CLINICAL PRACTICE GUIDELINE
Guideline coverage includes NICU KEMH, NICU PMH and NETS WA

Hypoglycaemia

This document should be read in conjunction with the Disclaimer

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 foetus 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 PMH for hypoglycaemia is a blood glucose level (BGL) < 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 PIV	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.

Investigation of Neonatal Hypoglycaemia – "Hypoglycaemia Screen"

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

If the decision is made to investigate a neonate for unexplained or persistent hypoglycaemia then a "hypoglycaemia screen" should be performed.

Hypoglycaemia Screen
The blood samples **MUST** be collected at the time of hypoglycaemia, wherever safe prior to commencing supplementation:
• 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.

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 postnatal ward "Quick reference guide" for management.

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

- Infants of mother's with diabetes (insulin-dependent, type 2 DM or GDM).
- Infants that are small for gestational age (below the 10th percentile).
- Preterm infants (less than 37 weeks gestation).
- Infants of mother's that have received antenatal corticosteroids (regardless of gestation).

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 60-80mL/kg/day or 12.5mL/kg/feed if not contra-indicated.
- If enteral feeding is not possible then admit to NICU and give IV 10% Glucose.
  - Start at 60-80mL/kg/day (providing 4.9 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. • Please follow appropriate postnatal ward or SCN flowchart. • 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

Management of Hypoglycaemia

Asymptomatic Infants with PGL 1.5-2.5mmol/L

Needs paediatric registrar review - consider "hypoglycaemia screen" and need for admission to SCN.

Enterally Feeding

- Start enteral feeding at 60-80mL/kg/day if no contra-indications.
- If persistent or recurrent then increase feed volume to 15mL/kg/feed.
  - Provides GIR of 7 mg/kg/min; total fluids 120mL/kg/day.
  - Consider more regular feeds (2 hourly).
  - If no contraindications then feeds can be fortified.
- Admit to NICU if:
  - PGL remains between 1.5-2.5mmol/L despite the increased feeds to 15mL/kg/feed.
  - Infant is symptomatic (lethargic with inadequate feeds, seizure).

Parenteral Supplementation

- If unable to obtain IV access then consider glucagon (IM 100 micrograms/kg) and UVC.
- Commence IV supplementation with 10% dextrose at 80-100mL/kg/day (5.6-7mg/kg/hr).
  - Consider bolus of 2mL/kg of 10% dextrose.
- Monitoring
  - Repeat BGL after 30 minutes of treatment; if normal then check at 3 hours.
  - If 30 minute and 3 hour BGL is normal then can monitor 3-6 hourly or as directed.

Asymptomatic Infants with PGL < 1.5mmol/L

Admit to NICU if on the PNW immediately for IV supplementation.

- Take "hypoglycaemia screen" (above) if it does not delay treatment significantly.
- Commence IV supplementation with 10% dextrose at 100-120mL/kg/day (7-8.3mg/kg/hr).
  - 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 is required.
- Monitoring
  - Recheck BGL at 30 minutely intervals until PGL is ≥ 2.6mmol/L.
  - Once BGL is ≥ 2.6mmol/L then check 3 hourly.
  - If 2 consecutive 3 hourly BGL is normal then can extend to 6 hourly BGLs.

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 100-120mL/kg/day (7-8.3mg/kg/hr).
  ◦ If unable to obtain IV access then consider glucagon (IM 100 micrograms/kg).
  ◦ Given 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 BGL is ≥ 2.6mmol/L then check 3 hourly.
  ◦ If 2 consecutive 3 hourly BGL is normal then can extend to 6 hourly BGLs.

Persistent Hyperinsulinaemic Hypoglycaemia of Infancy (PHHI)

PHHI is commonly seen in infants born to a mother with gestational diabetes, however can occur in mother's 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 GIR of up to 10-12mg/kg/min.

Infant with PPHI requiring short term diazoxide:

- If GIR > 10mg/kg/min and has unstable BGLs 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.
  - An infant has passed if all PGLs are ≥ 3.0mmol/L.
  - 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 BGLs 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**.

The rationale behind the use of PET techniques in the context of focal HI is that **focal lesions contain a concentrated number of beta cells** (secondary to adenomatous hyperplasia), so the area of the focal lesion generates a stronger gamma-ray signal compared to the rest of the pancreas, where the beta cells are not concentrated. Focal lesions are then seen as bright spots over a darker background,

whereas cases of **diffuse disease show homogeneous distribution of the tracer** throughout the pancreas (see INTERPRETATION). Case reports have indicated that this technique is able to detect **ectopic foci of pancreatic beta cells**.

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.

