LRI Children's Hospital

Hypoglycaemia in Infants & Children (not for use in the NNU or for Children diagnosed with diabetes)

Staff relevant to:	Clinical staff working within the UHL Children's Hospital.
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Written by:	J Greening, J Forster
Trust Ref:	C19/2017

Contents

1. Introduction & Scope

Clinical hypoglycaemia has been defined as 'a plasma glucose concentration low enough to cause symptoms and/or signs of impaired brain function [1].This glucose concentration varies from one patient to another, depending on the availability of alternative fuels and previous blood glucose concentrations. Moreover, in neonates, a decrease in blood glucose is expected after delivery and is physiologically normal. Hypoglycaemia is, therefore, a spectrum and the blood glucose concentration should be interpreted together with the clinical history and concentrations of counter-regulatory hormones and intermediate metabolites [1].

Biochemical hypoglycaemia refers to the inadequacy of circulating levels of blood glucose (BG) and is accepted as laboratory blood glucose measurement of < 2.6mmol/l in a neonate. After 72 hours of age in a term baby, normal blood glucose levels are 3.5-5.5. Readings persistently below this level beyond 72 hours of age are abnormal [2, 6, 7]. Brain glucose utilisation becomes limited at approximate plasma glucose values of 3 to 3.6mmol/l, below which neuroglycopenic symptoms are triggered [1]. Therefore beyond neonatal period and in older children a value of BG 3mmol/l is recommended as lower limit for hypoglycaemia [1]. Hypoglycaemia may be associated with clinical symptoms and signs or be asymptomatic.

This guideline is for the use of Medical and Nursing staff managing and preventing hypoglycaemia in infants and children within the Children's Hospital. **For guidance in the treatment of hypoglycaemia in children with diabetes, please refer to** Diabetes (Including Diabetic Ketoacidosis) UHL Childrens Hospital Guideline **(C10/2019)**

Related documents:

- Consent to Examination or Treatment UHL Policy B35/2024
- IV (Intravenous Therapy) UHL Policy B25/2010
- Vascular Access in Adults and Children Policy and Procedures B13/2010
- Aseptic Non Touch Technique UHL Guideline B20/2013
- Infection Prevention UHL Policy B4/2005
- Prevention and Management of Symptomatic or Significant Hypoglycaemia in Neonates C22/2008
- Hypoglycaemia Fasting Provocation Test UHL Childrens Hospital Guideline C42/2020

2. Hypoglycaemia Management

For infants and children consider intervention at BG value ≤ 3mmol/l

In the absence of blood ketones (<0.1 mmol/l) a higher limit of BG 3.5 mmol/l must be used

Where there is an obvious precipitant cause (eg sepsis , prolonged starvation) you might consider discussing if investigation is indicated with senior colleague or the endocrine/metabolic oncall consultant.

This is because there is an increased risk of neuroglypenia and brain insult in the absence of alternative brain fuel such as lactate and ketones that may be driven by hyperinsulinaemic state [4].

PLEASE REFER TO THE ALGORITHM: QUICK GUIDE FLOW CHART FOR EMERGENCY MANAGEMENT AND INVESTIGATION OF HYPOGLYCAEMIA (PAGE 3). [IF IN DOUBT, CONTACT THE ON-CALL PAEDIATRIC ENDOCRINOLOGY AND METABOLIC CONSULTANTS VIA SWITCH BOARD – AVAILABLE 24 HRS- [see Page 9]

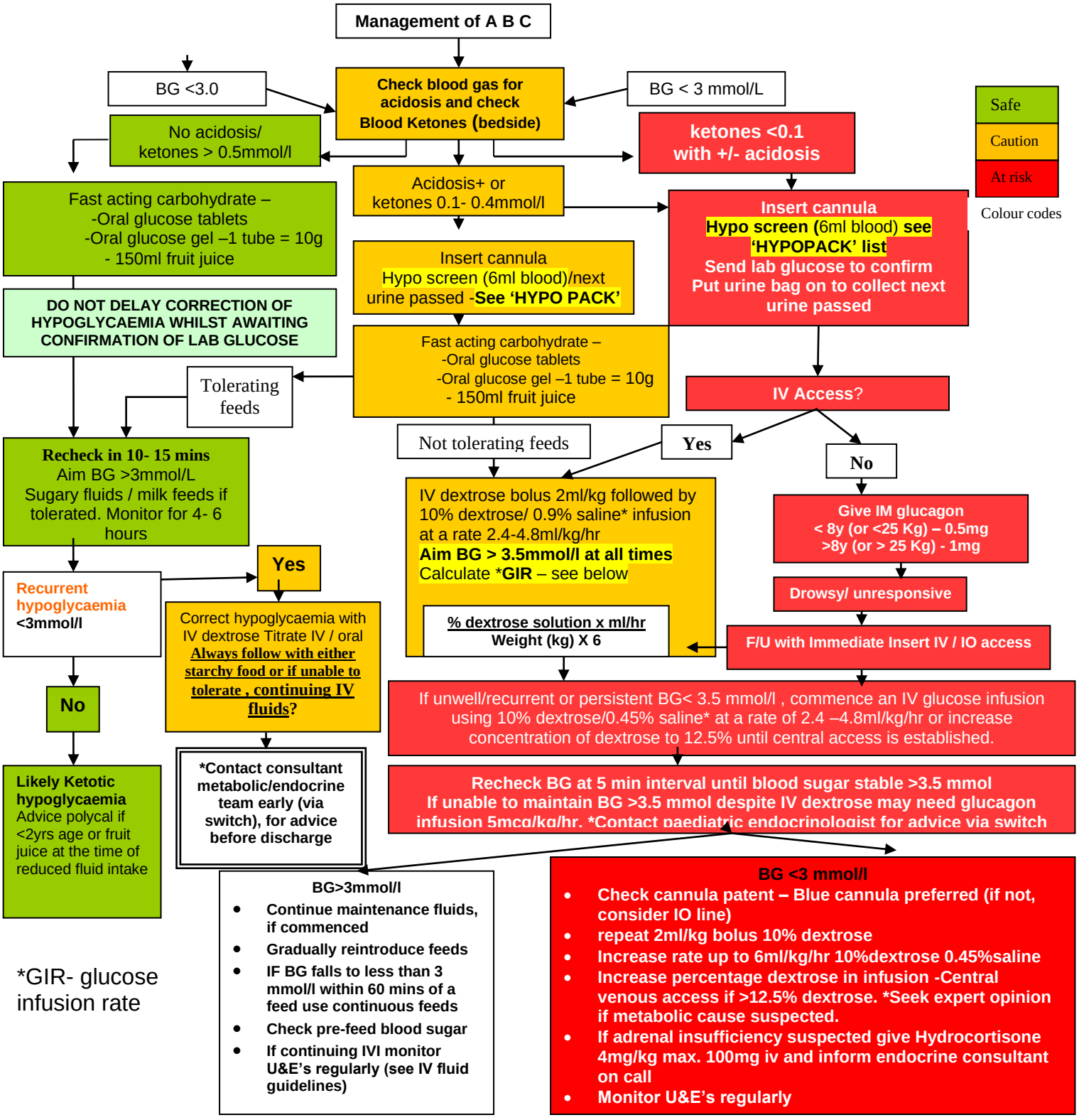
Background:

