CLINICAL GUIDELINE	
Hypoglycaemia	
Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

For **Postnatal Ward** monitoring and management click **here**.

Asymptomatic hypoglycaemia is a common transient problem in most neonates. Symptomatic hypoglycaemia is an emergency and requires intravenous treatment.

Symptoms include:

- CNS excitation: irritability, jitteriness, seizures.
- CNS depression: Hypotonia, lethargy, poor feeding, apnoeas.
- Non-specific: temperature instability, sweating, tachycardia.

The fetus under normal conditions derives all its glucose from the mother. At birth all infants must initiate glucose production and absorption. Most are able to mobilise glycogen, initiate gluconeogenesis and produce glucose at a rate of 4 – 6 mg/kg/min. This is usually adequate to maintain euglycaemia - normal blood glucose.

The definition used at KEMH and PCH for hypoglycaemia is a blood glucose of < 2.6mmol/L.

Cause /Risk Factors for Hypoglycaemia

The cause/risk factors for hypoglycaemia can be divided into:

Inadequate supply or reduced glycogen stores	Increased utilisation	Hormone/metabolism imbalance
Prematurity Small for gestational age Poor feeding Tissued IV	Infection RDS Hypothermia Perinatal asphyxia Hypothermia Erythroblastosis foetalis	Persistent hyperinsulinaemic hypoglycaemia of infancy. Inborn errors of metabolism. Pancreatic tumour. Congenital adrenal hyperplasia. Hypopituitarism. **Syndromes:** Beckwith-Wiedemann.

Persistent or recurrent hypoglycaemia (≥ 2 episodes of hypoglycaemia) warrants further investigation. It is commonly caused by hyperinsulinism secondary to maternal diabetes however other differentials should be considered such as CAH, syndromes and inborn errors of metabolism.

Infants at Risk of Hypoglycaemia

It is important to explain to the parents of at-risk infants that their infant is more likely than others to develop hypoglycaemia, and that their infant will need close monitoring of blood glucose. Refer to "Quick reference guide" for management.

Infants at risk of hypoglycaemia that require early energy provision and BGL monitoring:

- Infants of mothers with diabetes (insulin-dependent, type 2 DM or GDM).
- Infants who are small for gestational age (< 10th percentile) refer to Appendix 1
- Preterm infants (<37 weeks gestation).
- Infants large for gestational age (>4.5kg or >97th centile) refer to Appendix 1
- Infants of mothers who received antenatal corticosteroids >34 weeks gestation.
- Infants of mothers who received beta blockers in the 3rd trimester.

Early Energy Provision - Within 1-2 Hours of Birth

- Offer early skin to skin under warm blankets.
- Encourage early first breast feed followed by 3 hourly feeds/more frequent if demanding.
- If poor breast feeding consider supplemented enteral feeding 3 hourly.
  - Start at 60/kg/day (7.5mL/kg/feed) if not contra-indicated.
- If enteral feeding is not possible then admit to NICU and give IV 10% Glucose.
  - Start at 60mL/kg/day (providing 4.2 mg/kg/min of glucose).

Glucose Monitoring of at Risk Infants
• Whole blood glucose (blood gas analyser) or plasma glucose (biochemistry lab) should be performed. Reagent strips should not be used for PGL monitoring for infants. • For at risk infants, first sample done pre-second feed (3-4 hours of age). • If infant feeding well and PGL ≥ 2.6mmol then repeat PGLs 6 hourly (pre-feed) – if 2 consecutive PGLs are ≥ 2.6mmol/L then stop regular monitoring and test only if infant becomes symptomatic

Investigation of Neonatal Hypoglycaemia – "Hypoglycaemia Screen"

If hypoglycaemia is persistent/recurrent (≥ 2 episodes), resistant to treatment, or glucose delivery rate is > 10mg/kg/min then investigate further (see below for hypoglycaemia screen).

Hypoglycaemia Screen
The critical blood samples **MUST** be collected at the time of hypoglycaemia, wherever safe prior to commencing supplementation: **DO NOT** administer sucrose before heel stab/ venepuncture.
• 1 mL of clotted blood and 1 mL of heparinised blood (2 small red top and 2 small green top tubes). Request insulin, cortisol, growth hormone, glucose, ketones or β-hydroxybutyrate. • Blood gas analysis: lactate. • The NEXT urine passed is important (aim for 5 mL urine). Request ketones, amino acids and organic acids.
Contact the Biochemical Genetics Unit for any queries regarding these investigations.

Management of Hypoglycaemia

Asymptomatic Infants with PGL 1.5-2.5mmol/L

Needs paediatric RMO/ registrar review - consider "hypoglycaemia screen" and need for admission to SCN.
Enteral Feeding
• Start enteral feeding at 60-80mL/kg/day if no contra-indications.
• If persistent or recurrent hypoglycaemia, then increase feed volume to 12.5mL/kg/feed (100ml/kg/day).
• Consider more regular feeds (2 hourly)
• Admit to SCN if:
  ◦ PGL remains between 1.5-2.5mmol/L despite the increased feeds.
  ◦ Infant is symptomatic (lethargic with inadequate feeds, seizure).
Parenteral Supplementation
• If unable to obtain IV access then consider glucagon (IM 100 micrograms/kg) and consider siting a UVC.
• Commence IV supplementation with 10% dextrose at 80-100mL/kg/day (5.6-7mg/kg/min).
  ◦ Consider bolus of 2mL/kg of 10% dextrose.
• Monitoring
  ◦ Repeat PGL after 30 minutes of treatment; if normal then check at 3 hours.
  ◦ If 30 minute and 3 hour PGL is normal then can monitor 3-6 hourly or as directed.

