Newborn hypoglycaemia
Queensland Maternity and Neonatal Clinical Guideline: Newborn hypoglycaemia

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Hypoglycaemia and blood sugar level monitoring
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This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible to:

- Discuss care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes the use of interpreter services where necessary
- Advise consumers of their choice and ensure informed consent is obtained
- Provide care within scope of practice, meet all legislative requirements and maintain standards of professional conduct
- Apply standard precautions and additional precautions as necessary, when delivering care
- Document all care in accordance with mandatory and local requirements

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Flow chart: Newborn hypoglycaemia: prevention and detection

Preventative care for well newborns at risk for hypoglycaemia

For care associated with symptomatic hypoglycaemia and with BGL screening ≤ 2.6 refer to Management flow chart

Risk factors
- Preterm (< 37 weeks gestation)
- SGA (< 10th percentile)
- LBW (< 2500 grams)
- Maternal diabetes (IDM)
- LGA (> 90th percentile)/macrosomia
- Severe intrapartum asphyxia/ resuscitation at birth
- Polycythaemia
- Unwell babies (e.g. infection)
- Inadequate feeding
- Hypothermia or labile temperature
- Obvious syndromes
- Maternal drug therapy (e.g. β blocker)
- Family history of metabolic disorders

At birth
- Keep baby warm (36.5-37.2°C)
  - Dry baby
  - Early skin-to-skin contact
- Initiate early feeds within 30-60 minutes of birth
  - Support mother’s choice of newborn feeding
  - Gavage feeds if < 35 weeks
  - If enteral feeding is not possible or contraindicated:
    - Commence IVT 10% Glucose at 60 mL/kg/day (4.2 mg/kg/min) → Refer to Flow chart: Newborn hypoglycaemia BGL < 2.6
- Avoid separation of mother and baby
  - If no other indication, neonatal unit/SCN admission not required

Ongoing care
- Keep baby warm
- Further skin-to-skin contact
- Discuss preventative care with parents
  - Encourage mother to observe for feeding cues
- Pre-feed observations for minimum of 24 hours include:
  - Level of consciousness
  - Tone
  - Temperature
  - Respiration
  - Colour/perfusion
- Feeds:
  - At least 3 hourly or more frequently if baby demanding
- BGL:
  - Pre second feed – this should be within 2-3 hours of birth
  - Every 4-6 hours pre-feed

Fed effectively? No

Symptomatic or unwell?

Be proactive
- Breastfeeding babies:
  - Hand express, give colostrum/EBM
- BGL
  - At 2 hours of age
- Ongoing:
  - Keep warm
  - Skin-to-skin contact
  - Observations

BGL ≥ 2.6?

No

Symptomatic or unwell?

Yes

Yes

Medical review required
- If BGL ≥ 2.6 – consider other causes especially infection
- Commence IVT 10% Glucose at 60 mL/kg/day (4.2 mg/kg/min)

Referral to Management flow chart: Newborn hypoglycaemia: BGL < 2.6

Symptomatic or unwell?

No

BGL ≥ 2.6?

Yes

*All BGL measurements in mmol/L

Queensland Maternity and Neonatal Clinical Guideline: MN13.8-V4-R18 Newborn hypoglycaemia: Prevention and detection

Refer to online version, destroy printed copies after use
Flow chart: Newborn hypoglycaemia: management

**Newborn hypoglycaemia: BGL < 2.6**

- **BGL < 1.5 or unrecordable**
  - **Do not delay treatment**
    - Notify paediatric/medical staff
    - Confirm BGL < 2 with ABG machine or laboratory
    - Admit to neonatal unit
    - Consider diagnostic samples (e.g. hypoglycaemia screen)
    - **Urgent treatment with IVT**
      - 10% Glucose at 60 mL/kg/day (4.2 mg/kg/min) or as per age appropriate rate
    - Consider a 2 mL/kg bolus of 10% Glucose, if administered:
      - Increase back-ground IVT rate or concentration
    - **Comment IVT**, if not already infusing:
      - 10% Glucose at 60 mL/kg/day (4.2 mg/kg/min) or as per age appropriate rate
      - IM Glucagon (200 microgram/kg) if IV access delayed
    - Next BGL after 30 minutes
    - As required:
      - Increase IVT rate to 80 to 100 mL/kg/day
      - Risk of fluid overload (increase concentration rather than volume)
      - Max of 100 mL/kg/day on day 1 of life
      - BGL 30 minutes after IVT changes
    - Always calculate infused IV Glucose in mg/kg/min
    - BGL hourly until ≥ 2.6
    - Continue feeds if not contraindicated

- **BGL 1.5-2.5**
  - **Feed immediately**:
    - Give additional EBM (if available)/formula
    - Guide 60 mL/kg/day, i.e. 7.5 mL/kg/3 hours
    - If not enterally feeding proceed to **Comment IVT box**
    - Confirm BGL < 2 with ABG machine or laboratory
    - Notify paediatric/medical staff
    - BGL in 30-60 minutes

