EMERGENCY MANAGEMENT OF HYPOGLYCAEMIA IN CHILDREN

Excluding children with diabetes mellitus

Clinical Guideline

Principal Authors	Dr Allison Low Consultant Paediatrician Barnsley Hospital NHS Foundation Trust
Ratification Group	Guideline Development Group Care of the Acutely III Child Clinical Network South Yorkshire Children and Young People's Alliance
Peer Reviewer	Dr Elspeth Ferguson Consultant Endocrinologist Sheffield Children's Hospital NHS Foundation Trust

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Purpose of Guidance

This guideline has been created with the aim of standardising care throughout the South Yorkshire Integrated Care System footprint, with agreed definitions for hypoglycaemia, a standard hypoglycaemia screen, and a standardised treatment plan to ensure equity for all of our children and young people..

Scope of Guidance

This pathway is intended for primary use by staff working in the four acute hospital trusts in the South Yorkshire Integrated Care Board providing children's services:

- Barnsley Hospitals NHS Foundation Trust
- Doncaster & Bassetlaw Hospitals NHS Foundation Trust
- Rotherham NHS Foundation Trust
- Sheffield Children's NHS Foundation Trust

This includes but is not limited to Doctors, Nurses, and Allied Health Professionals.

The guideline applies to children in the **Emergency Department**, Assessment Unit, or **Paediatric Ward.** It is not applicable to newborns under 48 hours old.

The guideline may be referred to by other healthcare providers at their discretion but does not replace or override any guidance intended for that environment. It may not be relevant for use in Primary Care or other non-acute healthcare settings, and its use therein is at the discretion of the presiding clinician.

Please note that guidelines for children with Inherited Metabolic Diseases are covered in the BIMD Group Guidelines





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Version Control

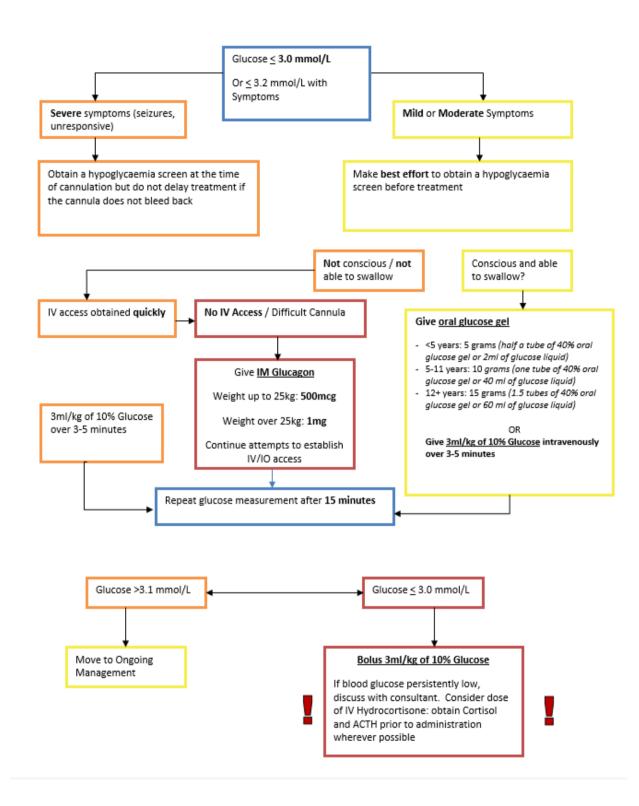
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Date	Version	Comments	Changes Made
June 2023	1 [Original]	None	Guideline Created





Hypoglycemia Flow Chart







Introduction and Background

Paediatric hypoglycaemia is a common presentation, and severe or prolonged cases can lead to permanent brain injury or death. Causes of hypoglycaemia include endocrine and metabolic disorders. Children with these disorders are at risk of future episodes of hypoglycaemia with neurological injury, so investigation of a possible underlying endocrine or metabolic cause should be undertaken at the first presentation. Investigations for many of these conditions can only be performed and interpreted when the child is hypoglycaemic. A hypoglycaemia screen is therefore an essential component of care.