Extrauterine adaptation of glucose homeostasis occurs after birth by gluconeogenesis. Following the clamping of the umbilical cord, blood glucose concentration decreases rapidly followed by a gradual stabilisation over the next 6-12 hours. Studies have demonstrated a wide range of glucose concentrations during the first 72 hours, with values ranging from 1.3-2 mmol/l in healthy breast fed infants [2, 6]. Low plasma glucose activates a number of counter-regulatory pathways resulting in increased systemic lipolysis with ketone utilisation by the brain [6]. Other alternative fuels such as pyruvate and lactate are also utilised by the brain and, as a result of these, the healthy newborn infant is probably not at risk of hypoglycaemia associated neuronal injury over the first few days. In contrast, preterm infants and those with altered homeostasis due to hyperinsulinemic states or intrauterine growth restriction may not produce alternative metabolites and are, therefore, at higher risk [2, 10, 11].

In majority of healthy neonates, the frequently observed low blood glucose concentrations are not related to any significant problem and merely reflect normal processes of metabolic adaptation to extra-uterine life [2]. However, when low blood glucose levels are prolonged or recurrent, they may result in acute systemic effects and cause long-term neurological damage or death [8, 11]. In addition, in a small number of infants, who may have maladaptation of glucose homeostasis, blood glucose monitoring with proactive recognition and treatment is essential [15].

Algorithm (1) Flow Chart towards Emergency Management and Investigation of Hypoglycaemia

*For contact details of the endocrine and metabolic teams please see Page 9



*GIR- glucose infusion rate

"HYPO PACK" Investigations for Hypoglycaemia: Labels can be printed from ICE.

Symptoms:

The following are typical symptoms and signs of hypoglycaemia but please be aware that this list is not exhaustive and a blood sugar should be checked in any unwell child.

Neonate	***Infant and older child***
• Pallor • Sweating • Tachypnoea • Jitteriness • Apnoea • Hypotonia • Feeding difficulties • Irritability • Abnormal cry • Convulsions	• Anxiety • Tremor • Palpitations • Weakness • Nausea & Vomiting • Hunger • Abdominal pain • Headache • Confusion • Coma • Visual Disturbance • Convulsions

