Key points
- Hypoglycaemia is defined as a true blood glucose (TBG) concentration < 2.6 mmol/L and should always be treated
- Newborns are screened for hypoglycaemia based on risk factors, starting at 1-2 hours after birth
- TBG should be used in preference to a blood sugar level (BSL) when available, and for ongoing screening in all infants who have had a BSL < 2.6mmol/L.
- 40% oral glucose gel rubbed into the buccal mucosa is the first-line treatment for hypoglycaemia in well newborns ≥ 34 weeks’ gestation
- An episode of hypoglycaemia should last no longer than 2 hours without medical evaluation

1. Purpose
This guideline outlines the requirement for management of hypoglycaemia in newborn infants at the Women’s. Where processes differ between campuses, those that refer to the Sandringham campus are differentiated by pink text or have the heading Sandringham campus.

2. Definitions
**Hypoglycaemia:** TBG < 2.6 mmol/L

**Clinical signs** which suggest clinically significant hypoglycaemia are non-specific and include jitteriness, irritability, high pitched cry, cyanotic episodes, apnoea, seizures, lethargy, hypothermia, hypotonia or altered or poor feeding. Most babies with hypoglycaemia will have no clinical signs.

**True Blood Glucose (TBG):** as measured by the glucose-oxidase method on a blood gas analyser in NICU, an iSTAT on the postnatal wards/ birth centre or SCN, or by laboratory measurement.

**Blood Sugar Level (BSL):** as measured using a non-glucose oxidase method with a blood glucose monitor and reagent strips in birth centre and postnatal wards. These measurements are less accurate at lower BSL. Therefore a TBG should be performed for any BSL < 2.6 mmol/L.

3. Responsibilities
All medical and nursing/midwifery staff caring for newborn infants.

4. Guideline
Neonatal hypoglycaemia is common, preventable and can both cause and potentiate neonatal brain injury. Although there is ongoing debate regarding the lowest threshold of blood glucose concentration that is considered safe, emerging evidence shows that even single episodes of hypoglycaemia in the neonatal period may be associated with adverse learning outcomes, with a dose-dependent relationship between severe hypoglycaemia and impaired executive function and visual-motor outcomes. In well, term infants, the normal post-partum blood glucose nadir occurs at ~ 90 minutes, with mean minimum blood glucose concentrations of 3.3 mmol/L.

Currently, intermittent TBG monitoring is the only method to screen babies for hypoglycaemia, but may miss up to 25% of hypoglycaemic episodes in at risk infants. The use of an enzymatic method to evaluate all blood glucose concentrations reduces the number of false-positive and false-negative results for hypoglycaemia, and decreases the number of repeat heel-prick tests required. TBG should be used in preference to a BSL when available, and for ongoing screening in all infants who have had a BSL < 2.6mmol/L.
4.1 **Identification of infants who require screening for hypoglycaemia**

Do not measure blood glucose levels in well, term infants.

Infants who have one or more of the following risk factors require screening for hypoglycaemia:

- All low birthweight infants (< 2,500g), regardless of gestation
- All preterm infants (< 37 weeks’ gestation)
- Small for gestational age infants (< 10th centile), as per table 1
- Macrosomic or large for gestational age infants (> 90th centile), as per table 1
- Infants of mothers with type 1, type 2 or gestational diabetes
- Infants of mothers treated with β-blockers
- Infants with clinical signs of hypoglycaemia
- Infants with poor feeding or limited/no enteral intake
- Unwell infants (including birth asphyxia, sepsis, polycythaemia)

<table>
<thead>
<tr>
<th>Birth gestation (completed weeks)</th>
<th>10th centile (grams)</th>
<th>90th centile (grams)</th>
</tr>
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<td>4200</td>
</tr>
<tr>
<td>41</td>
<td>3100</td>
<td>4400</td>
</tr>
</tbody>
</table>

4.2 **Management of infants with risk factors for hypoglycaemia**

All newborns with risk factors for hypoglycaemia should be offered a breastfeed within 1 hour of birth, then at least 3-hourly.

- Infants of mothers who choose to formula feed should be offered the equivalent of 60ml/kg/day
- Infants who are unable to feed enterally, for any reason, should have IV access obtained and intravenous glucose/nutrition commenced within 1 hour of birth

Infants with > 2 risk factors for hypoglycaemia are at increased risk of severe hypoglycaemia and should be referred to the neonatal RMO/ paediatrician after birth and assessed for potential NICU/ SCN admission.

4.3 **Screening newborns at risk for hypoglycaemia in birth centre and postnatal wards**

- BSL should be measured no more than 2 hours after birth in infants with risk factors for hypoglycaemia
- If BSL < 2.6 mmol/L at any time, ongoing measurement should be by TBG (blood gas analyser, iSTAT,)
- Measurement should continue prior to each feed (~Q3H) for 48 hours, or until 3 consecutive BSL/ TBGs ≥ 2.6 mmol/L and feeding is assessed as adequate
- Neonatal RMO/ paediatrician to review infants daily until discharged from neonatal/ paediatric care.
Infants managed for hypoglycaemia in the postnatal ward do not require routine neonatal outpatient follow-up.

