

# Unexplained hypoglycaemia – Management in children

## Purpose

This document provides clinical guidance for all staff involved in the care and management of a child presenting to an Emergency Department (ED) in Queensland with unexplained hypoglycaemia.

This guideline has been developed by the department of Metabolic Medicine at the Queensland Children's Hospital in consultation with senior ED clinicians and Paediatricians across Queensland. It has been endorsed for statewide use by the Queensland Emergency Care of Children Working Group in partnership with the Queensland Emergency Department Strategic Advisory Panel and the Healthcare Improvement Unit, Clinical Excellence Queensland.

### Key points

- Hypoglycaemia is defined as a blood glucose level (BGL) of  **$\leq 2.6$  mmol/L** using a blood gas machine, iSTAT, or formal laboratory testing.
- Ketotic hypoglycaemia (KH) of childhood is the most common cause of hypoglycaemia in children.
- In the absence of a history of prolonged fasting (over 30 hours) **and** blood ketones  $>4$ , all children with a formal BGL  $\leq 2.6$  mmol/L should be investigated for an underlying disorder.
- Management of hypoglycaemia includes administration of a Glucose 10% bolus followed by a Glucose 10% + Sodium Chloride 0.9% IV infusion (which needs to be mixed onsite).
- Fluids containing less than Glucose 10% (such as Glucose 5% + Sodium Chloride 0.9%) are unsuitable.
- **Hypoglycaemia is a medical emergency. If left untreated it can cause convulsions, irreversible brain damage and death.**

## Introduction

Maintaining glucose homeostasis relies on:

- an intact system of endocrine hormones (insulin, glucagon, growth hormone, cortisol)
- a system of intact metabolic pathways to be able to use fat, protein and glucose
- suitable substrates that are able to be metabolised to produce glucose/ketones for energy in times of fasting e.g. glycogen, protein, fat.

Some children become symptomatic of hypoglycaemia or hypoglycaemic faster than others.



Hypoglycaemia is defined as a blood glucose measurement (BGL) of  $\leq 2.6$  mmol/L using a blood gas machine, iSTAT, or formal laboratory testing.

As glucometers are unreliable at measuring low levels of glucose it is suggested that 3.0 mmol/L be considered a reasonable level to begin formal investigations.

### Possible causes of hypoglycaemia

Severe vomiting or diarrhoeal illness

Prolonged fasting

Underlying medical conditions including:

- liver disease (i.e. end stage liver failure)
- hyperinsulinism
- hormone deficiencies such as hypopituitarism
- neonatal sepsis
- metabolic causes

Ingestions (in younger children)

Drugs and alcohol (in an adolescent)

The most common cause of hypoglycaemia in children is ketotic hypoglycaemia (KH) of childhood. This is a physiological condition that is a variant of normal and expected in a fasting state. Most children grow out of KH by mid-late primary school age.

In the absence of a history of prolonged fasting (over 30 hours) **and** blood ketones  $>4$ , all children with a BGL  $\leq 2.6$  mmol/L should be investigated for an underlying disorder.

This is a critical time to obtain samples and gain a diagnosis.

Refer to the [Queensland Newborn Hypoglycaemia Guideline](#) for the management of newborns prior to initial discharge from hospital. The management of children with a diagnosis known to present with hypoglycaemia is beyond the scope of this guideline. Manage these children as per their emergency sick day management plan.

## Assessment

A child with hypoglycaemia may appear drowsy, listless and lethargic.

A thorough history and examination is important to identify other precipitating causes that need further investigation.

### History

History taking should include the following:

- How long has the child fasted before becoming hypoglycaemic?
- Has the child suffered symptoms of vomiting, diarrhoea or fasted in the last three days?
- Is the child sometimes difficult to wake in the morning?

