HYPOGLYCAEMIA RISK MANAGEMENT FOR NEWBORNS

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Background

Glucose is an essential substrate for brain function and development. Hypoglycaemia is defined as a low blood glucose level (BGL). Healthy term babies experience a normal physiological decline in BGL during the first 2 hours of life. Thereafter the BGL rises steadily until homeostasis is reached at about 3 - 4 hours after birth. An early low BGL in the majority of healthy, well-grown, term newborns is not pathological and likely reflects normal metabolic adaptation.

Prolonged, recurrent, or severe hypoglycaemia may however cause acute systemic effects and long-term neurological sequelae. There is uncertainty regarding the level and duration of hypoglycaemia that causes long-term sequelae, and the tolerance level that may exist at differing gestations. It remains unclear whether asymptomatic hypoglycaemia is associated with long-term sequelae.

BGL measurement is targeted to those with risk factors for hypoglycaemia.

RHH Postnatal Ward / NPICU risk stratification:

1. Postnatal Ward management (i.e. medium risk), Chart 1 & 2
2. Infants for management in NPICU or SCN (i.e. high risk), Chart 1 & 3

- Interpret BGL results carefully as they cannot accurately predict ongoing hypoglycaemia.
- Adherence to a strict early feeding regimen, when appropriate, is essential.
- Recognize signs suggestive of hypoglycaemia - such infants should be considered unwell/symptomatic and managed accordingly (see Chart 1).

Hypoglycaemia can often be prevented or minimized by early feeding and avoiding hypothermia. Encourage early skin-to-skin contact, monitor the baby’s temperature closely and nurse baby in an incubator if required.
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Chart 1 - Care Pathway

Maternal diabetes  
All types

- Poor recent diabetic control*
- IV glucose during labour
- GA less than 37 weeks
- Small or large for GA†
- Low birth weight (< 2.5 kg)
- Wasted‡

Small for GA†, wasted# or macrosomic¥

- Less than 2 kg
- Macrosomia¥

Preterm, less than 37 weeks GA

- Less than 34 weeks
- Less than 2 kg

Symptomatic/unwell, or other risks

- Unwell, ‘symptomatic’:
  - Poor sucking/feeding£
  - Excessive jitteriness, tremors or seizures
  - Irritability
  - Hypotonia, lethargy
  - Hypothermia
  - Agnoea, cyanosis
  - Respiratory distress
  - Peripartum asphyxia
  - Sepsis
  - Maternal drugs, eg. β-blockers
  - Risk of metabolic disease
  - Beckwith-Wiedemann syndrome (BWS)‡
  - Other medical reason

No to all

Yes to any

1st FEED WITHIN 1st HR OF LIFE & 1ST BGL AT 4 HRS OF LIFE
  - See Chart 2 - Postnatal Ward management

REVIEW BY NICU REGISTRAR/ADMIT TO SCN or NICU, WITH 1st BGL BY 1 HR OF LIFE (EARLIER IF UNWELL)

- Early feed if clinically appropriate
- See Chart 3: NICU/SCN management of term/near term babies

GA = Gestational age
*Poor diabetic control may be defined by 34:
  - most recent HbA1c greater than 7.5%
  - Recent BGLs greater than 8 mmol/L (including during labour)
†Small (<10th centile) and large (>90th centile) for GA thresholds: see Chart 4
#Wasted = poor fat stores regardless of birth weight
¥Macrosomia: babies resembling ‘infants of diabetic mothers’ in the absence of maternal diabetes- increased subcutaneous fat stores, plethoric (i.e. polycythaemic) appearance, small head relative to body size. Macrosomic babies may or may not be large for gestational age
£Poor feeding: e.g. babies not demand feeding, babies demanding fewer than 3 feeds in the first 24 hours.
‡Beckwith-Wiedemann syndrome (BWS): often large for gestational age, may exhibit exomphalos & macroGLOSSIA – refer if suspected.
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Chart 2 – Postnatal Ward Management

**Chart 2 – POSTNATAL WARD MANAGEMENT - BABY AT RISK OF HYPOGLYCAEMIA** (see Chart 1 for criteria)

- **BGL < 1.5 mmol/L, or unwell**
  - Call NPICU Reg/SRMO immediately
  - Admit to SCN/NPICU (see Chart 3)

