bicarbonate <5mmol/L)
> Decreased level of consciousness
> Age < 2 years
> If 1:1 nursing cannot be provided in HDU/Paediatric Ward.

Monitoring

Successful management of DKA requires frequent and meticulous monitoring of the patient's clinical and biochemical response to treatment, so that timely adjustments to fluid and electrolyte therapy can be made.

A second venous sampling line should be inserted where possible.

MONITOR AND RECORD THE FOLLOWING:

- **Hourly vital signs:** pulse rate, respiratory rate and blood pressure
- **Hourly or more frequent neurological observations** to detect the warning signs of cerebral oedema:
  - Headache, irritability or agitation
  - Deterioration in GCS or specific neurological signs
  - Inappropriate slowing of pulse rate
  - Rising blood pressure
  - Decreased oxygen saturation/abnormal breathing pattern.
- **Hourly fluid input and output** (urinary catheterisation may be necessary if patient unconscious or in very young children with severe DKA).
- **Hourly venous blood glucose** (capillary blood glucose may be inaccurate in the presence of poor peripheral perfusion and acidosis).
- **Electrolytes, urea, creatinine, calcium and acid base** should be measured **2 hours after the initiation of treatment and then every 2-4 hours until acidosis has resolved.** Hourly electrolytes may be necessary as clinically indicated in severe cases.
- **Blood ketones (βOHB) should be measured every 2 - 4 hours until cleared.** Point of Care βOHB measurements correlate well with the reference method up to 3mmol/L, but are not accurate >5mmol/L.
- **ECG monitoring** may be helpful to detect hyperkalaemia or hypokalaemia:
  - ECG signs of hyperkalaemia: Tall, peaked and symmetrical T waves with shortening of the QT interval.
  - ECG signs of hypokalaemia: Prolongation of the PR interval, T wave flattening and inversion, ST depression, prominent U waves and apparent long QT interval (due to fusion of T and U waves).

Calculations

Corrected Na = Measured Na + [0.4 x (Glucose – 5.5)] mmol/L

Anion gap = (Na + K) – (Cl + HCO_3) Normal: less than 17 mmol/L

Effective osmolality = [2x (Measured Na)] + [Glucose] + [Urea] mmol/L

Base excess due to Chloride = (Sodium – Chloride) - 32

Ongoing Management

Fluids

Fluid replacement should always begin before starting insulin therapy.

Following the initial bolus/es, the fluid deficit should be replaced evenly over 48 hours in addition to the maintenance fluid requirement.

In moderate/severe acidosis only allow sips of water /ice to suck and include in fluid balance.

It is essential that all fluids given are documented carefully, particularly those given in PED and during transfer.

Fluid requirement = Maintenance + Deficit

Fluid deficit

Fluid deficit estimation should be based on the degree of metabolic acidosis:

> Assume 5% dehydration in mild DKA (pH 7.2 -7.3 +/or bicarbonate 10-15)
> Assume 7% dehydration in moderate DKA (pH 7.1 - 7.2 +/or bicarbonate 5-10)
> Assume 10% dehydration in severe DKA (pH < 7.1 +/or bicarbonate < 5)

The initial 10mL/kg rehydration bolus given to non-shocked patients should be subtracted from the estimated fluid deficit.

Resuscitation boluses in children with shock should NOT be subtracted from the estimated fluid deficit.

Fluid requirement calculation

Fluid requirement (mL/hr) = Maintenance (mL/hr) + ({Deficit – initial bolus (mL)} / 48hr)

> Calculate the fluid deficit (either 5%, 7% or 10% dehydration depending on degree of metabolic acidosis), subtract the initial 10mL/kg rehydration bolus and then divide evenly over 48 hours.
> Add fluid deficit to the maintenance fluid requirement to calculate total fluid requirement.
> Base fluid calculations on actual weight on admission where possible.
> To avoid excessive fluid replacement in overweight and obese children, **a maximum weight of 80kg or the 97th weight centile for age (whichever is lower)** should be used for the calculation of both fluid deficit and maintenance fluids and the maximum IV fluid rate should not exceed 250mL/hr.
> If IV fluids have been given elsewhere, prior to assessment, this volume should be included in the fluid calculations
> Urinary losses should not be added to the calculation of replacement fluid.