While diarrhoea and vomiting can themselves contribute to hypoglycaemia, it is often the stress of an intercurrent illness that reveals an underlying metabolic problem. Hypoglycaemic children with diarrhoea and vomiting, therefore, still require a hypoglycaemia screen.

There is no national or international definition for hypoglycaemia. The National Metabolic Network Guidelines define hypoglycaemia as a blood glucose $\leq 2.6 \text{ mmol/L}$, while the Pediatric Endocrine Society in America advises a threshold of <3.3 mmol/L. The British Society of Paediatric Endocrinology and Diabetes advise that hypoglycaemia definitions range from $\leq 2.6 \text{ to } \leq 3.0$, but that no consensus has been obtained (personal communication, A Low and T Mushtaq, 2022). The issue is further complicated by the use of point-of-care devices, such as a blood glucose meters or gas machines, which are known to be inaccurate at lower ranges.

For the purpose of this guideline, a child with a blood glucose of ≤3.0mmol/L should be considered hypoglycaemic. However, hypoglycaemia should still be considered in the presence of suggestive signs and symptoms in patients with glucose levels between 3.0 and 3.2 mmol/L. If there is doubt, if the child is unable to communicate symptoms due to age or co-morbidity, or if the child is generally unwell, treat as hypoglycaemia.

A blood glucose measurement of \leq 3.0mmol/L (or 3.0 – 3.2 with symptoms) on a point of care test should always be confirmed with a lab glucose, but a hypoglycaemia screen should be undertaken and treatment given without waiting for the results.





Recommendations

- Identify hypoglycaemia using a point of care testing device
- Obtain a hypoglycaemia screen before treatment, while the child is hypoglycaemic, to investigate for underlying endocrine or metabolic conditions
- All units should have "hypo packs" with the correct blood bottles available to facilitate prompt and complete hypoglycaemia screens
- Treat hypoglycaemia promptly to prevent hypoglycaemic brain injury
- Ensure that hypoglycaemia screen results are reviewed and acted on appropriately





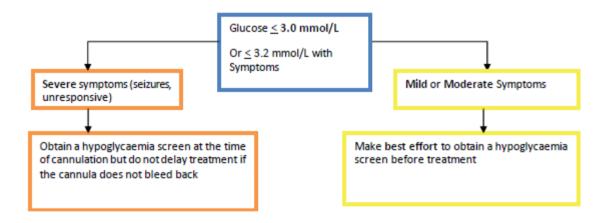
Initial Clinical Management

Initial symptoms of hypoglycaemia can be non-specific and include the following:

Irritability	Altered Behaviour	Sweating	Hunger	Dizziness
Shaking	Palpitations	Drowsiness	Generally Unw	ell Appearance

As hypoglycaemia progresses, patients may become **unconscious** or develop **seizures**, which can lead to significant neurological injury.

If there is any suspicion of hypoglycaemia, conduct a bedside blood glucose test.



Complete Screening

Sending a hypoglycaemia screen is a priority in patients with hypoglycaemia. A completed screen may prevent a later planned admission for a supervised fast, and its associated risks.

Obtain a full hypoglycaemia screen **before** starting treatment to enable identification of underlying pathology unless this is not safe or not possible. Capillary samples are acceptable.





Bloc	d Tests
Bedside	Laboratory
✓ Glucose	✓ Glucose
✓ Ketones	✓ Lactate
✓ Blood Gas	✓ Insulin & C-Peptide
	Discuss with laboratory if concern about Factitious or Induced Illness – see FII section
	 Intermediary Metabolites
	Also referred to as Free Fatty Acids and/or 3-hydroxybutyrate [also called β -OH butyrate]
	✓ Cortisol
	✓ Acylcarnitine Profile
	✓ Ammonia
	Free flowing & transported to the lab within 15 minutes
	✓ Plasma Amino Acids
	✓ U&E
	Not part of hypo screen but likely required
	 Any other blood tests required for clinical condition
Urin	e Tests
Bedside	Laboratory
✓ Urine Dip for	✓ Organic Acids
Ketones	 Toxicology for Specific Medication
Only if not able to	If indicated by history e.g., sulphonylureas OR if concern about factitious or induced illness
obtain via point-oi	
care blood test	