  - **BGL increased or is > 2?**
    - Yes
    - **Monitor BGL 4-6 hourly pre-feeds for the first 24 hours**
    - **BGL ≥ 2.6?**
      - Yes
      - **BGL ≥ 2.6 for 12 hours?**
        - Yes
        - **Reduce IV gradually as enteral feeds increase**
        - Check BGL pre-feed
        - **BGL ≥ 2.6 for 24 hours with enteral feeds and no IV Glucose**
        - **Discharge and follow-up**
          - As per underlying cause
          - Discuss with paediatrician/neonatologist
          - May require long term follow-up
          - Ensure BGL ≥ 2.6 for 3 consecutive normal feeds prior to discharge
      - No
      - **BGL ≥ 2.6?**
        - No
        - **BGL < 2.6?**
          - Yes
          - **BGL ≥ 2.6 for 12 hours?**
            - Yes
            - **Discharge and follow-up**
            - **As per underlying cause**
            - **Discuss with paediatrician/neonatologist**
            - **May require long term follow-up**
            - **Ensure BGL ≥ 2.6 for 3 consecutive normal feeds prior to discharge**
          - No
          - **BGL < 2.6?**
            - Yes
            - **BGL ≥ 2.6 for 24 hours with enteral feeds and no IV Glucose**
            - **Discharge and follow-up**
            - **As per underlying cause**
            - **Discuss with paediatrician/neonatologist**
            - **May require long term follow-up**
            - **Ensure BGL ≥ 2.6 for 3 consecutive normal feeds prior to discharge**
          - No
          - **BGL < 2.6?**
            - Yes
            - **BGL ≥ 2.6 for 24 hours with enteral feeds and no IV Glucose**
            - **Discharge and follow-up**
            - **As per underlying cause**
            - **Discuss with paediatrician/neonatologist**
            - **May require long term follow-up**
            - **Ensure BGL ≥ 2.6 for 3 consecutive normal feeds prior to discharge**

  - **Glucose > 10 mg/kg/min? and/or**
  - **Baby > 72 hours of age? and/or**
  - **BGL difficult to control?**
    - Yes
    - Refer to Level 6 neonatologist/paediatrician through RSQ
    - Ensure paediatric endocrinology consult
    - Collect diagnostic samples (e.g. hypoglycaemia screen), if not collected already
    - Consider **pharmacological intervention** in order of preference:
      - Glucagon: 10-20 microgram/kg/hour IV infusion
      - Hydrocortisone: 1-2 mg/kg 6 hourly IV or oral
      - Diazoxide: initial dose 5 mg/kg/dose bd oral
      - Hydrochlorothiazide: 1-2 mg/kg/dose bd oral
      - Octreotide: 2-5 micrograms/kg 6-8 hourly subcutaneous

*All BGL measurements in mmol/L*
Table 1.1

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABG</td>
<td>Arterial blood gas</td>
</tr>
<tr>
<td>AMH</td>
<td>Australian Medicines Handbook</td>
</tr>
<tr>
<td>bd</td>
<td>Twice a day</td>
</tr>
<tr>
<td>BGL</td>
<td>Blood glucose level</td>
</tr>
<tr>
<td>BNF</td>
<td>British National Formulary</td>
</tr>
<tr>
<td>EBM</td>
<td>Expressed breast milk</td>
</tr>
<tr>
<td>EDTA</td>
<td>Ethylenediaminetetraacetic acid</td>
</tr>
<tr>
<td>Hb</td>
<td>Haemoglobin</td>
</tr>
<tr>
<td>Hct</td>
<td>Haematocrit</td>
</tr>
<tr>
<td>IDM</td>
<td>Infant of a diabetic mother</td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>IVT</td>
<td>Intravenous therapy</td>
</tr>
<tr>
<td>MCADD</td>
<td>Medium-chain acyl-CoA dehydrogenase deficiency</td>
</tr>
<tr>
<td>mmol/L</td>
<td>Millimole per litre</td>
</tr>
<tr>
<td>min</td>
<td>Minute</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>RSQ</td>
<td>Retrieval Services Queensland</td>
</tr>
<tr>
<td>SCN</td>
<td>Special care nursery</td>
</tr>
<tr>
<td>SGA</td>
<td>Small for gestational age</td>
</tr>
<tr>
<td>UVC</td>
<td>Umbilical venous catheter</td>
</tr>
<tr>
<td>&gt;</td>
<td>Greater than</td>
</tr>
<tr>
<td>≥</td>
<td>Greater than or equal to</td>
</tr>
<tr>
<td>&lt;</td>
<td>Less than</td>
</tr>
</tbody>
</table>

**Definition**

Jitteriness is not a definitive sign of hypoglycaemia as many babies will appear jittery on handling and in response to stimuli. The operational definition is excessive repetitive movements of one or more limbs, which are unprovoked and usually relatively fast. It can be distinguished from seizure activity by the ability to stop the movements by holding the affected area/limb in flexion.
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1 Introduction

At birth, all babies must absorb glucose and initiate glucose production. Most are able to mobilise glycogen, initiate gluconeogenesis and produce glucose at a rate which is usually adequate to maintain normal blood glucose levels.