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- How long does the child usually fast overnight?
- Was the hypoglycaemia precipitated by a protein meal?
- Has the child had recent exposure to fruit or honey (consider hereditary fructose intolerance)?
- Could the child have had any medications or alcohol? (especially insulin, metformin, beta-blockers, quinine, chloroquine, salicylates and valproate)

## Examination

### Red flags to suggest an underlying disorder

- midline defects – consider pituitary hormone deficiencies
- organomegaly – consider storage disorders such as glycogen storage disease
- small genitalia in a male child – consider pituitary hormone deficiencies
- hyperpigmentation – consider adrenal insufficiency
- short stature
- macrosomia
- growth hormone deficiency or overgrowth syndrome
- hyperinsulinism – especially in an infant
- hypoglycaemia precipitated by shorter (<6 hour) fasting period



Seek senior emergency/paediatric advice as per local practice if suspect an underlying disorder.

## Investigations

The presence of blood or urinary ketones at the time of presentation is essential to differentiating possible causes of the hypoglycaemia and obtaining a final diagnosis. Blood ketones can be rapidly performed in ED and should be measured at the same time as formal confirmation of blood glucose. If testing urinary ketones, it is important to obtain the first urine passed after the hypoglycaemia is confirmed.



## Blood collection

### Ideal blood collection for the initial investigation of unexplained hypoglycaemia

Preferred blood collection (volume 5 mL)				
Tube type	Tube description		Volume required	Tests required
Serum	Red or yellow pedi-pot		3 mL	<ul style="list-style-type: none"> <li>free fatty acids</li> <li><math>\beta</math>hydroxybutyrate</li> <li>cortisol</li> <li>growth hormone</li> <li>insulin</li> <li>E/LFTs</li> </ul>
Lithium heparin no gel	Green pedi-pot or adult pot		0.5 mL	<ul style="list-style-type: none"> <li>acylcarnitine</li> <li>plasma amino acids</li> </ul>
Fluoro-oxalate	Grey pedi-pot		1 mL	<ul style="list-style-type: none"> <li>glucose</li> <li>lactate</li> </ul> <p><b>Can be performed on VBG</b></p>
EDTA	Purple pedi-pot		0.5 mL	<ul style="list-style-type: none"> <li>ammonium</li> </ul> <p><b>Notify and send to lab urgently. Check with lab if needs to be on ice</b></p>

### Prioritised blood collection for child with blood collection difficulties

Essential blood collection (required volume 2 mL)				
Tube type	Tube description	Volume	Tests required	
Lithium heparin- no gel	Green pedi-pot or adult pot	0.5 mL	<ul style="list-style-type: none"> <li>acylcarnitine</li> <li>plasma amino acids - may be done from a newborn screening card if collection is difficult.</li> </ul>	
Fluoro-oxalate	Grey pedi-pot	1 mL	As per table above	
Serum	Red or yellow pedi-pot	0.5 mL	<ul style="list-style-type: none"> <li>cortisol</li> <li>insulin</li> </ul>	
Second priority investigations (2 mL volume)				
Tube type	Tube description	Volume	Tests required	
Serum	Red or yellow pedi-pot	0.5 mL	<ul style="list-style-type: none"> <li>growth hormone</li> </ul>	
EDTA	Purple pedi-pot	0.5 mL	As per table above	
Serum	Red or yellow pedi-pot	1.0 mL	<ul style="list-style-type: none"> <li>E/LFTs</li> </ul>	

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## Urine

A urine metabolic screen includes urine amino acids and organic acids.

### Critical urine sample

The **first** urine passed after the episode of hypoglycaemia (BGL  $\leq$  2.6 mmol/L) is the **CRITICAL SAMPLE**. It must be collected and sent for a urine metabolic screen regardless of age and time since hypoglycaemic episode.

## Management

Refer to Appendix 1 for a summary of the management of a child presenting to ED with hypoglycaemia.



**ALERT** – Hypoglycaemia is a medical emergency. If left untreated it can cause convulsions, irreversible brain damage and death.

### Acute management

Obtain IV/IO access rapidly for child with BGL  $<$  3.0 mmol/L on a glucometer.

Upon obtaining IV access:

- obtain formal BGL on blood gas machine, iSTAT or formal laboratory testing
- draw 5 mL of blood (ideally) for further investigations (See Investigations section)
- measure blood ketones using a blood ketone monitor

### Management of child with formal BGL $>$ 2.6 mmol/L

- If low normal BGL, push fluids with initial high sugar content (apple juice, flavoured ice block) followed by more complex carbohydrates
- If formal BGL is greater than 3.0 mmol/L, do not send bloods for further investigation

### Management of child with hypoglycaemia (formal BGL $\leq$ 2.6 mmol/L)

Children with a history of prolonged fasting (over 30 hours) and blood ketones  $>$ 4 can be managed as KH.