Initial assessment

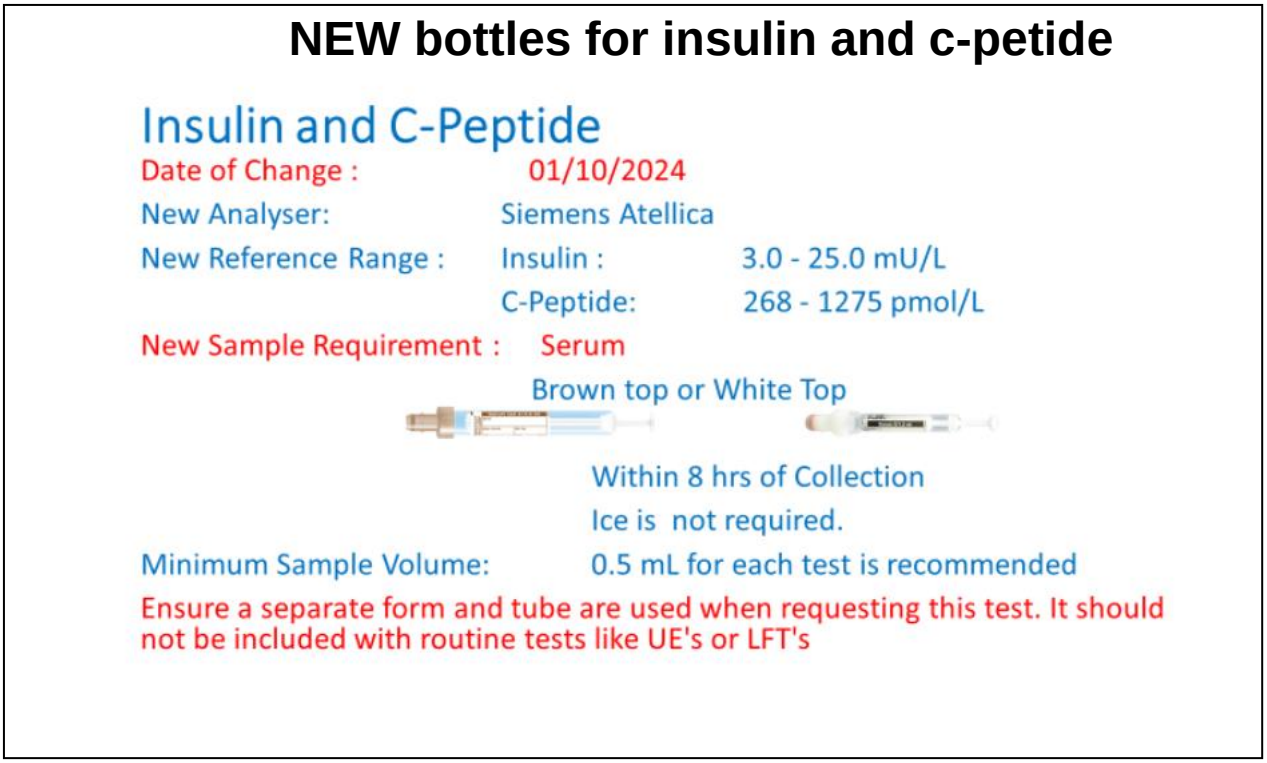
History	***Signs***

• Age
• Feeding History
• Birth history and weight
  ○ Perinatal stress
  ○ Infant of a diabetic mother
  ○ Syndrome associated with hypoglycaemia
  ○ Family hx of hypoglycaemic disorder
• Neonatal jaundice
• Tolerance to fasting/illness
• Drug ingestion
• Family history and parental consanguinity
	• Features of sepsis
	• Hepatomegaly
	• Encephalopathy
	• Optic atrophy/cataracts
	• Genitalia appearance
	• Midface abnormalities
	• Syndromic features
	• Skin pigmentation

Investigative work up for Hypoglycaemia:

Access the cannula. Take 0.5 mls of blood and discard. Then take at least 10 mls of blood from the cannula and fill it in the respective sample bottles.

Priority tests to be taken at the time of hypoglycaemia	Also to be taken at or around the time of hypoglycaemia	1st urine after the hypoglycaemic episode
• Glucose • Lactate • Insulin • C-peptide • 3 BOHB • NEFA • Growth Hormone • Cortisol	• Acylcarnitine • Plasma amino acids • Ammonia • Electrolytes • Liver function	• Urine organic acids



- **Please note that separate (hand-written) forms are required for specimens as marked 1-9 in the table below**

- **Please ensure that the samples are taken to the lab (Level 4, Sandringham building) with the ammonia <u>on ice immediately.</u> If no porter available a member to staff to take**

A total of 10 mls in 9 blood specimen bottles required (3 orange, 3 yellow, 1 white 2 brown)
<u> RED- Time critical samples – must be collected at the time of hypoglycaemia</u>**

Table 2: Fasting Provocation test for Hypoglycaemia – Time critical samples

Lab	Investigation	Specimen type	Volume	Blood taken	Time taken
BLOOD					
Bedside	**Blood glucose stix**		**1 drop**		
Bedside	**Blood gas (capillary /venous)**		**0.5 ml**		
Fast-track 1	**Glucose**	Fluoride oxalate (YELLOW top)	**0.5 ml**		
Fast-track 2	**Lactate** **On ice**	Fluoride oxalate (YELLOW top)	**1.0 ml**		
Fast-track 3	**Ammonia** On ice	Lithium Heparin (Orange top)	**1.0 ml**		
Fast-track 1	**U&E's, *Cortisol and Growth Hormone**	White (WHITE top)	**1.0 ml**		
Specials 4	**Insulin**	Brown or white top	**0.5 ml**		
Specials 5	**C-peptide**	Brown or white top)	**0.5 ml**		
Specials 6	***Free Fatty Acids and 3β-hydroxybutyrate**	Fluoride oxalate (YELLOW top)	**1.0 ml**		
Specials 7	***Acylcarnitine profile, Gal-1-Put**	Lithium Heparin (ORANGE top)	**1.0 ml**		
Specials 8	**Serum amino acids**	Lithium Heparin (ORANGE top)	**1.0 ml**		
URINE					
Bedside	**Urine dip – ketones**				
Specials 9	**Urine organic acids**	Urine sample (universal pot)	**5 ml**		

Miscellaneous Testing: Alcohol, Salicylates, Blood cultures, LFT, U&E

Put urine bag on child or collect next passed urine **to send for** urine organic acids **check for ketones by doing a dipstick test**

After obtaining all the samples, treat hypoglycaemia as below

Emergency management of hypoglycaemia:

<u>If child is conscious and not vomiting</u>-

- Give oral glucose dextrogel ½ tube (5g) for infants < 6 months and 1 tube if > 6 months.
- In an older child give oral glucose 10–20 g.
- 2 scoops of polycal in 30 ml milk or water, 200 ml milk or 2 teaspoons sugar, followed by a snack of starchy carbohydrates or a milk feed in infants

<u>In patients with altered consciousness</u> –

- give 2 ml/kg 10% glucose as intravenous bolus followed by infusion containing 10% glucose
- If no IV access available give stat glucagon IM: 0.5mg for patients < 8 yrs age or <25 kg,

  1 mg for patients > 8 yrs age or >25 kg.