4.4 Management of hypoglycaemia in birth centre and postnatal wards
Refer to Appendix 1.

Indications for NICU admission

- TBG < 1.5 mmol/L at any time
- TBG < 2.6 mmol/L 2 hours after initiation of treatment
- TBG < 2.6 mmol/L on ≥ 3 consecutive pre-feed samples
- Baby appears unwell

4.5 Management of infants with risk factors for, or diagnosis of hypoglycaemia, in NICU/SCN
All preterm infants (< 37 weeks’ gestation) are at risk of hypoglycaemia due to inadequate glycogen stores, inefficient or absent enteral feeding, blunted counter-regulatory responses to low blood glucose concentrations and transient hyperinsulinism resulting from perinatal stress (hypoxia, intrauterine growth restriction, etc). The normal post-birth blood glucose nadir occurs earlier with decreasing gestational age. For infants who are admitted to NICU/SCN with multiple risk factors for hypoglycaemia, and those who are in NICU/SCN due to other illnesses, hypoglycaemia may also be early and severe.

Prevention of hypoglycaemia

Provide an exogenous glucose source within one hour of birth
- Breastfeed/EBM
- Formula (with maternal consent and if medically appropriate)
- IV glucose

Ensure normothermia
Small, early enteral feeds may aid glucose regulation in very preterm infants

Screening for hypoglycaemia

All blood glucose measurements are TBG.

Measure TBG one hour after birth.

Screening should continue pre-feeds, or twice daily if on IV fluids with stable blood glucose:
- Screening may be discontinued when infant is on full enteral feeds with 3 consecutive TBG readings ≥ 2.6mmol/L
- Screening should be recommenced if the feeding regimen changes (e.g. transition from full top ups to exclusive breast feeds) or if the infant’s clinical condition changes

Note that infants born preterm are at increased risk of hypoglycaemia occurring beyond the usual 48 hour screening period.

Management of infants with risk factors for hypoglycaemia in NICU/SCN
Refer to Appendix 2.
Calculate and document IV glucose delivery rate in mg/kg/min

Continue enteral feeds as tolerated and support breastfeeding (do not make nil orally unless enteral feeding contraindicated).

Increase feeds gradually, reducing IV glucose infusion accordingly when TBG readings are stable (at least 2 consecutive readings ≥ 2.6mmol/L).

Infants on 3 hourly sucking feeds may be discharged to postnatal ward as soon as TBG ≥ 2.6 mmol/L on 3 consecutive occasions. If hypoglycaemia has occurred, complementary feeds after breastfeeding may be necessary for a day or two until maternal breastmilk supply is established.

Infants admitted to NICU/ SCN for management of hypoglycaemia should remain under neonatal/ paediatric care in the postnatal ward for at least 72 hours.

Only infants admitted to NICU/ SCN for management of hypoglycaemia who receive IV glucose for more than 3 days, and/or glucagon infusion, and/or diazoxide will be reviewed in the general neonatal outpatient clinic.

### 4.6 Complicated hypoglycaemia

#### Persistent hypoglycaemia

Persistent hypoglycaemia occurs when hypoglycaemia persists beyond 4 hours despite treatment, or where episodes of hypoglycaemia occur ≥ 3 times in 24 hours.

Persistent hypoglycaemia may reflect hyperinsulinism, inadequate availability of substrate or increased metabolic demand.

Management options include:

- **Increase glucose supply**
  - Increase frequency of enteral feeds (Q2H)
  - Increase TFI up to 90ml/kg/day (IVF only) or 120ml/kg/day (enteral as tolerated) on day 1
  - Increase concentration of delivered dextrose
    - 12.5% dextrose may be given via a peripheral venous cannula
    - 15% dextrose MUST be given via central venous line
  - Calculate glucose infusion rates using a glucose calculator

- **Glucagon**:
  - May be used as an intramuscular injection for the acute management of hypoglycaemia, or as a continuous infusion where hypoglycaemia is treatment resistant
  - Allows mobilisation of hepatic glycogen stores
  - Less likely to be useful in infants < 34 weeks (due to minimal glycogen stores) or infants >24 hours postnatal age with inadequate feeding (stores deplete within 24 hours).
  - Glucagon I.M. injection may be repeated once if initial response was good (TBG ≥ 2.6 mmol/L).
  - See Neonatal Medicines Information

Any baby in whom hypoglycaemia persists beyond postnatal day 3 should be investigated for other causes of hypoglycaemia (see 4.7 Investigations for aetiology of severe or prolonged hypoglycaemia).