See Appendices 2 and 3 for further information.

Type of fluid

Fluid replacement should begin with 0.9% sodium chloride or Plasma-Lyte 148 with added potassium.

Potassium levels will fall once insulin is commenced.

All fluid replacement (excluding any initial boluses given) **should contain 40mmol/L of potassium** (as potassium chloride or potassium dihydrogen phosphate), **unless evidence of renal failure** (anuria or potassium greater than 5mmol/L) **persists after initial boluses are given.**

Monitor glucose levels hourly

- **When the blood glucose level falls below 15mmol/L**, add 5% glucose to IV fluids and continue/reduce insulin to 0.05units/kg/hr**.** If continuing insulin at 0.1units/kg/hr, add 10% glucose to IV fluids (Appendix 4).
- DO NOT reduce insulin infusion below 0.05units/kg/hr, if blood ketones >1mmol/L
- **If blood glucose falls below 6mmol/L,** add more glucose to the IV fluids. Do not reduce insulin infusion below 0.05units/kg/hr, if blood ketones >1mmol/L
- **If blood glucose falls below 4mmol/L,** give a bolus of 2mL/kg of 10% glucose and increase the glucose concentration in the IV fluids. Do not reduce insulin infusion below 0.05units/kg/hr, if blood ketones >1mmol/L

Calculate and monitor corrected sodium 2 – 4 hourly

Fluid and electrolyte replacement should be reviewed 2-4 hourly and ongoing fluid therapy determined by the **corrected sodium level.**

Corrected Na = Measured Na + [0.4 x (Glucose – 5.5)] mmol/L

Serum sodium is an unreliable measure of the degree of extracellular fluid contraction, due to the dilutional effect of hyperglycaemia and the resultant fluid shift from the intracellular fluid to the extracellular fluid. The serum urea and haematocrit are more useful markers of severe extracellular fluid contraction.

- As the plasma glucose concentration falls, measured and corrected sodium should rise steadily.
- **A fall in corrected serum sodium is one of the few biochemical correlates of impending cerebral oedema**
- If the corrected sodium fails to rise, and particularly if it falls, a careful re-evaluation of the fluid replacement is required.
- **Adjust IV fluids to promote an increase in corrected sodium**
  - A fall in Na_{corr} of >5mmol/L in 4-8hours suggests too much fluid replacement
  - A rise in Na_{corr} of >5mmol/L in 4-8hrs suggests insufficient fluid replacement
- Effective osmolality = 2 x (Measured Na) + Glucose + Urea (mmol/L) may be a useful guide to fluid and electrolyte therapy. A fall in serum osmolality of >3mosm/kg/hr has been suggested as a risk factor for cerebral oedema
- Fluid replacement should always be with a solution that has a tonicity ≥ 0.45% sodium chloride with added potassium. If there are concerns about hyperchloraemic acidosis and AKI due to high chloride load, alternative fluid options include:
  - 0.45% sodium chloride with 5% glucose
  - Plasma-Lyte 148 (contains 5 mmol/L potassium chloride)

Potassium

- **Potassium replacement is always required in DKA, as total body potassium is substantially depleted**
- Serum potassium levels at presentation may be normal, increased or decreased. Hypokalaemia at presentation represents a significant total body potassium deficit, whereas hyperkalaemia implies reduced renal function
- Insulin administration and the correction of acidosis will drive potassium back into the cells, decreasing serum potassium levels**. Therefore, potassium replacement should always precede insulin therapy, unless hyperkalaemia or anuria is present**.
- **If serum K^+ < 2.5 mmol/L** discuss with PICU Consultant for advice as cardiac monitoring will be required. **Do not start insulin until potassium >2.5mmol/L**

- **If serum K^+ 2.5 - 3.5 mmol/L** administer **40mmol potassium per litre** of IV fluids and monitor K^+ hourly
- **If serum K^+ 3.5 - 5.0 mmol/L** administer **40mmol potassium per litre** of IV fluids to maintain K^+ at 3.5-5.0 mmol/L
- **If serum K^+ > 5.0 mmol/L** do not give IV potassium. Monitor K^+ hourly until K^+ < 5.0mmol/L
- The maximum recommended rate of intravenous potassium replacement is 0.25mmol/kg/hour (or a concentration of 60mmol/L in large peripheral IV line).
- Potassium dihydrophosphate may be used together with potassium chloride or acetate (e.g. 20mmol/L potassium dihydrophosphate and 20mmol/L potassium chloride) to reduce the risk of hyperchloraemic metabolic acidosis, however hypocalcaemia can result if potassium phosphate is used alone (Appendix 4).