FDOPA Scan

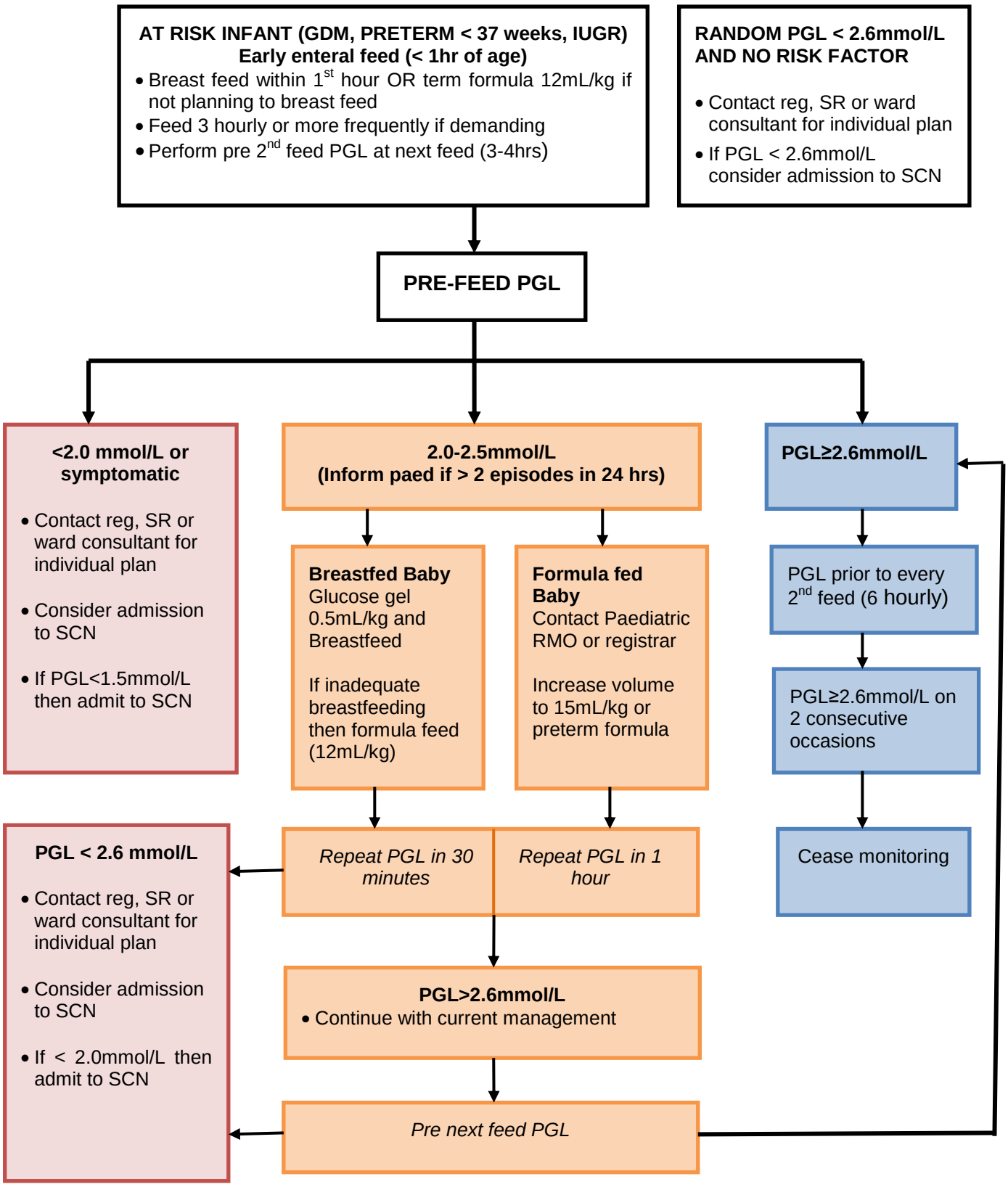
An FDOPA scan may be required for work-up of an infant suspected to have a pancreatic/ectopic source for inappropriate insulin secretion. The decision to undertake and F-DOPA scan must be made in conjunction with endocrinology, neonatology and the parents. Parents will be counselled regarding the need and the logistical requirements for an F-DOPA scan. This will require a 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 F-DOPA 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 that affects beta cell activity 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 BGL > 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.



Pink boxes: infants require an individualised plan as they have moderate to severe hypoglycaemia or they have not responded well to intervention (glucose gel, increased calories).
Orange boxes: intervention is divided into breastfed babies and formula fed babies.

Note: if more than 2 pre-feed PGLs are < 2.6mmol/L in a 24 hour period, please inform paediatric team.

References

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Related WNHS policies, procedures and guidelines

Neonatal Medication Protocols - Diazoxide
- Glucagon

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