In addition to treating the hypoglycaemia, blood and urine should be collected from all remaining children to screen for an underlying disorder (refer to Investigation section).



**ALERT** - Hypoglycaemia should be treated with **Glucose 10% + Sodium Chloride 0.9%** IV fluids. A **Glucose 5%** infusion is usually **not** sufficient to maintain BGL or clear ketones.



Management of hypoglycaemia in children	
<b>Initial bolus dose (IV)</b>	2 mL/kg of 10% glucose
<b>Following IV bolus</b>	Commence an infusion of <b>Glucose 10% + Sodium Chloride 0.9%</b> at maintenance rate. Take a 1L bag of Glucose 5% with Sodium Chloride 0.9%, withdraw 100 mL of fluid from the bag and discard. Inject 100 mL of 50% glucose into the bag and mix well. Refer to <a href="#">QCH IV Fluid Guideline</a> . If dehydrated, commence maintenance fluids plus replacement of deficit over 24 hours.
<b>Monitoring</b>	IV site hourly for signs of extravasation due to the hyperosmolality of the infusion (see <a href="#">Insertion and management of peripheral and central venous access devices</a> (QH only))

IM glucagon is unlikely to benefit a child with KH.

IO route is recommended if unable to obtain IV access.



Consider seeking senior emergency/paediatric advice as per local practice for child with a BGL  $\leq 2.6$  mmol/L, a history of fasting over 30 hours **and** blood ketones  $>4$ .



Seek senior emergency/paediatric advice as per local practice for child BGL  $\leq 2.6$  mmol/L without a history of fasting over 30 hours **and** blood ketones  $>4$ . Additional investigations are required.

## Ongoing management



Seek senior emergency/paediatric advice as per local practice if no clinical improvement following initial glucose bolus and IV fluid infusion. Consider seeking paediatric metabolic advice.



Seek relevant specialist advice as clinically indicated by results of the hypoglycaemia screen for ongoing investigations and management.

Review the IV fluid calculation and glucose concentration for children with ongoing symptoms of clinical concern following initial bolus and IV infusion. Consider alternate/concurrent diagnoses.

On admission to the ward or SSU:

- Continue Glucose 10% + Sodium Chloride 0.9% at maintenance rate (plus additional fluids to replace deficit if dehydrated).
- administer Ondansetron for children over 12 months of age with nausea or vomiting (note ketones alone can cause nausea which may not settle until ketones have cleared).
- encourage oral fluids (see below) and diet, preferably with foods containing carbohydrates.
- once tolerating oral intake IV fluids may be discontinued or changed to Glucose 5% + Sodium Chloride 0.9% at a reduced rate.
- organise discharge medications (glucose gel and glucose 10% polymer, +/- Ondansetron) early in admission.



**Ondansetron for the management of nausea or vomiting in children**

<b>Dose</b>	<p>Given orally or sublingually at a dose of 0.15 mg/kg (maximum 8 mg). Tablets and wafers are available in 4 mg and 8 mg doses. Recommended doses are as follows:</p> <ul style="list-style-type: none"> <li>• 8-15 kg: 2 mg</li> <li>• 15-30 kg: 4 mg</li> <li>• greater than 30 kg: 8 mg</li> </ul> <p>Not recommended for children aged less than 6 months, weight less than 8 kg or with ileus.</p>
<b>Considerations</b>	<p>Ondansetron prolongs the QT interval in a dose-dependent manner. Exercise caution in children who have or may develop prolongation of QTc (such as those with electrolyte disturbances, heart failure or on medications that may lead to a prolongation of the QTc).</p>

**Fluids**

Appropriate oral fluids include:

- 10% glucose polymer (Polyjoule, CarbPlus, SOS formulas)
- 100% apple juice

The following fluids are **unsuitable**:

- glucolyte (2.5% glucose + 3% sucrose)
- hydralyte ice blocks (1.6% glucose)

**Monitoring**

Children with hypoglycaemia require routine observation as dictated by their clinical condition.