**Hyperinsulinism**

Hyperinsulinism is a common, transient phenomenon in infants of diabetic mothers, but may also be seen in relation to other conditions such as Beckwith-Weidemann syndrome. Any infant requiring a glucose infusion...
rate of >10mg/kg/min should be investigated for hyperinsulinism.

Special considerations for infants with hyperinsulinism:

- Bolus enteral feeds may stimulate insulin release and cause paradoxical hypoglycaemia.
- Enteral feeds may need to be restricted to ~10% of total daily fluid allowance. Continue small enteral feeds where possible.
- Blood glucose concentrations should be maintained ≥ 3.3 mmol/L.
- Hyperinsulinism prevents the normal counterregulatory responses to hypoglycaemia and impairs production of alternative cerebral fuels.
- **Diazoxide** is an anti-hypoglycaemic agent which blocks glucose-mediated pancreatic insulin secretion. It should only be used after consultation with an endocrinologist. Further information can be found in Neonatal Medicines Information.

### 4.7 Investigations for aetiology of severe or prolonged hypoglycaemia

Most cases of neonatal hypoglycaemia are transient, related to aberrant metabolic transition from fetal to neonatal life. In cases where hypoglycaemia is prolonged (beyond 48-72 hours), severe (glucose infusion rate > 10mmol/kg/min) or associated with a dysmorphic infant, further investigations should be undertaken.

**Physical examination**

Omphalocoele, ear notching, hemihypertrophy, macrosomia (Beckwith-Wiedemann syndrome)

Micropenis, ambiguous genitalia, midline facial deformity (hypopituitarism, septo-optic dysplasia)

Dysmorphic features, especially facial midline defects

**Blood tests**

A hypoglycaemia screen may be performed to investigate the hormonal response to low blood glucose concentrations. This should be performed when TBG < 2.6 mmol/L (preferably < 2mmol/L) and is most useful if done more than 48 hours after birth. If there are concerns that hypoglycaemia may be the result of an inborn error of metabolism, ammonia, lactate and acyl-carnitine samples should be sent urgently regardless of TBG value. Discuss with neonatal consultant.

**Tier 1 investigations - venous or arterial samples** – to exclude hyperinsulinism and panhypopituitarism

- Paired insulin and glucose concentrations
- Cortisol
- Growth hormone
- Sodium, potassium (blood gas analyser)

If insulin secretion is not suppressed and the diagnosis of hyperinsulinism is established, continue to treat, in severe cases with input from the paediatric endocrinologists at RCH. Genetic testing for hyperinsulinsim (ABCC8, KCNJ11 and other gene mutations) may be considered in severe and persistent cases with a suggestive family history and/or ethnic background.

If the insulin concentration is suppressed, the diagnosis of hyperinsulinism is not established and tier 2 testing should be performed.

Any abnormal growth hormone or cortisol levels require tier 2 testing.

**Tier 2 investigations - to exclude panhypopituitarism and congenital adrenal hyperplasia:**

- 17-hydroxyprogesterone (17-OHP)
- Thyroid function (TSH and FT4)
- Urine osmolality and specific gravity
- Cranial ultrasound
- Eye examination by ophthalmologist
- Growth hormone and cortisol (if not already done with tier 1 testing)

**Tier 3 investigations – to exclude inborn errors of metabolism**

If hypoglycaemia persists despite normal 1st and 2nd line investigations, or where there are clinical features consistent with metabolic disease (encephalopathy, cardiomyopathy), the following tests should be performed without delay and advice sought from the RCH metabolic team:

- Ammonia level (free flowing sample)
- Lactate and pyruvate (arterial sample)
- Free fatty acids and acyl carnitine profile
- Triglyceride level
- Urine organic acids
- Urine metabolic screen, including reducing substances and ketones
- Plasma amino acids

Accelerated completion of the newborn screening test - call the VCGS screening laboratory and ask for the infant to be flagged as having a possible metabolic disorder. The metabolic screen will then be expedited.

5. **Evaluation, monitoring and reporting of compliance to this guideline**

Compliance to this guideline will be monitored via clinical incidents reported through VHIMS.