Insulin

There is some evidence that cerebral oedema is more likely to occur if insulin is started early.

NEVER give a bolus dose of IV insulin

Start IV insulin infusion 1 hour after starting IV fluid therapy when:

- The circulating blood volume has been restored or initial 10ml/kg rehydration bolus has been given
- The serum potassium is >2.5mmol/L and potassium replacement has been started (unless hyperkalaemic)

IV Insulin Infusion Dose: 0.05 - 0.1units/kg/hour

- An insulin infusion rate of 0.05units/kg/hr is sufficient in most cases and may reduce the risk of hypoglycaemia
- **An insulin infusion rate of 0.05units/kg/hr** is recommended for transfer, in young children <5yrs of age (who may be more sensitive to insulin) and in children with known diabetes and partial insulin treatment
- **An insulin infusion rate of 0.1units/kg/hr** may be required in severe DKA, particularly in adolescents (who may be more resistant to insulin)

Use 50units of regular insulin (Actrapid) diluted in 50mLs of 0.9% sodium chloride; (1unit = 1mL) (Appendix 4).

- Prime the IV tubing by flushing the insulin infusion solution through all IV tubing before connecting to the patient (to saturate the insulin binding sites in the tubing)
- The insulin infusion should be replaced every 24 hrs to avoid inactivation of insulin
- During the first 60-90 minutes of rehydration, the blood glucose may fall substantially even without insulin therapy
- After the initial fluid bolus, the desired rate of fall in blood glucose is 2-5mmol/hour
- **The insulin infusion should not be stopped or reduced below 0.05units/kg/hr until DKA has resolved** (pH> 7.30 and bicarbonate >15mmol/L or βOHB <1mmol/L) without consultation with senior staff
- If patient is on insulin pump therapy, suspend and remove the pump when starting an IV insulin infusion
- In unusual circumstances where IV insulin infusion is not possible and provided peripheral perfusion is not impaired, the use of 1-2 hourly IM or SC injections of rapid acting insulin (0.1units/kg/hour) has been shown to be effective.

If the biochemical parameters of DKA (pH, bicarbonate, ketones, Anion Gap) do not improve:

- Reassess adequacy of resuscitation
- Recalculate the IV fluid replacement
- Review the insulin therapy (delivery and dose calculation)
- Consider possible causes (e.g. sepsis, hyperchloraemic acidosis, salicylate or other prescription or recreational drugs)

Phosphate

- Intracellular phosphate is depleted in DKA and insulin administration results in a fall in plasma phosphate as phosphate re-enters the cells
- Potassium dihydrophosphate may be safely used as an alternative or in combination with potassium chloride.
- Supplements are not required unless there is severe, symptomatic hypophosphataemia.
- **Careful monitoring of serum calcium is recommended as administration of phosphate may induce hypocalcaemia.**

Bicarbonate

- Even severe acidosis is reversible by fluid and insulin replacement
- **Bicarbonate therapy has not been shown to confer clinical benefit in DKA and may increase the risk of cerebral oedema**

Complications of DKA and its Treatment

Cerebral Oedema

Hypertonic Sodium Chloride (3%) or Mannitol (20%) should always be immediately available during the treatment of DKA and the dose calculated in advance.