Asymptomatic Infants with PGL < 1.5mmol/L

Admit to SCN immediately for IV supplementation.
• Take hypoglycaemia screen (above) if it does not delay treatment significantly.
• Commence IV supplementation with 10% dextrose at 100mL/kg/day (7mg/kg/min).
  ◦ If unable to obtain IV access then consider glucagon (IM 100 micrograms/kg).
  ◦ Consider bolus of 2mL/kg of 10% dextrose.
  ◦ If hypoglycaemia continues then aim to increase GIR by 2-3mg/kg/min (Increase total fluids by 20-30mL/kg/day or increase dextrose concentration by 2.5-5%).
  ◦ If needing > 12.5% dextrose then central access (UVC) is required.
• Monitoring
  ◦ Recheck PGL at 30 minutely intervals until PGL is ≥ 2.6mmol/L.
  ◦ Once PGL is ≥ 2.6mmol/L then check 3 hourly.
  ◦ If 2 consecutive 3 hourly PGL is normal then can extend to 6 hourly PGLs.

Symptomatic Infants – Seizures, Reduced Consciousness

Admit to NICU for urgent IV supplementation
• Take hypoglycaemia screen if it does not delay treatment significantly.
• Commence IV supplementation with 10% dextrose at 100mL/kg/day (7mg/kg/min).
  ◦ If unable to obtain IV access then give glucagon (IM 100 micrograms/kg) and consider siting UVC.
  ◦ Give bolus of 2mL/kg of 10% dextrose; repeat until seizure has stopped.
• Monitoring
  ◦ Recheck PGL at 15-30 minutely intervals until PGL is ≥ 2.6mmol/L.
  ◦ Once PGL is ≥ 2.6mmol/L then check 3 hourly.
  ◦ If 2 consecutive 3 hourly PGL is normal then can extend to 6 hourly PGLs.

Persistent Hyperinsulinaemic Hypoglycaemia of Infancy (PHHI)

PHHI is commonly seen in infants born to a mother with gestational diabetes, however can occur in mothers with a normal glucose tolerance test. It is diagnosed by finding an elevated insulin level during a period of hypoglycaemia. Infants with PHHI may require a significantly higher glucose delivery rate of up to 10-12mg/kg/min.

Infant with PPHI requiring short term diazoxide:

- If glucose delivery rate > 10mg/kg/min and has unstable PGLs then consider diazoxide.
- Please discuss with endocrinology if patient is to commence on diazoxide.
- Once infant is ready for discharge then a prolonged fast is required (6 hours).
  - 3 hour pre-feed PGL, then hourly up to 6 hours.
  - If during the fast the PGL drops below 3.0mmol/L then a hypoglycaemia screen should be sent and endocrinology informed.

- Endocrinology should be informed of all babies that have received diazoxide and are being discharged home as they will organise a 6 week follow-up in their outpatient clinic.

Congenital Hyperinsulinism of Infancy (CHI)

Infants that cannot be weaned off diazoxide or have unstable PGLs on diazoxide may require further investigations to exclude CHI.

CHI is a clinically and genetically heterogeneous disease, is characterized by the unregulated secretion of insulin from pancreatic beta-cells. It is the commonest cause of PHHI. The most common and severe forms of CHI are caused by inactivating mutations in ABCC8 and KCNJ11 genes, encoding the two subunits of the pancreatic beta-cell ATP-sensitive potassium channel (KATP). There are two histopathological forms of CHI, **focal and diffuse**.

FDOPA Scan

An FDOPA scan may be required for work-up of an infant suspected to have a pancreatic/ ectopic source of inappropriate insulin secretion. 18F-FDOPA PET/CT is indicated for distinguishing between diffuse and focal disease, thus allowing focused surgical approaches to children with focal CHI. Diffuse HI requires a 95% or higher pancreatectomy with the subsequent increased risk of iatrogenic diabetes. In contrast, focal HI can be cured with the selective resection of the area of dysregulated insulin secretion

The decision to undertake an F-DOPA scan must be made in conjunction with endocrinology, neonatology and the parents. Parents will be counselled regarding the need and the logistical requirements. This will require transport to Sir Charles Gardiner hospital, central access for high concentration dextrose infusion that may require a general anaesthetic and likely a general anaesthetic for the scan as the infant is required to be still.