✓ Capillary samples are acceptable

- ✓ Inform the lab **BEFORE** sending a hypo screen
- ✓ Use a hypoglycaemia pack, if available
- ✓ All bottles must be FULL
- ✓ Components in **bold** are priorities

Partial Screening

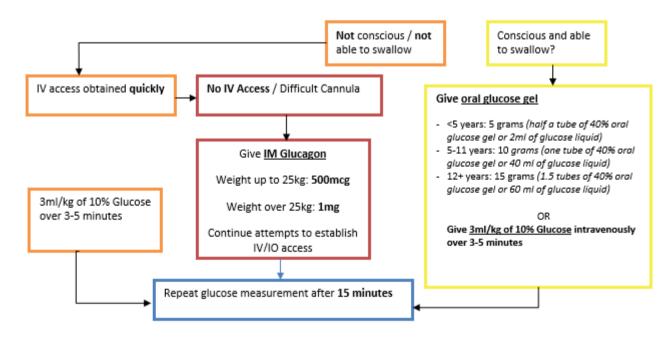
For some patients, a full/complete hypoglycaemia screen is not possible despite best efforts.





Situation	Appropriate Tests
 Difficulty obtaining sufficient volume of blood Ketones available (POCT) and result <0.6 If ketones are <0.6 on POCT or negative on urine dipstick, this suggests the patient has NOT had an appropriate ketotic response to the hypoglycaemia 	Most important investigations Insulin Cortisol Acyl-Carnitine Profile Full screen should still be taken wherever possible
✓ Patient no longer hypoglycaemic	Acyl-Carnitine Profile
An acylcarnitine profile is most useful during hypoglycaemia but can sometimes be diagnostic during normoglycaemia. Cortisol response is often detectable up to an hour after the event.	Cortisol Ammonia Plasma Amino Acids

After screening, proceed to initial treatment below.







Actions After Initial Treatment

If BG remains ≤3.0 mmol/L (or ≤3.2 mmol/L if symptomatic):

Bolus 3 ml/kg of 10% Glucose

If blood glucose is persistently low, discuss with consultant

Consider dose of <u>IV Hydrocortisone</u>: obtain cortisol and ACTH samples prior to administration if possible.

Emergency IV hydrocortisone doses by age:

<1 year 25mg IV or IM

1-5 years 50mg IV or IM

6 years and over 100mg IV or IM

If BG ≥4mmol/L:

→ Move to Further Management section

If BG has improved but remains <4mmol/L:

- ➔ If the patient is symptomatic, give IV bolus treatment (3 ml/kg of 10% Glucose) and monitor response.
- → In patients who are clinically well, start maintenance fluids (see Further Management section) and monitor blood glucose.
- → Blood glucose levels should be maintained \geq 4 mmol/L on maintenance fluids.
- → An infusion of up to 12.5% Glucose can be used peripherally.





12.5% Glucose is produced by using a bag of 0.9% Sodium Chloride with 10% Glucose, and replacing some of the volume of this bag with a solution of 50% Glucose. The following formula will give the correct concentration:

30ml of 50% Glucose + 470ml of (10% Glucose + 0.9% Sodium Chloride) = 500ml of 12.5% Glucose

If solutions above 12.5% are required this must be discussed with PCCU urgently as central access is required in these situations. In addition, a discussion with Endocrinology and/or Metabolic Medicine input (available in working hours at Sheffield Children's Hospital) will be necessary.

Any glucose infusion stronger than 12.5% <u>cannot</u> be infused peripherally

To facilitate discussion with specialist teams, calculate the <u>Glucose Infusion Rate (GIR)</u>. A normal rate is between 4-6mg/kg/minute, and rates >8mg/kg/minute may indicate hyperinsulinism.

[Concentration of glucose (%) x Infusion rate (ml/hr)]

[Weight (kg) x 6]

Patients with recurrent hypoglycaemia, refractory hypoglycaemia, or with features suggesting an endocrine or metabolic cause for their hypoglycaemia should be discussed with the appropriate specialist team.





Further Management

Resolved Hypoglycaemia

If blood glucose levels are maintained ≥4mmol/L, monitor glucose using a point of care device hourly for four hours and then as indicated.