**BGL monitoring**

BGL monitoring is **not** required for children receiving a Glucose 10% infusion as the risk of hypoglycaemia is minimal unless hyperinsulinism is suspected.

Consider BGL monitoring for the following children:

- symptoms of clinical concern such as pallor, vomiting, tachycardia or drowsiness
- ketones that are absent or inappropriately low (consider hyperinsulinism and continue BGL monitoring until insulin level is known).

**It is the treating doctor's responsibility to document if BGL monitoring is required.**

**Ketone monitoring**

Test urine for ketones after 12 - 24 hours of treatment to ensure urine ketones have cleared or are clearing. If ketones are present, continue to monitor 12 – 24-hourly until cleared.



## Escalation and advice outside of ED

Clinicians can contact the services below if escalation of care outside of senior clinicians within the ED is needed, as per local practices. Transfer is recommended if the child requires a higher level of care.

Reason for contact	Who to contact
<b>Advice</b> (including management, disposition or follow-up)	Follow local practice. Options: <ul style="list-style-type: none"> <li>onsite/local paediatric service</li> <li>Queensland Lifespan Metabolic Medicine Service via <a href="#">Children's Advice and Transport Coordination Hub (CATCH)</a> on 13 CATCH (13 22 82) (24-hour service)</li> <li>local and regional paediatric videoconference support via Telehealth Emergency Management Support Unit <a href="#">TEMSU</a> (access via QH intranet) on 1800 11 44 14 (24-hour service)</li> </ul>
<b>Referral</b>	First point of call is the onsite/local paediatric service

### Inter-hospital transfers

<b>Do I need a critical transfer?</b>	<ul style="list-style-type: none"> <li>discuss with onsite/local paediatric service</li> <li>view <a href="#">Queensland Paediatric Transport Triage Tool</a></li> </ul>
<b>Request a non-critical inter-hospital transfer</b>	<ul style="list-style-type: none"> <li>contact onsite/local paediatric service</li> <li>contact RSQ on 1300 799 127 for aeromedical transfers</li> <li>contact <a href="#">Children's Advice and Transport Coordination Hub (CATCH)</a> on 13 CATCH (13 22 82) for transfers to Queensland Children's Hospital</li> </ul>
<b>Non-critical transfer forms</b>	<ul style="list-style-type: none"> <li><a href="#">QH Inter-hospital transfer request form</a> (access via QH intranet)</li> <li><a href="#">aeromedical stepdown</a> (access via QH intranet)</li> <li>commercial aeromedical transfers:           <ul style="list-style-type: none"> <li><a href="#">Qantas</a></li> <li><a href="#">Virgin</a></li> <li><a href="#">Jetstar</a></li> </ul> </li> </ul>

## Disposition

All patients with unexplained hypoglycaemia require a period of observation. Admission to an inpatient service is usually required but admission to an SSU (where relevant) may be considered.

Children with refractory BGLs despite IV therapy or rebound hypoglycaemia on cessation of fluids require admission to an inpatient service.



## Discharge from the ward or SSU

On discharge, caregiver/s should be provided with:

- script for the following:
  - 1 tube of glucose gel
  - +/- Ondansetron
  - +/- 1 can of 10% glucose polymer with the age-appropriate recipe (Lucozade is an appropriate alternative if aged over 5 years)
- education including:
  - signs, symptoms and emergency management of hypoglycaemia
  - written instructions on management to prevent a recurrent hypoglycaemic episode as per Appendix 2 - [Sick Day Plan](#)
  - advice against purchasing a glucometer or monitoring BGLs at home (as results can be inaccurate and misleading)

## Follow-up

In the event that an overnight fast rather than an intercurrent vomiting illness precipitated the hypoglycaemic episode, discuss with the on-call Metabolic Physician, Queensland Children's Hospital. The administration of night time cornstarch may be required on discharge.

## First presentation of unexplained hypoglycaemia

- formal written referral to the Department of Metabolic Medicine, Queensland Children's Hospital to review results of initial metabolic screening. Consultation can be conducted via telehealth if required.