Protocol for F-DOPA scan (Please see Appendix A for full F-DOPA information)

1. Inform consent from parents is required for the F-DOPA scan; central access and anaesthetic.
2. Contact SCGH nuclear medicine scan to organise date (Dr Nelson Loh).
3. Contact anaesthetic department and submit off-site anaesthetic request.
4. Inform NETS WA team to organise scheduled transport (Fellow and nurse are required).
5. Protocol prior to scan:
   a) Insertion of central access 3-4 days prior to scan.
   b) Glucagon must be stopped for 48 hours.
   c) Octreotide and diazoxide ideally should be ceased however may be continued if clinician feels it is unsafe to cease.
   d) Prescribe high concentration dextrose to maintain PGL > 3mmol/L.
   e) Low-protein diet: TPN should be avoided for 12 hours before the procedure. Patient can have milk feeds (up until the anaesthetic fast) and IV glucose.
   f) Bladder catheterisation: there is renal/urinary excretion of F-DOPA- if an ectopic focus is being pursued, IDC in situ is required.
   g) 6 hour fast prior to scan is required.

Follow-up for Infants with Evidence of Hypoglycaemia

All infants who have been symptomatic or had persistent asymptomatic hypoglycaemia need follow up, the intensity of which needs to be graded to the severity. Discuss with Neonatologist. An MRI of the brain should be considered for all infants with severe and/or prolonged hypoglycaemia, or who developed hypoglycaemic seizures.

AT-RISK INFANT

(GDM, PRETERM < 37 weeks, SGA, LGA, antenatal steroids >34 weeks, maternal beta blockers)

Early enteral feed (< 1hr of age)

- Breastfeed within 1st hour OR term formula 7.5mL/kg if not planning to breastfeed
- Feed 3 hourly or more frequently if demanding
- Perform pre 2nd feed PGL at next feed (3-4hrs)

RANDOM PGL < 2.6mmol/L AND NO RISK FACTOR

- Contact RMO, reg, SR or ward consultant for individual plan

PRE-FEED PGL

< 2.0mmol/L or symptomatic

- Contact RMO, reg, SR or ward consultant for individual plan
- Consider admission to SCN
- If PGL<1.5mmol/L then admit to SCN

2.0-2.5mmol/L

(Inform paed if > 2 episodes in 24 hrs)

Breastfed Baby
Glucose gel 0.5mL/kg and Breastfeed

If inadequate breastfeeding then give 7.5mL/kg term formula.

Formula fed Baby
Contact Paediatric RMO or registrar

Give 7.5mL/kg of term formula.

Repeat PGL in 30 minutes

Repeat PGL in 1 hour

PGL < 2.6 mmol/L

- Contact RMO, reg, SR or consultant for individual plan
- Consider increasing feeds to 10-12.5mL/kg.
- If <2.0mmol/L, consider admission to SCN

PGL ≥2.6mmol/L

- Continue with current management

Pre next feed PGL

PGL ≥ 2.6mmol/L

PGL prior to every 2nd feed (6 hourly)

PGL ≥ 2.6mmol/L on 2 consecutive occasions

Cease monitoring

Related CAHS internal policies, procedures and guidelines
Neonatal Medication Protocols - • Diazoxide • Glucagon

References and related external legislation, policies, and guidelines
1. WHO, 1997 – Hypoglycaemia of the Newborn Review of the literature. WHO Geneva. 2. Akerblom H.K. Savilahti E. Vaarala O1996 Cows milk protein and insulin-dependent diabetes mellitus. Scandinav Journ of Nutrition 3. Hawdon J M. Aynsley-Green A. (1999) Disorders of blood glucose homeostasis in the neonate in Textbook of Neonatology 3rd edition p947. 4. Vogel A. Hutchison BL. Mitchell EA. 1999. Factors associated with the duration of breastfeeding. Acta Paediactrica. 88:12: 1320-6. 5. Arthur, P.G., Kent, J. and Hartmann, P.E. (1994). Metabolites of lactose synthesis in milk from diabetic and non diabetic women during lactogenesis II. Journal of Paediatric Gastroenterology and Nutrition. 19 pp 100-108. 6. http://www.cps.ca/english/statements/FN/fn04-01.htm 7. Harris DL, Weston PJ, Battin MR, Harding JE. The sugar babies study, A RCT of dextrose gel for treatment of neonatal hypoglycemia; J of Paed and child health 47, (Supplement 1) 2011, 8-59

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Document Owner:	Neonatology		
Reviewer / Team:	Neonatal Coordinating Group		
Date First Issued:	July 2006	Last Reviewed:	September 2018
Amendment Dates:	5th February 2021	Next Review Date:	6th September 2021
Approved by:	Neonatal Coordinating Group	Date:	6th September 2018
Endorsed by:	Neonatal Coordinating Group	Date:	
Standards Applicable:	NSQHS Standards:  Child Safe Standards: 1,10		

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Appendix 1

Centile Chart for Hypoglycaemia

Birth weight of term babies at the **10th centile**			Birth weight of term babies at the **97th centile**	
Male (weight)	Female (weight)	**Gestation (weeks)**	Male (weight)	Female (weight)
1900	1800	**35**	3280	3200
2170	2050	**36**	3550	3500
2400	2300	**37**	3800	3800
2600	2500	**38**	4020	4020
2800	2650	**39**	4280	4250
3000	2800	**40**	4500	4450
3200	3000	**41**	4750	4680
3400	3150	**42**	5020	4920