Certain groups of babies may be unable to make the appropriate metabolic adaptations to extra uterine life and are considered ‘at risk’ of severe and/or persistent hypoglycaemia. Current evidence has not identified a specific blood glucose threshold, range of thresholds or duration of low blood glucose that is predictive of acute or chronic adverse outcomes, the most serious of which are neurological sequelae.2 Thresholds have been identified for treatment, however thresholds should be considered in the context of the baby’s alternative energy substrates (ketone, lactate and pyruvate), pathology, altered physiology and metabolism.3 Persistent and/or recurrent hypoglycaemia should be investigated and treated.3

1.1 Management principles
The basic tenets of newborn hypoglycaemia management are:

- Prevent babies from becoming hypoglycaemic
- Detect those babies that are hypoglycaemic
- Treat those babies that are hypoglycaemic
- Find a cause if the hypoglycaemia is severe, persistent or recurrent

1.2 Definition
For the purpose of this guideline, the most widely used definition of hypoglycaemia is a:4,5,6

- Formal blood glucose level (BGL) of less than 2.6 mmol/L [refer to Section 1.4 Equipment]

For definitions of severe, persistent or recurrent hypoglycaemia refer to Section 6.

1.3 Parent information
Provide parents and carers with opportunities for informed discussion [refer to Disclaimer (page 2)]. Ensure verbal and written information contains content on:

- Definition
- Preventative care
- Symptoms
- Tests
  - Babies at risk of hypoglycaemia will require close monitoring
- Treatment

1.4 Equipment
A BGL may be measured using a:

- Formal measurement:
  - Blood gas machine/analyser – use a capillary tube or blood gas syringe
  - Biochemical laboratory – use, in order of preference, either a fluoride oxalate (grey top), clotted (red top), or heparin (green top) tube – confirm with local pathology service

- Bedside glucometer:
  - Considered a screening tool
  - Use a glucometer that uses a glucose oxidase test strip with electrochemical sensor
  - Although newer generation glucometers have improved accuracy7,8,9, glucometers are less accurate than formal measurements in lower BGL ranges

To ensure accurate BGL measurement, all monitoring equipment requires:

- Maintenance – refer to the manufacturer’s instructions for requirements including:
  - Calibration process and intervals
- Approval by pathology services
- Data quality monitoring
- Adequate training of clinical staff in its use
- Avoidance of delay between blood sample collection and analysis
1.5 Documentation
Document all care as per mandatory\textsuperscript{10} and local requirements. As newborn hypoglycaemia may be a symptom of an underlying disease process, ensure accurate documentation of:\textsuperscript{1}

- Time of feeding in relation to BGL
- Clinical signs noted including pre-feed observations [refer to Section 4.1 Observations]
- BGL
- Treatment and response to treatment
- Follow-up

2 Babies at risk of newborn hypoglycaemia
Risk for newborn hypoglycaemia may be due to maternal and/or neonatal factors.\textsuperscript{4,11,12}

2.1 Maternal risk factors
- Maternal diabetes mellitus\textsuperscript{4,11,13,14,15} – risk correlates with quality of control more than category of diabetes\textsuperscript{11,12}
- Intrapartum administration of Glucose\textsuperscript{4,11,12,13,14}
- Maternal drug therapy\textsuperscript{4,11,12,14,15,16} including:
  - β-blockers\textsuperscript{1,4,11,12,15}
  - Oral hypoglycaemic agents\textsuperscript{1,4,11,12,15}
  - Valproate\textsuperscript{17}
- Family history of metabolic disorders (e.g. Medium-chain acyl-CoA dehydrogenase deficiency (MCADD))\textsuperscript{1} – refer for specialist consultation