Please note, this MUST be immediately followed by IV or IO access with infusion of Dextrose to maintain normal glycaemic state (BG>3.5mmol/L). Monitor BG at least 1hrly until stable.

GLUCAGON IS RARELY EFFECTIVE IN METABOLIC PATIENTS PLEASE REFER TO SPECIFIC METABOLIC GUIDELINES IN https://bimdg.org.uk/

Specific management for differing types of hypoglycaemia (Follow algorithm pg. 3)

1) Non-Ketotic hypoglycaemia

If blood ketones < 0.1 mmol/l and glucose requirement (GIR) is >8 mg/kg/min in an infant consider the diagnosis of hyperinsulinism. To calculate glucose requirement use the formula below.

Glucose Infusion Calculator

Glucose infusion rate (**GIR**) in mg / kg / min =	$\frac{\%\ \text{dextrose solution} \times \text{ml/hr}}{\text{Weight} \times 6}$

Please see appendix 2 protocol to manage an infant with hyperinsulinism (if suspected, MUST CONSULT PAEDIATRIC ENDOCRINOLOGIST ON-CALL VIA SWITCH). If inborn error of metabolism is suspected, contact paediatric metabolic consultant on-call or (Sheffield- out of hours) see HTTPS://BIMDG.ORG.UK/EMERGENCY-GUIDES/ emergency management guidelines (https://https://bimdg.org.uk/emergency-guides/.org.uk/) for specific disorder and seek advice from metabolic consultant via switch.

2) Ketotic hypoglycaemia (KH)

KH is the most common cause of hypoglycaemia in young nondiabetic children with or without metabolic disorder, chronic conditions such as gastrointestinal, endocrine or heart disease, Problems are usually precipitated by an intercurrent illness associated with anorexia or vomiting. A range of metabolic disorders can cause hypoglycaemia with ketosis.

For any patient presenting with ketotic hypoglycaemia as the very first presentation, please refer to the flow chart for management (Algorithm 1, page 3).

If this patient is known to have underlying metabolic condition and presents with ketotic hypoglycaemia, please refer to https://bimdg.org.uk/ for specific guidelines on management. ***BIMDG have outlined specific emergency guidelines to treat and prevent high catabolic state,*** speak to metabolic team early, patient will usually have an emergency protocol and open access to emergency department and must be seen without delay. The fasting tolerance is shorter during infections in many IEMs depending on the metabolic condition [3]. As well as increasing the tendency to hypoglycaemia, catabolism often leads to the accumulation of toxic metabolites. It is, therefore, important to minimise catabolism, primarily by maintaining a high glucose intake with additional measures in specific disorders (https://bimdg.org.uk/). Please ensure you contact the Metabolic team consultant (via switch) for advice in such instance.

It is recommended to prevent ketotic hypoglycaemia with additional support of 'emergency regimen' of drinks containing soluble glucose polymer to provide large amounts of carbohydrate and calories at the time of reduced intake/losses. See Appendix 3.

If children are unable to tolerate the oral emergency regimen, they need admission and intravenous glucose. Patients should receive this treatment even if their blood glucose is normal as its primary purpose is to reduce catabolism and prevent problems [3, 14]. Patients with fatty acid oxidation defects, for example, can develop arrhythmias or encephalopathy without hypoglycaemia, presumably due to accumulation of toxic metabolites. If it occurs, hypoglycaemia is a relatively late feature [16].

Fasting Provocation Test for hypoglycaemia (MUST be only done after discussion with endocrine/metabolic consultant)
A fasting provocation test is occasionally indicated to help establish a diagnosis. This should never be completed without consulting a Paediatric endocrinologist/ metabolic consultant and a separate protocol is available for this.

Contact details of Metabolic team : [0900-1700hr service provided 5/7 a week]

Consultants :
Dr J Forster **0300 303 1573**
Dr Emily Sivers

Clinical nurse specialist Metabolic Team : 01162047854 / 07921545407
Email: (paediatric metabolic team) PMT@uhl-tr.nhs.uk

OOH service via hospital switch board or Sheffield Switch board over weekends

Contact details of Endocrine team : [0900-1700hr service provided 5/7 a week]

Dr J Greening	**0300 303 1573/ 01162586796**
Dr Subbarayan	**0300 303 1573/ 01162586796**
Dr S Shenoy	**0300 303 1573/ 01162586796**

Clinical Nurse Specialist Endocrine
Pauline Jones: 07921 545 455
Katie Parkin 07484015480

Email: paediatricendocrineteam@uhl-tr.nhs.uk

OOH service via hospital switch board ask for the East Midland Paediatric Endocrine Consultant oncall service. 0300 303 1573

Interpreting the Results of the Hypoglycaemia Screen [3,9]

Low Ketones (<0.5mmol/L)	Fatty acid oxidation defects or defects in ketogenesis Hyperinsulinism of infancy
Raised Insulin (Insulin > 3mu/L When BG < 2.6mmol/L)	Hyperinsulinism of infancy Beckwith- Weidman syndrome Pancreatic islet cell adenoma Insulin poisoning Maternal diabetes
Hyperammonia	Fatty acid oxidation defects Some organic acidaemia Urea cycle disorders Liver dysfunction Hyperinsulinism
Metabolic acidosis	Fatty acid oxidation defects MCAD, LCAD Defects in ketogenesis Sepsis Glycogen storage disorders Organic acid disorders
Deranged LFT's	Most metabolic conditions in extremes Sepsis Liver disease Glycogen storage disease Galactosaemia Fat oxidation defects Hereditary fructose intolerance
Low cortisol	Adrenal insufficiency Congenital adrenal hyperplasia ACTH deficiency/ Hypopituitarism