## Subsequent presentations

- liaise with Department of Metabolic Medicine, Queensland Children's Hospital to determine the need for further outpatient follow-up and if needed book into local General Paediatric outpatient clinic.

## Related documents

- [Sick day plan](#)

## References

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3. Hofmann, G.F., Nyham, W.L., Zschocke, J., Kahler, S.G., Mayatepek, E. (2002), *Inherited Metabolic Diseases*, Lippincott Williams & Wilkins: Philadelphia, pp.132-144.
4. McGill, J. (2003), 'Inborn errors of metabolism,' in *Practical Paediatrics*, 7<sup>th</sup> edn, Elsevier: Victoria, p. 318-326.
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## Guideline approval

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### Disclaimer

This guideline is intended as a guide and provided for information purposes only. The information has been prepared using a multidisciplinary approach with reference to the best information and evidence available at the time of preparation. No assurance is given that the information is entirely complete, current, or accurate in every respect. We recommend hospitals follow their usual practice for endorsement locally including presenting it to their local Medicines Advisory Committee (or equivalent) prior to use.

The guideline is not a substitute for clinical judgement, knowledge and expertise, or medical advice. Variation from the guideline, taking into account individual circumstances may be appropriate.

This guideline does not address all elements of standard practice and accepts that individual clinicians are responsible for:

- Providing care within the context of locally available resources, expertise, and scope of practice
- Supporting consumer rights and informed decision making in partnership with healthcare practitioners including the right to decline intervention or ongoing management
- Advising consumers of their choices in an environment that is culturally appropriate and which enables comfortable and confidential discussion. This includes the use of interpreter services where necessary
- Ensuring informed consent is obtained prior to delivering care
- Meeting all legislative requirements and professional standards
- Applying standard precautions, and additional precautions as necessary, when delivering care
- Documenting all care in accordance with mandatory and local requirements

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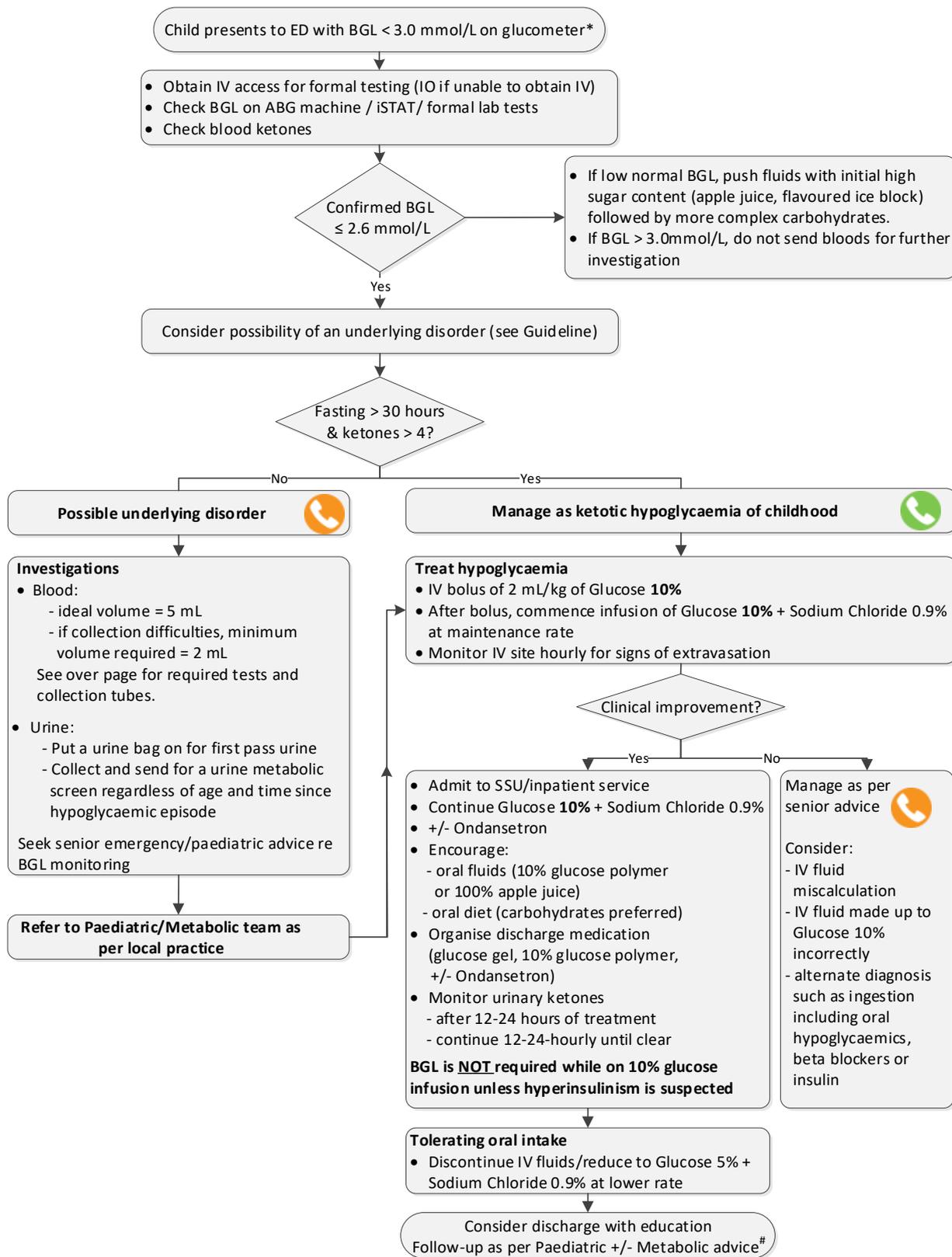
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\*Excluding children with a diagnosis known to present with hypoglycaemia (manage as per their emergency sick day plan).