- **BGL 1.5 – 2 mmol/L, well**
  - Immediate complementary feed 5-10 mL/kg (EBM &/or formula)
  - Repeat BGL 1 hour after complementary feed

- **BGL > 2 mmol/L*, well**
  - Feed 3-4 hourly (breast, formula, complementary &/or nasogastric) with pre-feed BGLs
  - Consult NPICU Reg/SRMO if BGL 2-2.5 mmol/L beyond 24 hrs of life

- **TBGL ≤ 2 mmol/L**
  - Notify NPICU Reg/SRMO
  - Perform TBGL

- **Cease BGLs when:**
  - 3 consecutive BGLs > 2.5 mmol/L and baby feeding well

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*BGL = True blood glucose level, via NPICU blood gas machine or laboratory.

*BGLs of 2-2.5 mmol/L are acceptable in the first 24 hours only, in well babies in whom postnatal ward management is indicated
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Chart 3 – NPICU / SCN Management

- Aim for admission to NPICU/SCN within 1st hour of life
- True blood glucose level (TBGL) by 1 hour of life + avoid hypothermia
- Attempt to complement breast feeds with EBM/formula 30-60 mL/kg/day (term/ near-term babies)

TBGL < 1.5 mmol/L
- Notify NPICU Reg/RMO
- Bolus 2-3 mL/kg IV 10% dextrose*
- IV dextrose infusion 60-90 mL/kg/day
- Consider NG feed if IV delayed
- Discuss management with NPICU Senior Reg/Consultant if ongoing TBGL < 2.5 mmol/L

TBGL 1.5-2.5 mmol/L
- Notify NPICU Reg/RMO
- Feed 2 hourly
- Complement breast feeds with EBM/formula volume of 60 mL/kg/day (Day 0, term/near term babies), if tolerated

TBGL > 2.5 mmol/L
- Early breast feeding (+/- complement feeds), or formula
- Feed 3 hourly, 60 mL/kg/day (term/near term babies)
- Aim for TBGL > 2.5 mmol/L
- Change to 3 hourly feeds after 24 hrs if TBGL > 2.5 mmol/L
- If next pre-feed TBGL 1.5-2.5 mmol/L, increase feeds to 90 mL/kg/day, if tolerated.
- If subsequent TBGL 1.5-2.5 mmol/L, commence IV dextrose.
- Consider transfer to Postnatal Ward when 3 consecutive pre-feed TBGL > 2.5 mmol/L and sucking all feeds well. BGLs may be ceased in this context

*Avoid repeated boluses of 10% dextrose as this may induce rebound hypoglycaemia
Chart 4 – Small and large for gestational age thresholds
(from Fenton, BMC Pediatrics 2003; 3:13 – Revised Babson and Benda Chart; as used in the RHH NPICU)

<table>
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<tr>
<th>Gestation (weeks)</th>
<th>Small for gestational age (&lt; 10th centile)</th>
<th>Large for gestational age (&gt; 90th centile)</th>
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<tr>
<td>41</td>
<td>&lt; 3100 g</td>
<td>&gt; 4400 g</td>
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<td>&gt; 3300 g</td>
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<tr>
<td>35</td>
<td>&lt; 2000 g</td>
<td>&gt; 3000 g</td>
</tr>
</tbody>
</table>

Objective
To provide optimal BGL management in the Labour Ward, the Postnatal Ward, NPICU and the Special Care Nursery (SCN) in infants at risk of hypoglycaemia.

Definition of hypoglycaemia and operational thresholds
As clinically important hypoglycaemia cannot be precisely defined pragmatic operational thresholds, are recommended to guide therapy in order to keep babies in a safe BGL range.

The most commonly used operational threshold for symptomatic hypoglycaemia is to maintain a BGL of greater than 2.5 mmol/L. For at risk but well term or near-term infants some units favour...
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an operational threshold of greater than 2 mmol/L in the first 24 hours. The World Health Organisation recommends that asymptomatic preterm babies maintain a BGL greater than 2.5 mmol/L (Lucas et al\textsuperscript{11}). BGL varies before and after feeding. Our unit accepts a pre-feed BGL greater than 2 mmol/L within the first 24 hours of life for well babies that are appropriate for Postnatal Ward management.\textsuperscript{12,13} A BGL operational threshold of greater than 2.5 mmol/L is generally appropriate for all other babies.