Low sodium + High Potassium	Adrenal disorders
GH deficiency	Panhypopituitarism Isolated GH deficiency
Raised lactate	Metabolic liver disease Prolonged convulsion Fructose 1,6-bisphosphatase Glycogen storage disorders(GSD 1) Sepsis
Urine	Specific amino or organic acid disorders

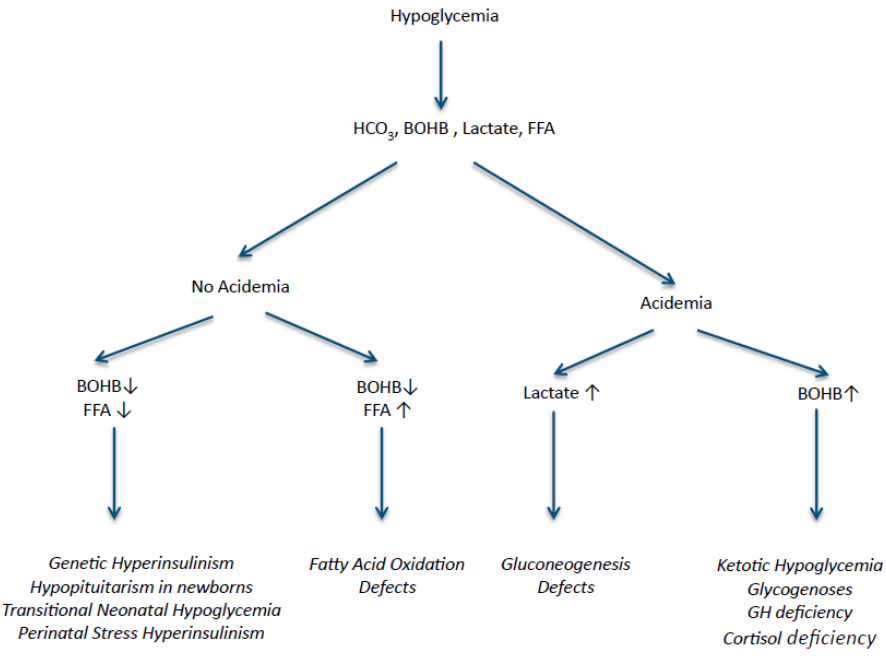


Figure. Algorithm showing how the major categories of hypoglycemia can be determined with information from the critical sample. *GH*, growth hormone.

3. Education and Training

Training of junior medical staff and nursing: at induction and adhoc ward training of how to follow the pathway.

Education: presentation of abnormal results at in-house endocrine/metabolic meetings + children's hospital grand round.

4. Monitoring and Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead	Reporting arrangements
100 % compliance of hypo screens with full panel obtained	Audit / Chem path	Yearly	JEG	Local clinical practice team
>95% complication of contact with speciality team if hypopack blood taken	Monitor via monthly Biochemistry meeting/ audit	Monthly	JEG	Local clinical practice team

5. Supporting Documents and Key References

1. Paul S. Thornton et al,Recommendations from the Pediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants,and Children, .jpeds.2015.03.057, p238-245
2. Guftar Shaikh et al, Standardised practices in the networked management of congenital hyperinsulinism: a UK national collaborative consensus Front. Endocrinol., 30 October 2023 Sec. Pediatric Endocrinology Volume 14 - 2023 | https://doi.org/10.3389/fendo.2023.1231043
3. Thornton PS, Stanley CA, De Leon DD, et al. Recommendations from the Pediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants, and Children. J Pediatr 2015;167:238–45.
4. Stanley CA, Rozance PJ, Thornton PS, et al. Re-evaluating “transitional neonatal hypoglycemia”: mechanism and implications for management. J Pediatr 2015;166:1520–5.e1.
5. Morris AAM; Thekekara A; Wilks Z; Clayton PT; Leonard JV; Aynsley-Green A; Evaluation of fasts for investigating hypoglycaemia or suspected metabolic disease. Archives of Disease in Childhood. 1996;75(2):115-119
6. Cornblath M, Hawdon JM, Williams AF, et al. Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds. Pediatrics 2000;105:1141–5.
7. Güemes M, Rahman SA, Hussain K. What is a normal blood glucose? Arch Dis Child Sep 2015. doi:10.1136/archdischild-2015-308336
8. Hay, W.W., Jr., et al., Knowledge gaps and research needs for understanding and treating neonatal hypoglycemia: workshop report from Eunice Kennedy Shriver National Institute of Child Health and Human Development. J Pediatr, 2009. **155**(5): p. 612-7.
9. Lucas, A., R. Morley, and T.J. Cole, Adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia. BMJ, 1988. **297**(6659): p. 1304-8.
10. McKinlay, C.J., et al., Neonatal Glycemia and Neurodevelopmental Outcomes at 2 Years. N Engl J Med, 2015. **373**(16): p. 1507-18
11. Saudubray JM, De Lonlay P, Touati G, et al. Genetic hypoglycaemia in infancy and childhood: pathophysiology and diagnosis. J Inherit Metab Dis 2000;23:197–214.
12. Sprague JE, Arbelaez AM. Glucose counterregulatory responses to hypoglycemia. Pediatr Endocrinol Rev 2011;9:463–73; quiz 74–5.
13. Cryer PE. Hypoglycemia, functional brain failure, and brain death. J Clin Invest 2007;117:868–70.