# Make an outpatient referral to the Metabolic team, Queensland Children's Hospital if an overnight fast precipitated hypoglycaemic event.

Consider seeking senior emergency/paediatric advice as per local practice

Seek senior emergency/paediatric advice as per local practice. Consider seeking paediatric metabolic advice.



## Blood collection for initial investigations of unexplained hypoglycaemia

Preferred blood collection (minimum volume 5 mL)				
Tube type	Tube description		Volume required	Tests required
Serum	Red or yellow pedi-pot		3mL	<ul style="list-style-type: none"> <li>free fatty acids</li> <li>βhydroxybutyrate</li> <li>cortisol</li> <li>growth hormone</li> <li>insulin</li> <li>E/LFTs</li> </ul>
Lithium heparin no gel	Green pedi-pot or adult pot		0.5mL	<ul style="list-style-type: none"> <li>acylcarnitine</li> <li>plasma amino acids</li> </ul>
Fluoro-oxalate	Grey pedi-pot		1mL	<ul style="list-style-type: none"> <li>glucose</li> <li>lactate</li> </ul> <p><b>Can be performed on VBG</b></p>
EDTA	Purple pedi-pot		0.5mL	<ul style="list-style-type: none"> <li>ammonium</li> </ul> <p><b>Notify and send to lab urgently. Check with lab if needs to be on ice.</b></p>

## Recommended blood collection for child with collection difficulties

Essential blood collection (required volume 2 mL)			
Tube type	Tube description	Volume	Tests required
Lithium heparin- no gel	Green pedi-pot or adult pot	0.5 mL	<ul style="list-style-type: none"> <li>acylcarnitine</li> <li>plasma amino acids - may be done from a newborn screening card if collection is difficult.</li> </ul>
Fluoro-oxalate	Grey pedi-pot	1 mL	As per table above
Serum	Red or yellow pedi-pot	0.5 mL	<ul style="list-style-type: none"> <li>cortisol</li> <li>insulin</li> </ul>
Second priority investigations (2 mL volume)			
Tube type	Tube description	Volume	Tests required
Serum	Red or yellow pedi-pot	0.5 mL	<ul style="list-style-type: none"> <li>growth hormone</li> </ul>
EDTA	Purple pedi-pot	0.5 mL	As per table above
Serum	Red or yellow pedi-pot	1.0 mL	<ul style="list-style-type: none"> <li>E/LFTs</li> </ul>

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Queensland Paediatric Guideline

Metabolic

## Sick Day Plan

### 10% Carbohydrate Solution

#### Why does my child have a Sick Day Plan?

Your child has a sick day plan because he or she has had at least one episode of a low blood sugar level. This plan aims to prevent blood sugars from dropping to a level that can harm your child.