Cerebral oedema should be suspected, if a patient with DKA develops any of the following:

- Headache
- Agitation or irritability
- Unexpected fall in heart rate
- Unexpected increase in BP
- Deterioration in level of consciousness
- Abnormalities in breathing pattern
- Oculomotor palsies
- Abnormal posturing
- Pupillary inequality or dilatation

Immediately exclude hypoglycaemia and treat for cerebral oedema with:

- **IV 3% Sodium Chloride (3mL/kg) over 15 minutes OR IV Mannitol 20% (0.5-1g/kg) over 15 minutes**

  The effect of treatment should be apparent within 15 minutes. If no improvement after initial dose, repeat IV 3% Sodium Chloride OR IV Mannitol 20% infusion
- **Halve the rate of IV fluid administration**
- **Elevate the head of the bed**
- **Inform Consultant immediately**
- Intubation and ventilation may be necessary, however aggressive hyperventilation has been associated with poor outcome. If assisted ventilation is required maintain pCO_2 above 26mmHg (3.5kPa)
- Cranial imaging should only be considered after the child has been stabilised. Intracranial events other than cerebral oedema can occur which may require emergency neurosurgery (e.g. intracranial haemorrhage) or anticoagulation (cerebrovascular thrombosis).

Other Complications

> **Hypoglycaemia and hypokalaemia** - Avoid by careful monitoring and adjustment of glucose and potassium content of the IV fluid replacement. Consideration should be given to adding more glucose if blood glucose is falling rapidly, even if still above 6mmol/L (see Appendix 4)

> **Hyperchloraemic metabolic acidosis** - The use of large amounts of 0.9% sodium chloride during the management of DKA can be associated with the development of hyperchloraemic metabolic acidosis. The preferential renal excretion of ketones instead of chloride leads to hyperchloraemia. Direct monitoring of ketones and calculation of the component of the base deficit due to chloride will help differentiate whether the persisting acidosis is due to ongoing ketosis or hyperchloraemia. Acidosis due to hyperchloraemia will correct spontaneously and does not need specific treatment. It should not delay transition to oral fluids and subcutaneous insulin.

> **Sepsis** - A raised WCC is common in DKA, but fever, raised lactate and raised inflammatory markers may all indicate an intercurrent infection. See Sepsis in Children Clinical Guideline.

> **Aspiration pneumonia** - Avoid by using a nasogastric tube in a vomiting child with impaired consciousness

> **Abdominal pain** - Is common in DKA and may be due to liver swelling, gastritis, ileus or bladder retention. If abdominal pain persists once DKA has resolved a surgical opinion should be sought. A raised amylase is common in DKA.

Transfer to Oral Fluids and Subcutaneous Insulin

Oral fluids

> In severe dehydration and acidosis, only allow sips of water or ice to suck (include in fluid balance).

> Oral fluids should only be offered after substantial clinical improvement and cessation of vomiting (mild acidosis and ketosis may still be present).

> When oral fluids are tolerated the IV fluids should be reduced accordingly.

> The insulin infusion can be increased to cover oral carbohydrate intake prior to the commencement of subcutaneous insulin. The basal insulin infusion rate is usually doubled for 30 minutes for snacks and doubled for 60 minutes for meals.

Transfer to subcutaneous insulin can be made when ketoacidosis has resolved and oral intake is tolerated

> Do not change from intravenous insulin to subcutaneous insulin until ketones (βOHB) <1mmol/L and the child with DKA is alert and tolerating fluids without nausea or vomiting.

Note: Patients with DKA are at risk of persistent hyperchloraemic acidosis, βOHB and Anion Gap are better indicators of DKA correction than pH and bicarbonate alone

	Anion Gap	βOHB
DKA	>12	>1mmol/L
Hyperchloraemic acidosis	≤12	<1mmol/L

> The subcutaneous insulin dosage and regimen will vary with the patient's age and circumstances, and should be discussed with the Paediatric Endocrinology Team. For a child who is restarting insulin pump therapy, a change of insulin and a new infusion set is required.

> The most convenient time to change to subcutaneous insulin is before a meal. If ketoacidosis resolves between usual meal times, the insulin infusion rate can be reduced by 25-50% to keep the blood glucose in the target range until SC insulin is started.

> The insulin infusion should be discontinued 15-30 minutes after subcutaneous rapid acting insulin (Fiasp, Novorapid or Humalog) is given or insulin pump therapy is restarted.

> Blood glucose monitoring should continue at 2- 4 hourly intervals.

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APPENDICES

Appendix 1: Glasgow Coma Scale (GCS)

The GCS consists of three parameters and is scored between 3 and 15; 3 being the worst and 15 the best. One of the components of the GCS is the best verbal response, which cannot be assessed in non-verbal young children. A modification of the GCS was created for children too young to talk.