14. National Metabolic Biochemistry Network. Best Practice Guidelines for the Investigation of Hypoglycaemia in Children. 2012. http://www.metbio.net/ metbioGuidelines.
15. Wong CP; Forsyth RJ; Kelly TP; Eyre JA: Incidence, aetiology and outcome of non-traumatic coma: a population based study. Archives of Disease of Childhood. 2001;84(3):193-199
16. Bonham JR. Investigation of hypoglycaemia in childhood. Ann Clin Biochem 1993;30:238-247
17. Aynsley-Green A. Glucose, the brain and the paediatric endocrinologist. Hormone Res 1996;46:8-25
18. Glycaemic emergencies. BNF June 2004
19. Hypoglycaemia of the newborn. Review of the literature. WHO 2006
20. Huidekoper H, Duran M, Turkenburg M, et al. Fasting adaptation in idiopathic ketotic hypoglycemia: a mismatch between glucose production and demand. Eur J Pediatr 2008;167: 859–65.
21. Lang TF, Hussain K. Chapter six—Pediatric hypoglycemia. In: Gregory SM, ed. Advances in clinical chemistry. Elsevier, 2014:211–45.
22. Bodamer OA, Hussein K, Morris AA, et al. Glucose and leucine kinetics in idiopathic ketotic hypoglycaemia. Arch Dis Child 2006; 91:483–6.

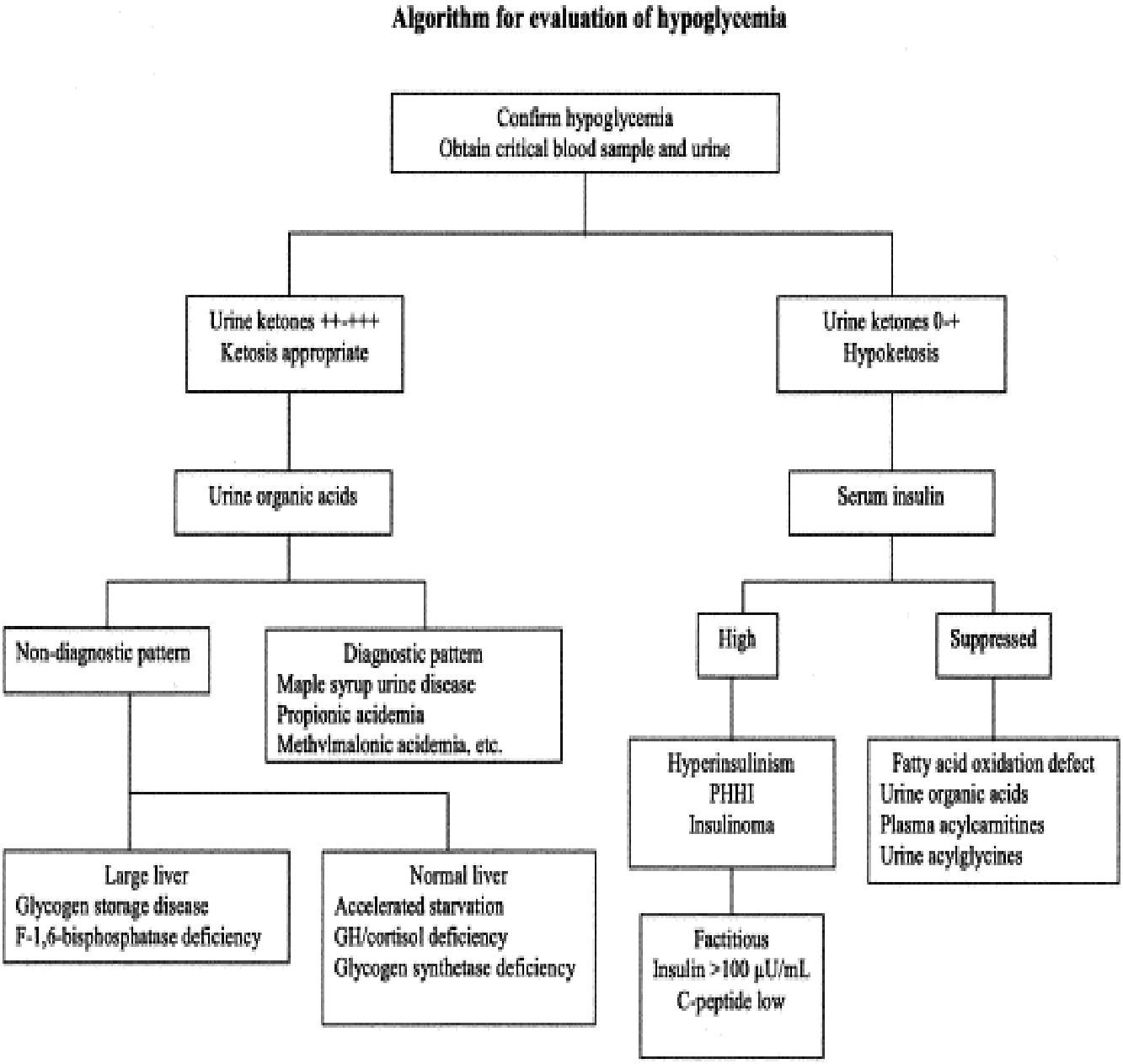
6. Key Words

Hypoglycaemia, Glucose, Ketotic

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) J Greening - Cons Paediatrician	**Executive Lead** Chief Medical Officer
Details of Changes made during review: **Related documents hyperlinks updated** **Age for intervention consider intervention at BG value ≤ 3mmol/l** **Updated with New blood bottles for C-Peptide and Insulin** **Updated that bloods for C-Peptide and Insulin no longer need to be on ICE** **Clarifies that bloods for Ammonia must be on ICE** **Contact details for Metabolic Team and Enodcrine Team updated** **Appendix 3: Protocol for management of hyperinsulinaemic hypoglycaemia in neonates** **Reviewed and updated : Aiming to maintain Blood Glucose level changed from 3 to >3.5mmol/l- 4mmol/l** **Removed referral to HI Service at Great Ormond Street** **Summary of drug dosages used in hyperinsulinism updated** **References updated**	

Appendix 1: Algorithm for evaluation of hypoglycaemia



Appendix 2: causes of hypoglycaemia.