RHH operational safe thresholds for newborns:
- Well babies less than 24 hours old and appropriate for Postnatal Ward management (see Chart 1): BGL greater than 2 mmol/L
- All other newborns: BGL greater than 2.5 mmol/L

A low BGL in at risk newborns is most likely to occur within the first 24 hours of life.

The following should be avoided if possible, or treated aggressively if they occur, to reduce the risk of neurological sequelae:
- BGL less than 1.5 mmol/L
- Clinical signs of hypoglycemia
- Prolonged hypoglycemia (greater than 4 hours)
- Recurrent hypoglycemia (if more than 1 episode, consider uncommon causes)
- Ongoing clinical signs despite normalized BGL (consider alternative diagnoses)

Ultimately, BGLs of greater than 2.5 mmol/L (preferably BGL greater than or equal to 3 mmol/L) are targeted once treatment is commenced for neonatal hypoglycaemia.

**Diagnosis**

A clinical diagnosis of hypoglycaemia can be difficult and is often missed. Therefore it is essential that all infants:
- at risk of hypoglycaemia, or
- with clinical signs suggestive of hypoglycaemia,

are fed early whenever possible and are tested with bedside blood glucose monitoring (glucometer); see Chart 1.

**SIGNS OF HYPOGLYCAEMIA**

Neonatal hypoglycaemia may manifest with a range of non-specific symptoms (see Chart 1).
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Babies at risk of hypoglycaemia (Charts 1 - 4)

A wide range of factors may cause deviations in the normal postnatal adaptive response of glucose homoeostasis (see Chart 1).

ADDITIONAL EXPLANATORY NOTES TO CHARTS

- **Infants of mothers with poorly controlled diabetes mellitus** are at **highest risk**. These babies are often macrosomic with associated increased subcutaneous fat, plethora and a small head in relation to body size. They may also be growth restricted.

- **Small for gestational age** (SGA) or **low birth weight** (< 2500 g): In the absence of other risk factors or symptoms, a baby must have a birth weight of at least 2 kg to be considered appropriate for Postnatal Ward management.

- **Macrosomic infants**:
  - Macrosomic ('large bodied') babies resemble 'infants of diabetic mothers' in the absence of maternal diabetes; they have increased subcutaneous fat stores, plethora (secondary to polycythaemia) and small head relative to body size (refer to birth centile chart). This appearance is suggestive of hyperinsulinism. Most, but not all macrosomic infants are large for gestational age (LGA - see Table 4 above).

  These babies may include:
  - Babies born to mothers who did not have a diabetic screening test during the pregnancy (i.e. possible missed diagnosis of gestational diabetes).
  - Babies born to mothers who were normal on antenatal testing for diabetes but with clinical features resembling 'the infant of a diabetic mother' (see above). This group includes those babies with primary hyperinsulinism (rare).

- **Beckwith-Wiedemann syndrome**:
  - Often large for gestational age, hyperinsulinism, exomphalos, macroglossia and other signs.

Decisions as to where 'at risk' infants are monitored, whether admission to NPICU/SCN is warranted, how they are treated and whether feeds can be started should be made in consultation with the NPICU medical team. Some signs such as initial poor feeding or excessive jitteriness may not of course necessitate admission to NPICU/SCN in an otherwise well baby. They should however be discussed with and reviewed by the NPICU Registrar.

See also: [Neonatal and Paediatric ICU, Tasmania – Admission Guideline P&N-1-0015](#)
Testing method

The gold standard measurement for blood glucose levels is a laboratory performed enzymatic determination (e.g. hexokinase or glucose-oxidase method). Blood gas analyzers can also measure BGL and they are as accurate and reliable as the laboratory test.

For practical reasons, bedside glucometers are now established in clinical practice. Most devices read less accurately at lower BGLs. Deviations can be between 0.2-0.6 mmol/L when true blood glucose levels are between 2.0 and 2.6 mmol/L. Glucometers usually overestimate the true blood glucose level (i.e. they tend to read falsely high rather than falsely low). This should be taken into consideration. Glucometers should be calibrated regularly.