Best eye response	Best verbal response	Best verbal response (nonverbal children)	Best motor response
1. None 2. To pain 3. To speech 4. Spontaneous	1. None 2. Incomprehensible sounds 3. Inappropriate words** 4. Confused conversation* 5. Fully orientated	1. None 2. Inconsolable, irritable, restless, cries 3. Inconsistently consolable and moans; makes vocal sounds 4. Consolable crying, interacts inappropriately 5. Smiles, orients to sound, follows objects and interacts	1. None 2. Extension to pain (decerebrate posture) 3. Flexion to pain (decorticate posture) 4. Withdrawal from pain 5. Localises pain 6. Obeys commands

*Attention can be held; responds in a conversational manner, but shows some disorientation.
**Inappropriate words, no sustained conversational exchange.

Appendix 2: Fluid Calculations

Fluid Requirements = Maintenance + Deficit

Calculate **MAINTENANCE (mL/hr)** fluid requirements based on weight as follows:

- for first 10kgs give 4mL/kg/hr
- for next 10kgs add 2mL/kg/hr
- for additional weight over 20kgs add 1mL/kg/hr

For example, in a child weighing 30 kg maintenance fluid = 40 + 20 + 10 = 70mL/hr

Calculate total **DEFICIT*(mL) = body weight (kg) x % dehydration x 10**

- Estimation of % dehydration should be based on degree of metabolic acidosis
  - Assume 5% dehydration in mild DKA
  - Assume 7% dehydration in moderate DKA
  - Assume 10% dehydration in severe DKA
- **Subtract 10ml/kg rehydration bolus given to non-shocked patients from the DEFICIT, but do NOT subtract resuscitation boluses given for shock**
- Then replace the total **DEFICIT** evenly over 48hours

EXAMPLE 1:

30kg child with moderate DKA (7% dehydrated), who is not in shock and has received a 10mL/kg rehydration bolus

Maintenance = **70mL/hr**

+ (7% Deficit – Rehydration Bolus) ÷ 48hrs = (2100 - 300 = 1800mls) ÷ 48hrs = **37.5mL/hr**

Total fluid replacement = 70 + 38 = **108mL/hr over 48hours**

EXAMPLE 2:

30kg child with severe DKA and in shock (≥10% dehydrated) who has received a 20ml/kg resuscitation bolus

Maintenance **70mL/hr**

+ (10% Deficit) ÷ 48 hrs = 3000ml ÷ 48hrs = **62.5mL/hr**

Total fluid replacement = 70 + 63 = **133mL/hr over 48hours**

Appendix 3: IV fluid requirement (mL/hr) following initial bolus/es

Requirement = Maintenance + Replacement of Deficit over 48hours

	Mild DKA pH 7.2-7.3, Bicarbonate10 -15	Moderate DKA pH 7.1-7.2, Bicarbonate 5 - 10	Severe DKA pH <7.1, Bicarbonate <5	Severe DKA Resuscitation boluses given for shock
Weight (kg)	**Maintenance + 5% deficit – 10mL/kg rehydration bolus (mL/hr)**	**Maintenance + 7% deficit – 10mL/kg rehydration bolus (mL/hr)**	**Maintenance + 10% deficit – 10mL/kg rehydration bolus (mL/hr)**	**Maintenance + 10% deficit (mL/hr)**
5	24	26	29	30
6	29	32	35	37
7	34	37	41	43
8	39	42	47	49
9	44	47	53	55
10	48	53	59	61
11	51	56	63	65
12	54	59	67	69
13	57	62	70	73
14	60	66	74	77
15	63	69	78	81
16	65	72	82	85
17	68	75	86	89
18	71	79	90	94
19	74	82	94	98
20	77	85	98	102
22	80	90	103	108
24	84	94	109	114
26	88	99	115	120
28	91	103	121	126
30	95	108	126	133
32	99	112	132	139
34	102	117	138	145
36	106	121	144	151
38	110	126	149	157
40	113	130	155	163
42	117	135	161	170
44	121	139	167	176
46	124	144	172	182
48	128	148	178	188
50	132	153	184	194
55	141	164	198	210
60	150	175	213	225
65	159	186	227	240
70	168	198	241	250
75	178	209	250	250
80	187	220	250	250