Hyperinsulinism
Transient: Infant of diabetic mother, perinatal asphyxia, rhesus disease, intra-uterine growth retardation, Beckwith-Wiedemann syndrome, 'idiopathic'.
Congenital Hyperinsulinism due to gene mutations.
Carbohydrate deficient glycoprotein syndrome (CDG).
Defects in the metabolism of fatty acids (SCHAD).

Hormonal deficiency
Cortisol, growth hormone, ACTH, glucagon, adrenaline rarely hyothyroidism.

Defects in hepatic glycogen release/storage
Glycogen storage diseases: Glucose-6-phosphatase, Amylo-1,6-glucosidase deficiency, Liver phosphorylase deficiency.
Hepatic glycogen synthase deficiency.

Defects in gluconeogenesis
Fructose-1,6-bisphosphatase deficiency, phosphoenolpyruvate carboxykinase (PEPCK) deficiency.

Defects of fatty acid oxidation
Medium Chain Acyl-CoA Dehydrogenase Deficiency.
Long Chain Acyl-CoA Dehydrogenase Deficiency (+ VLCAD).
Short Chain Acyl-CoA Dehydrogenase Deficiency.
Multiple Acyl CoA Dehydrogenase deficiency (MADD)
Carnitine deficiency (primary and secondary).
Carnitine palmitoyl transferase deficiency (CPT 1 and 2).

Defects in ketone body synthesis or utilization
HMG CoA synthase deficiency, HMG CoA lyase deficiency, beta-ketothilase defeciency

Metabolic conditions (relatively common ones)
Organic acidaemias (Propionic, Methylmalonic).
Maple syrup urine disease, galactosaemia, fructosaemia, tyrosinaemia.
Glutaric aciduria type 2.

Defects in glucose transport
Defects of transporters GLUT2

Drug induced
Sulphonylurea, Insulin, Beta-blocker, Salicylates.

Miscellaneous causes (mechanism not clear)
Ketotic hypoglycaemia (the commonest cause of hypoglycaemia).
Infections (sepsis, malaria), congenital heart disease.

Appendix 3: Protocol for management of hyperinsulinaemic hypoglycaemia in neonates

MANAGEMENT IN THIS GROUP OF PATIENTS MUST BE DISCUSSED WITH THE ON-CALL ENDOCRINE CONSULTANT VIA SWITCHBOARD.

Blood samples are taken at the time of hypoglycaemia (blood glucose < 2.6 mmol/l). Perform the hypoglycaemia screen as suggested in the protocol for the Investigation of hypoglycaemia.

Management

1. Give 2 ml/kg of 10% glucose as a slow IV injection, and then continue with a 10% glucose infusion at a rate of 6 to 8 mg/kg/minute (i.e. 3.6 ml/kg/hour of 10% glucose). **NB**: A large bolus of glucose should **not** be given, as this will cause unnecessary hyperglycaemia and may provoke further (i.e. reactive) hypoglycaemia.

2. Monitor blood glucose with regular BG stix, initially frequently to establish a plateau and then at 1 – 2-hourly intervals, aiming to maintain the blood glucose level at>3.5 mmol/l– 4 mmol/l.

3. If venous access is difficult, glucagon (0.5 mg in <8 yrs or <25 Kg; and 1 mg in >8 yrs or >25 Kg) by intramuscular injection can be given. An exaggerated hyperglycaemic response is consistent with a diagnosis of hyperinsulinism. The effect is usually transient.

4. If blood glucose concentrations drop to < 3.5 mmol/l, then the glucose infusion rate should be increased (often 10– 20 mg/kg/minute). If the glucose requirement is > 12 mg/kg/minute, consider starting a glucagon infusion (to discuss with the on-call paediatric endocrine consultant)

5. Consider starting therapy with diazoxide. 1st obtain an echocardiogram ,discuss fluid infusion rate with endocrinologist on call 2-15 mg/kg/day (start at the low end of the range), covered with a diuretic (e.g. chlorothiazide 7-10 mg/kg/day, divided into 12-hourly doses), if hyperinsulinism is confirmed. Chlorothiazide therapy is used to cover any fluid retention that may occur with diazoxide, and also because there is a synergistic effect between diazoxide and chlorothiazide.

6. Monitor U&Es carefully, and start potassium replacement as necessary.

7. Stop bolus feeding as it is a stimulus to insulin secretion and will exacerbate the hypoglycaemia.

8. If the patient requires high glucose infusion rates to maintain normoglycaemia, the diazoxide dose should be increased to 15 mg/kg/day with maximum doses of thiazide diuretic. Alternatively, the patient may be given octreotide 10 micrograms/kg/day and glucagon 5 microgram/kg/hour as a continuous infusion. (to discuss with the on-call paediatric endocrine consultant).