6. **References**


7. **Legislation/Regulations related to this guideline**

Not applicable.
8. Appendices
Appendix 1: Management of hypoglycaemia in birth centre/ postnatal wards.
Appendix 2: Management of infants in NICU/ SCN with hypoglycaemia or risk factors for hypoglycaemia
Appendix 3: Investigation pathway for causes of prolonged or severe hypoglycaemia
Appendix 1. Management of infants with hypoglycaemia in birth centre and postnatal wards

Infant identified as having risk factors for hypoglycaemia and hypoglycaemia screening initiated 1-2 hours after birth

Blood sugar level < 2.6 mmol/L

True blood glucose measure performed

**TBG < 1.5 mmol/L**
MET CALL / URGENT NEONATAL REVIEW
Give 0.5ml/kg 40% oral glucose gel
Admit to NICU/SCN for further treatment

**TBG 1.5 – 2.5 mmol/L**
Give 0.5ml/kg 40% oral glucose gel and offer a breast feed ± top up feed (EBM or 5-10 mls formula)

**TBG ≥ 2.6 mmol/L**
Continue to monitor TBG before feeds

Repeat TBG after 1 hour

**TBG < 1.5 mmol/L**
MET CALL / URGENT NEONATAL REVIEW
Give 0.5ml/kg 40% oral glucose gel
Admit to NICU/SCN for further treatment

**TBG 1.5 – 2.5 mmol/L**
Give 0.5ml/kg 40% oral glucose gel and offer a breast feed ± top up feed (EBM or 5-10 mls formula)

**TBG ≥ 2.6 mmol/L**
Continue to monitor TBG before feeds

Repeat TBG after 30 mins

**TBG < 2.0 mmol/L**
MET CALL / URGENT NEONATAL REVIEW
Admit to NICU/SCN for further treatment

**TBG 2.0 – 2.5 mmol/L**
Give a full feed (60ml/kg/d)
Neonatal medical assessment to arrange NICU/SCN admission (IV or NG required) and timing of next TBG

**TBG ≥ 2.6 mmol/L**
Continue to monitor TBG before feeds
Appendix 2. Management of infants in NICU/SCN with hypoglycaemia or risk factors for hypoglycaemia

Admission to NICU / SCN

- Unsuitable for enteral feeding or has failed hypoglycaemia treatment pathway (appendix 1)
  - Gain IV access
  - Start 10% glucose infusion

- TBG after 1 hour
  - TBG < 2.6 mmol/L
    - 2ml/kg 10% glucose bolus
    - Increase glucose delivery by 20ml/kg/day
    - Repeat TBG after 30 mins
  - TBG ≥ 2.6
    - Continue to monitor TBG before feeds / Q3-4 H

- TBG after 1 hour
  - TBG < 2.6 mmol/L
    - Give full 60ml/kg/d feed volume or 0.5 ml/kg 40% oral glucose gel (if ≥34 weeks’ gestation) or commence IV 10% glucose delivery
  - TBG ≥ 2.6
    - Continue to monitor TBG before feeds / Q3-4 H

- Breastfeed/NG if unable to suck
  - EBM as available or formula 60ml/kg/day

- Repeat TBG after 30 mins
  - TBG < 2.6 mmol/L
    - Give 0.5 ml/kg 40% oral glucose gel (if ≥ 34 weeks’ gestation) or commence IV 10% glucose delivery
  - TBG ≥ 2.6
    - Continue to monitor TBG before feeds / Q3-4 H

- TBG < 2.6 mmol/L
  - Commence IV 10% glucose delivery
  - Consider 2ml/kg 10% glucose bolus

- TBG < 2.6 mmol/L
  - Increase glucose delivery (increase volume or concentration of IV glucose)
  - Consider insertion of central line
  - Consider glucagon IM or infusion
  - Monitor glucose infusion rate
Appendix 3. Investigation pathway for causes of prolonged or severe hypoglycaemia

Hypoglycaemia
Assess antenatal risk factors (such as maternal metabolic disease/diabetes, IUGR). Assess clinical presentation: Risk for sepsis, polycthæmia, clinical signs of pituitary or adrenal disease, risk for metabolic disorders (encephalopathy, cardiac dysfunction, seizures).

- Glucose below 2.6 mmol/L despite treatment
- Glucose infusion rate more than 10 mg/kg/min
- Glucose infusion rate <=10 mg/kg/min but hypoglycaemia persists for 72 hours and unable to start weaning infusion rates
- Symptoms of Panhypopituitarism, Septo-Optic Dysplasia or Adrenal Hyperplasia
- Newborn with encephalopathy / seizures and/or poor cardiac function without clear cause.

TIER 1 TESTING
(Focus on diagnosis of Hyperinsulinism and screen for panhypopituitarism)

Insulin suppressed

NO

Treat the Hyperinsulinism

NO

Marked and prolonged hypoglycaemia

Consult with endocrinology for treatment and assess need for genetic testing (ABCC8, KCNJ11 etc.)

YES

TIER 2 TESTING
(Focus on panhypopituitarism and adrenal hyperplasia)

Tier 2 testing abnormal

NO

YES

TIER 3 TESTING
(Focus on metabolic disorders)

Tier 3 testing abnormal

NO

YES

Treat according to diagnosis

If hypoglycaemia still present and significant, review patient further with:
- Neonatologists
- Endocrinologists
- Geneticists
- Metabolic team

Discuss patient with neonatal consultant and consider contacting endocrinology team for advice