Maximum IV rehydration fluid rate = 250ml/hr

Appendix 4: How to make up special IV fluids

Available IV Fluids and Additives on SA Medicines Formulary:

- 0.9% Sodium Chloride (1L) – PED and PICU
- 0.9% Sodium Chloride and 40mmol/mL KCL (1L) – PED and PICU
- 0.9% Sodium Chloride with 20mmol/L of KCL (1L) – PED and PICU
- 0.9% Sodium Chloride with 5% Glucose and 20mmol/L of KCL (1L) – PED and PICU
- Plasma-Lyte 148 (1L) - PICU
- Plasma-Lyte 148 with 5% Glucose (1L) – PICU

Note: Plasma-Lyte 148 (1L) contains 5mmol/Litre KCL

- IV KCL 10mmol/10mL– PED and PICU
- IV KH_2PO_4 10mmol/10mL - PICU
- IV 50% Glucose (25g/50mL) – PED and PICU

To make up 0.9% Sodium Chloride with 5% Glucose:

- Remove100mls from 1 Litre bag of Sodium Chloride 0.9%
- Draw up 100mls of 50% Glucose using a syringe and add this to the above 1 litre bag to make glucose concentration 5%
- Mix well before administration

To make up 0.9% Sodium Chloride with 10% Glucose:

- Remove 200mLs from 1 Litre bag of Sodium Chloride 0.9%
- Draw up 200mLs of 50% Glucose using a syringe and add this to the above 1 litre bag to make glucose concentration 10%
- Mix well before administration

The above method can also be used with bags of 0.9% NaCl and KCl

To make up an IV Insulin Infusion:

Use 50 units of human neutral insulin (Actrapid) diluted in 50mL of 0.9% sodium chloride (1unit = 1mL)

- Prime the IV tubing by flushing the insulin infusion solution through all IV tubing before connecting to the patient (to saturate the insulin binding sites in the tubing)
- The insulin infusion should be replaced every 24 hrs to avoid inactivation of insulin

Appendix 5: Initial management of Hyperosmolar Hyperglycaemic State (HHS)

Features differentiating HHS from DKA:

Severe dehydration with shock more common

Marked hyperglycaemia – blood glucose >33mmol/L

No significant ketosis (blood ketones <3mmol/L) or acidosis (pH >7.3, bicarbonate >15mmol/L)

Serum osmolality usually >330mOsm/L

Often altered consciousness

Fluid therapy:

The goal of initial fluid therapy is to expand the intra and extravascular volume and restore normal renal perfusion.

The rate of fluid replacement is **more rapid** than is recommended in DKA

> **If shocked - Give an initial 20ml/kg bolus of 0.9% sodium chloride**

> Repeat boluses as needed to reverse shock

> Assume a fluid deficit of 12-15% of body weight

Fluid requirement = Maintenance + (Deficit - given over 48hrs) + Urine output

> Thereafter 0.45 -0.75% sodium chloride with added potassium (40mmol/L unless K>5mmo/L or anuric) should be administered to replace the deficit over 24-48 hours

> Unlike DKA, replacement of urinary losses is recommended (typical urine sodium concentration approximates 0.45% sodium chloride)

> Isotonic fluids should be restarted if perfusion or haemodynamic status appear inadequate as serum osmolality declines

> The goal is a gradual decline in corrected sodium and osmolality (there is no data on the optimal rate of decline in HHS, but 0.5mmol/L per hour has been recommended in hypernatraemic dehydration

> Monitor serum sodium 2 hourly and adjust concentration of the fluids to promote a gradual decline in corrected serum sodium levels

> If there is a continued fall in blood glucose level after the first few hours (>5mmol/L/hr), consider adding 2.5 -5% glucose to the rehydration fluid. If the glucose level fails to fall as expected, reassess renal function

Insulin therapy:

Blood glucose levels will fall with fluid alone and insulin is NOT needed early in treatment. Insulin administration is required at 0.025 – 0.05 units/kg/hr when serum glucose is not falling at a rate of at least 3mmol/L per hour with fluids alone.

Potassium:

Patients with HHS have extreme potassium deficits. A rapid insulin induced shift of potassium into the intracellular space can trigger an arrhythmia. Therefore potassium MUST be added to all fluids

For further information see ISPAD Guidelines.