Start fluid at normal maintenance rates: 0.9% Sodium Chloride + 10% Glucose +/- Potassium and maintain ongoing blood glucose ≥4mmol/L.

If levels increase to ≥8mmol/L on two consecutive occasions an hour apart, change the infusion to 0.9% Sodium Chloride + 5% Glucose +/- Potassium as required. Introduce carbohydrate-containing food and drink if tolerated. Stop fluids once oral intake has been tolerated and blood glucose remains ≥4mmol/L for at least two hours.

Discharge Planning

Prior to discharge, ensure that pre-feed blood glucose consistently remains ≥4mmol/L without intravenous fluids. Patients who required IV fluids should tolerate two consecutive meals - milk feeds for an infant - or a meal and a substantial snack for older children to ensure that their underlying illness has improved sufficiently to allow a safe discharge.

Patients who have required Endocrine or Metabolic Medicine input, or who have had persistent or recurrent hypoglycaemia may require a safety fast prior to discharge. This should be discussed with the relevant team.

All available hypoglycaemia screen results should be reviewed and acted upon during admission, with a plan to follow up outstanding results postdischarge.





History

Points to cover include

Previous hypoglycaemic episodes, including as a newborn

and/or symptoms that may have been indicative of past hypoglycaemia

- Time and content of last meal, and last carbohydrate-containing drinks in relation to time of hypoglycaemia
- ✓ Treatment given by paramedics
- ✓ Family history of hypoglycaemia
- ✓ Consanguinity
- ✓ Family history of unexplained deaths
- ✓ Ingestion of relevant substances, whether intentional or accidental

e.g. Alcohol, Oral Hypoglycaemic Agents, Beta Blockers, Aspirin

- ✓ Document all steroid medication, including inhaled
- ✓ Symptoms of any current illness

e.g. fever, diarrhoea, vomiting

Consider if this could be a presentation of induced illness

Examination

The following findings during examination can point towards a specific diagnosis.

Finding	Possible Diagnosis
✓ Failure to Thrive	 ✓ Inborn Error of Metabolism ✓ Growth Hormone Deficiency ✓ Hypopituitarism ✓ Other Endocrine Disorders
✓ Small Stature	✓ Hypopituitarism✓ Growth Hormone Deficiency





 ✓ Macrosomia ✓ Large Tongue ✓ Deep Grooves in Ears ✓ Hemihypertrophy 	✓ Beckwith-Wiedemann Syndrome
✓ Hepatomegaly	 ✓ Beckwith-Wiedemann Syndrome ✓ Glycogen Storage Disease ✓ Galactosemia
✓ Midline Facial Defects✓ Micropenis	✓ Hypopituitarism
✓ Increased Skin Pigmentation	✓ Adrenal Insufficiency

Investigations

Abnormality	Possible Cause
✓ Very Short Fasting Tolerance	✓ Glycogen Storage Disorder
✓ Low Levels of Free Fatty Acids✓ Low Levels of Ketones	✓ Hyperinsulinism✓ Hypopituitarism
✓ High Levels of Free Fatty Acids✓ Low Levels of Ketones	✓ Fatty Acid Oxidation Defect
✓ High Lactate	✓ Glycogen Storage Disorder✓ Sepsis
✓ Raised Ammonia	 ✓ Organic Acidaemia ✓ Tyrosinaemia ✓ Liver Dysfunction
✓ High Carnitine or Acylcarnitine Levels	✓ Fatty Acid Oxidation Defect
✓ Low Cortisol Levels	✓ Adrenal Insufficiency✓ Hypopituitarism
 Inappropriately Normal/High Insulin with Inappropriately Low C-peptide 	 Exogenous Administration of Insulin
✓ Abnormalities in Reducing Substances	✓ Galactosaemia✓ Fructosaemia





 Abnormalities in Organic Acids Abnormalities in Amino Acids 	✓ Urea Cycle Defect✓ Inborn Error of Metabolism
 Inappropriately High/Normal Insulin and Inappropriately High/Normal C-Peptide 	✓ Hyperinsulinism

Follow Up Actions

All hypoglycaemia screen results **must** be reviewed and acted upon. This may involve discussion with either Endocrinology or Metabolic Medicine teams, depending on the results.