#### When do I use the sick day plan?

- At the first sign of illness or if your child is eating less than normal.
- Offer your child small amounts of your chosen carbohydrate solution regularly.
- Write down how much your child drinks.

#### How do I make the carbohydrate solution?

- Using the recipe, put the required amount of water into a container and add the product.
- Use the scoop that comes with the product to make sure the dose is correct.
- Mix well and store in the fridge.

## Recipes

### Poly-Joule recipes

Options	Recipes	Where to buy
Poly-Joule	2 scoops (10 g) of Poly-Joule in 100 mL water	Poly-Joule can be ordered from your local pharmacy
Poly-Joule + Ribena	5 teaspoons Ribena syrup + 1 ½ scoop (about 8 g) Poly-Joule in 100 mL water	
Poly-Joule + cordial	3 teaspoons cordial syrup (regular cordial, NOT diet) + 1 ½ scoop (about 8 g) Poly-Joule in 100 mL water	

### CarbPlus recipes

Options	Recipes	Where to buy
CarbPlus	1 heaped scoop (11 g) CarbPlus in 100 mL water	CarbPlus can be ordered from your local pharmacy
CarbPlus + Ribena	1 teaspoon Ribena syrup + 1 level scoop (10 g) of CarbPlus in 100 mL water	
CarbPlus + cordial	1 teaspoon cordial syrup (NOT diet) + 1 level scoop (10 g) of CarbPlus in 100 mL water	

### Recipes using other products

Product	Recipe	Where to buy
SOS 10	Add contents of sachet to 200 mL of water	Phone Vitaflo Australia on 1800 230 889 or email: <a href="mailto:enquiry@vitaflo.com.au">enquiry@vitaflo.com.au</a>
Lucozade Energy	Add 55 mL of Lucozade Energy to 45 mL of water to make 100ml	Can be bought from the sport drink aisle of most large grocery stores



## Hypoglycaemia and Ketones

The blood sample taken from your child in the emergency department showed a low blood sugar level and ketones.

### What is hypoglycaemia?

Hypoglycaemia is the medical name given to a low blood sugar level (less than 2.6 mmol/L). A child with hypoglycaemia requires urgent medical treatment to increase the blood sugar level. Hypoglycaemic episodes can cause harm if not treated promptly.

### What are ketones?

Ketones are chemicals that occur as the body breaks down fat for energy.

### Why did this happen?

This is the body's normal response when you do not eat for a while. Your child may have had an illness (such as vomiting and diarrhoea) or injury which stopped them from eating.

### Signs and symptoms

- shakiness
- pale skin colour
- sweating
- hunger
- confusion, sudden moodiness or behaviour changes

### Investigating hypoglycaemia

Blood and urine samples are often collected to look for medical conditions that cause hypoglycaemia. These tests take some time to complete so the results are usually not ready when your child is well enough to go home. When you are discharged you will be given a follow-up appointment to receive these results.

These tests rule out all the known causes of hypoglycaemia for your child's age. If these tests are normal your child will likely have a condition called ketotic hypoglycaemia of childhood. This is very common in childhood and a condition most children grow out of by ten years of age.

### What is the treatment?

There are some steps you can take to stop your child having another episode of hypoglycaemia.

#### When your child is well:

- try some solutions from the Sick Day Plan so you know which one they like best
- keep a supply of the preferred drink in the house

#### When your child is unwell or not eating:

- do NOT give your child water
- try and get your child to eat some food or drink milk
- follow the Sick Day Plan to top up their diet
- once they are back to their usual diet you can stop the Sick Day Plan

Monitoring your child's blood sugar levels at home (using a glucometer) is not recommended. The results can be incorrect. It is better to look at your child's symptoms.

### When to seek medical help?

**In an emergency, always call 000 immediately.**

Contact your local doctor or visit the emergency department of your nearest hospital if your child has:

- more than three vomits
- any signs or symptoms of hypoglycaemia
- any other health problems that concern you