9. Venous access may become a problem, and insertion of a long line should be considered at an early stage.

10. If the child shows no signs of improvement, and is requiring maximal therapy, then the child needs to be referred to NORCHI centre at Manchester/ for further management.

11. May need fast provocation test, adequate blood glucose monitoring training for family and emergency hypoglycaemia correction kit/ open access letter prior to discharge. Contact endocrine team early for advise at least 48 – 72 hours prior to planned fast provocation test.

12. Summary of drug dosage used in hyperinsulinism:

Drug	Dose
Diazoxide	Total daily dose up to 2-15 mg/kg/day in 3 divided doses, in combination with a thiazide diuretic. (start at 2mg/kg/day)
Chlorothiazide	Starting dosage 7mg /kg/day in 2 divided doses
Octreotide	5-30micrograms/kg/day as a continuous iv or s/c infusion. Or s/c QDS dose
Lanreotide	Dosage in discussion with endocrinologist in conjunction with GOSH or Manchester NORCHI service
Sirolimus	Dosage in discussion with endocrinologist in conjunction with GOSH or Manchester NORCHI service
Glucagon infusion	5 -20 microgram/kg/hour to max 20 mcg/kg/hr by iv infusion. Start at 2.5 mcg/kg/hr

TABLE 2: Dextrose solutions: Conversion from ml/kg/day (dextrose solutions of different concentrations) to mg/kg/minute of dextrose

Daily fluid intake (ml/kg/d)	**10% Dextrose**	**12.5% Dextrose**	**15% Dextrose**	**17.5% Dextrose**	**20% Dextrose**	**22.5% Dextrose**	**25% Dextrose**
	mg/kg/min	mg/kg/min	mg/kg/min	mg/kg/min	mg/kg/min	mg/kg/min	mg/kg/min
40	2.77	3.47	4.16	4.86	5.55	6.25	6.94
50	3.47	4.34	5.2	6.07	6.94	7.81	8.68
60	4.16	5.20	6.25	7.29	8.33	9.37	10.41
70	4.86	6.07	7.29	8.50	9.72	10.93	12.15
80	5.55	6.94	8.33	9.72	11.10	12.50	13.88
90	6.25	7.81	9.37	10.93	12.50	14.06	15.62
100	6.94	8.68	10.41	12.15	13.88	15.62	17.36
110	7.63	9.54	11.45	13.36	15.26	17.18	19.08
120	8.33	10.41	12.50	14.58	16.66	18.75	20.82
130	9.02	11.28	13.54	15.79	18.05	20.31	22.56
140	9.72	12.15	14.58	17.01	19.44	21.87	24.30
150	10.41	13.02	15.62	18.22	20.83	23.43	26.04

TABLE 3: Making up dextrose solutions of different concentrations

Final dextrose concentration required	Volume of **50%** Dextrose	Volume of **10%** Dextrose	Total volume of final solution
12.5%	31.25 ml	468.75 ml	500 ml
15%	62.5 ml	437.5 ml	500 ml
17.5%	93.75 ml	406.25 ml	500 ml
20%	125 ml	375 ml	500 ml
22.5%	156.25 ml	343.75 ml	500 ml
25%	187.5 ml	312.5 ml	500 ml

Appendix 4: Emergency feed regimen

Age up to 1 year; Regimen recipes – 10% CHO solution; Provides – 40kcals/100ml

Glucose polymer to 10% CHO solution	Caloreen 	Maxijul 	Polycal 	Vitajoule 	SOS 10 
200ml recipes use cooled, boiled water. **Weight of product in own scoop**	20g Caloreen (2 level unpacked scoops) made up to 200ml with cooled boiled water. Scoop = 10g	20g Maxijul (6 level unpacked scoops) made up to 200ml with cooled boiled water. Scoop = 5g	20g Polycal (4 level unpacked scoops) made up to 200ml with cooled boiled water. Scoop = 5g	20g Vitajoule (2 level unpacked scoops) made up to 200ml with cooled boiled water. Scoop = 10g	1 sachet SOS 10 made up to 200ml with cooled boiled water. 1 pre-measured sachet = 21g
Feeding volumes:	**< 6months of age** 150ml/kg/day (up to maximum 1200ml) **7-12months of age** 120-150ml/kg/day (up to maximum 1200ml)				
Administration	Divide total volume over 24 hours: give 1 -2 hourly orally or tube feed (bolus or continuous)				

Age upto 2 year, Regimen recipes – 15% CHO solution ; Provides – 60kcals/100ml

Glucose polymer to 15% CHO solution	Caloreen 	Maxijul 	Polycal 	Vitajoule 	SOS 15 
200ml recipes use cooled, boiled water for tube feeds*. **Weight of product in own scoop**	30g Caloreen (3 level unpacked scoops) made up to 200ml with water*. Scoop = 10g	30g Maxijul (6 level unpacked scoops) made up to 200ml with water*. Scoop = 5g	30g Polycal (6 level unpacked scoops) made up to 200ml with water*. Scoop = 5g	30g Vitajoule (3 level unpacked scoops) made up to 200ml water*. Scoop = 10g	1 sachet SOS 15 made up to 200ml with water*. 1 pre-measured sachet = 31g
Feeding volumes:	**For children >10 kg fluid requirements can be calculated as:** **11-20 kg:** 100ml/kg for the first 10 kg, plus 50ml/kg for the next 10 kg **>20 kg:** 100ml/kg for the first 10 kg, plus 50ml/kg for the next 10 kg, plus 25ml/kg thereafter up to a maximum of 2500ml/day				
Administration	Divide total volume over 24 hours: give 1 -2 hourly orally or tube feed (bolus or continuous)				