For children who did not have a complete hypoglycaemia screen, or whose lab glucose was normal when the screen was sent, discuss plans for further investigations with the responsible consultant. Decisions about further investigation will be made on a case by case basis, balancing the risk of a possible undiagnosed endocrine/metabolic disorder against the risks of a supervised fast.

Red flags that warrant further investigation include:

History of Previous Hypoglycaemia	Consanguinity	Family history of unexplained death
History of Morning Drowsiness	Hepatomegaly	Abnormal newborn blood screening
	Unusual odour	

All children who have required management for hypoglycaemia should be offered follow-up within six weeks, usually in a general paediatric clinic.

As growth hormone is no longer included in the hypoglycaemia screen, retrospective and current height and weight measurements should be specifically reviewed.





Factitious or Induced Illness

Factitious or Induced Illness (FII) should be considered in recurrent unexplained hypoglycaemia, although it is extremely rare.

If FII is suspected, early discussion with Clinical Chemistry, Endocrine, and Metabolic Medicine teams is essential.

Some centres routinely test for exogenous/administered insulin and others do not: please discuss with your laboratory and be aware that you may need to request these investigations specifically.





Communication and Training

The main groups affected by this pathway, and consulted in its development, are as follows:

Acute	Clinical	Endocrinology	Metabolic	Emergency
Paediatrics	Chemistry	Endocrinology	Medicine	Department

Additional training requirements are not anticipated for the majority of groups as this pathway represents a streamlining of current practice to ensure equity across the region, and has been developed in consultation with Trusts to ensure that expectations are in line with the skills and training in their clinical teams.





Review Timeline

This policy will be reviewed in its entirety on a three-yearly basis, as is standard practice, by the members of the **Guideline Development Group** within the **Care of the Acutely III Child Clinical Network**. If significant issues are found before this time, a review will be conducted as necessary to ensure patient safety. As part of the audit process, there is scope to make minor amendments to the policy built into the document, and these will be reflected in the version control table visible at the front of this document.





References

Recommendations from the Paediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycaemia in Neonates, Infants, and Children

Paediatric Endocrine Society, USA

Hypoglycaemia Management in Non-Diabetic Children

Doncaster & Bassetlaw Hospitals Trust

Guidelines for Paediatric Hypoglycaemia & Prolonged Fast Test

Rotherham Hospital Trust

Hypoglycaemia (Non-Diabetic) in Children: Emergency Investigations and Management of

Sheffield Children's Foundation Trust

Investigation and Management of Hypoglycaemia on PCCU

Sheffield Children's Foundation Trust





Appendix I: Record of Regional Consultation

Partner Trusts	<u>Name</u>	<u>Role</u>
<u>Barnsley</u>	Dr Allison Low [author]	Consultant Paediatrician
Doncaster & Bassetlaw	<u>Dr Nagendra Rao</u> Dr Lovlin Joseph	<u>Consultant Paediatrician</u> Consultant Paediatrician
Rotherham	<u>Dr Louisa Hemington</u> Dr Naveen Naganna	<u>Consultant Paediatrician</u> Consultant Paediatrician
Sheffield Children's	<u>Dr Astha Soni</u>	<u>Consultant Paediatric Endocrinologist</u> Chair, CAIC Guideline Development Group
Other Key Participants		
Clinical Chemistry	Dr Katherine Wright	Consultant Biomedical Scientist Clinical Lead for Newborn Screening
Endocrinology	South Yorkshire Regional Endocrine Network	
Pharmacy	Mark Fairweather	Pharmacist, DBHFT
Metabolic Medicine	Dr Mark Sharrard	Consultant in Paediatric Metabolic Medicine





Appendix II: Results Table

Bloods				
Test	Date / Time Taken	Result		
Bedside Glucose				
Bedside Ketones				
Lab Glucose				
Lactate				
Insulin				
C-Peptide				
Cortisol				
Free Fatty Acids				
3-Hydroxybutyrate				
Growth Hormone				
Ammonia				
Plasma Amino Acids				
Acylcarnitine Profile				

Urine				
Test	Date / Time Taken	Result		
Ketones				
Organic Acids				
Toxicology				