The RHH Maternity unit and the NPICU/SCN use the ‘Nova Express – i’ beside glucometer. This guideline takes into consideration the characteristics of this device.

If a glucometer reads 2 mmol/L or less, it must be acted upon and a BGL must be repeated with a more reliable method (via the blood gas analyzer in NPICU or a blood glucose sample sent to the main laboratory).

Principles of management

EARLY FEEDING, BGL MONITORING, SUPPLEMENTATION

1. Early feeding, preferably exclusive breastfeeding, is often sufficient to meet the nutritional needs of the infant at risk of hypoglycaemia. For these infants early energy provision (within 1 hour of delivery) is of vital importance. If the baby is medically well enough to stay with the mother then skin-to-skin contact for as long as possible and assistance with the first feed should be the usual plan. The nursing staff assisting in these initial steps must ensure that the baby is demonstrating an efficient suck and swallow and therefore that feeding is nutritive. If non-nutritive sucking is evident, express and administer available expressed breast milk (EBM).

2. For babies monitored on the Maternity Ward the first BGL should be measured before the second feed, at around 4 hours of life, 2-3 hours after the first feed (but not prior to 2 hours of age unless the baby is symptomatic/unwell). High risk infants being monitored in the NPICU should have a BGL checked within the first hour of life.

3. During the first 2-3 days of life all infants at risk should be fed every 3 hours (8 times per day) if this is not contraindicated.

4. For breast fed infants with hypoglycaemia:

   - Supplementation is recommended in the first instance with EBM if available, or with formula if breast milk alone is unable to achieve and maintain acceptable BGLs.
Supplementation in the first 24 hours should equate to approximately 30 – 60 mL/kg/day, but may be increased to 90 mL/kg/day (if tolerated) if hypoglycaemia persists. Parental consent must be requested before supplementation with formula. It is important to emphasize to mothers that such supplementation is only considered a temporary measure and that breastfeeding and/or provision of expressed breast milk remains the ultimate goal.

5. Babies at risk should be fed when they show signs of hunger but should not be allowed to wait more than 3 hours between feeds.

6. BGLs should continue to be measured pre-feeds, until there are 3 consecutive pre-feed BGL measurements greater than 2.5 mmol/L and the baby is feeding well.

7. In the case of feeding difficulties due to a weak suck/swallow or anatomical problems, expressed breast milk (preferred) or formula may need to be administered via a nasogastric feeding tube. Early involvement of a lactation consultant and review by the NPICU Registrar is recommended. Admission to the Special Care Nursery and further investigation should be considered.

8. After BGL monitoring has been ceased the baby should continue to be monitored to ensure they continue to feed well and show no clinical signs suggestive of hypoglycaemia.

9. Those babies requiring treatment for hypoglycaemia should be observed in hospital for a minimum of 48 hours and not discharged home until BGL monitoring is ceased and they are feeding well.

10. Infants with symptomatic hypoglycaemia (see above) must be treated immediately and require admission to NPICU/SCN depending on the severity of the symptoms and the level of BGL (i.e. below 1.5 mmol/L). Inform the NPICU Pediatric team urgently.

Investigation of neonatal hypoglycaemia

When the cause of neonatal hypoglycaemia is not readily apparent in cases that are severe, refractory to treatment, or require prolonged infusion of high doses of dextrose (e.g. greater than 10 mg/kg/min), further investigations may be considered in discussion with the senior NPICU Registrar and/or the on-call NPICU Consultant. In this setting, when the true blood glucose is less than 2 mmol/L, test:

- Urine
  - ketones

- Blood:
  - laboratory (or blood gas machine) true blood glucose
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- insulin
- growth hormone
- cortisol
- free fatty acids

References


7. Stocker, M (Ed), (2007) “Care of the Newborn infant ≥34 0/7 gestational weeks with increased risk or occurrence of hypoglycaemia in the delivery suite and on the maternity ward”, Swiss Society of Neonatology Guidelines http://www.neonet.ch


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Key words

1. Glucose
2. BGL
3. BSL
4. blood glucose
5. Infants