2.2 Newborn risk factors
- Prematurity less than 37 weeks\textsuperscript{1,6,11,12,13}
- Small for gestational age\textsuperscript{1,2} (SGA) (less than 10\textsuperscript{th} percentile) or intrauterine growth restriction\textsuperscript{1,6,11,12,13,15}
- Low birth weight (less than 2500 gram)
- Large for gestational age (LGA)\textsuperscript{2} (greater than 90\textsuperscript{th} percentile)
- Other:
  - Macrosomia\textsuperscript{3,10}
  - Perinatal hypoxic-ischaemic insult\textsuperscript{4,11,12,13,14,15}
  - Respiratory distress\textsuperscript{15}
  - Sepsis\textsuperscript{4,11,12,15} or suspected infection\textsuperscript{15}
  - Hypothermia\textsuperscript{4,11,12,13,15}
  - Polycythaemia\textsuperscript{1,4,11,12}
  - Congenital cardiac abnormalities\textsuperscript{4,12}
  - Endocrine disorders\textsuperscript{4,11,12,15}
  - Family history of metabolic disorders\textsuperscript{1}
  - Inborn errors of metabolism\textsuperscript{4,11,12,15}
  - Rhesus haemolytic disease\textsuperscript{4,12,14}
  - Erythroblastosis fetalis\textsuperscript{4,15}
  - Obvious syndromes:
    - Beckwith-Wiedemann syndrome\textsuperscript{11,14,15}
    - Midline defects (e.g. cleft palate)\textsuperscript{11,15}
  - Inadequate feeding\textsuperscript{4,11,12,16}
  - Intravenous (IV) cannula infiltrated
  - Weaning of IV fluids
3 Prevention
Discuss preventative care with the parents/carers.

Keep the baby warm (36.5-37.2°C):
- At birth dry and remove wet linen
- Initiate early skin to skin contact (SSC)\(^{13,15}\) (baby’s gestation and condition permitting)
  - Encourage ongoing SSC to assist thermoregulation and promote frequent breastfeeds
  - If required, use warmed blankets, overhead heaters, incubators and heated mattresses as per local work instruction

Provide energy by:
- **Initiating early feeds within 30-60 minutes of birth**\(^{15}\) with:
  - Breastfeeding
  - Formula if mother plans to formula feed (start at 60 mL/kg/day, i.e. 7.5 mL/kg 3 hourly)
  - Gavage feeds if baby is less than 35 weeks gestation
  - If baby is not feeding well, it is still ideal to give colostrum (either from the breast or expressed)
- Whether breast or formula feeding, provide support and teach the mother to recognise and respond to early feeding cues – may not be present in the ‘at risk’ baby\(^1\)
- **For at risk babies – continue oral feeding at least three hourly**\(^{13}\) or more frequently in response to feeding cues
- Separation of mother and baby should be avoided to enable early feeds, frequent feeds and breastfeeding\(^{18}\)
- Ketones may be an important alternative to glucose for brain metabolism in the neonatal period and breastfeeding may enhance ketogenesis\(^{18}\)
- Refer to Queensland Clinical Guideline: Breastfeeding initiation\(^{19}\)
- If enteral feeding is not possible or contraindicated – commence IV therapy 10% Glucose at 60 mL/kg/day
4 Detection

4.1 Observations
Commence and continue pre-feed observations for a minimum of 24 hours for at risk babies. Assess and document:

- Level of consciousness
- Tone
- Temperature
- Respiration
- Colour/perfusion

4.2 Clinical signs

- The clinical signs of hypoglycaemia are neither sensitive nor specific
- Babies with signs suggestive of hypoglycaemia require urgent paediatric review

Babies with hypoglycaemia may display any of the following signs:

- Tremors/jitteriness
- Cyanosis
- Apnoeic episodes
- Tachypnoea
- Weak or high pitched cry
- Hypotonia
- Poor feeding/intolerance after feeding well
- Eye rolling
- Pallor
- Hypothermia
- Sweating
- Temperature instability
- Tachycardia

More severe signs:
- Changes in level of consciousness (e.g. irritability, lethargy, stupor, coma)
- Seizures
4.3 BGL screening

- Babies should have BGL screening if:
  - At least one risk factor is present\(^4,6,11\)
  - They are unwell\(^11\)
  - There are unexplained abnormal signs that may be due to hypoglycaemia\(^4\)

Routine BGL screening does not need to occur:
- In asymptomatic, appropriately grown term babies who do not have risk factors\(^2,4,12,15,20\)
- Within 2 hours of birth, if the baby is well, as will likely have low blood glucose\(^18,21\)

Prior to blood sampling:
- Ensure the baby receives appropriate pain reducing strategies (in accordance with local work instructions)
  - The use of oral sucrose is not contraindicated in babies of diabetic mothers
    - To avoid any effect on the newborn’s blood sugar, oral sucrose should preferably be given only a short duration (e.g. less than 30 seconds) before the blood sampling
- Confirm with blood gas analyser or laboratory analysis if glucometer BGL is less than 2.0 mmol/L
  - Do not wait for confirmation results – initiate appropriate treatment immediately\(^4\)

4.3.1 Factors affecting BGL results

Factors which may affect BGL results include\(^22\):
- The sample collection technique:
  - Squeezing a poorly perfused heel may cause haemolysis resulting in a falsely low BGL reading
  - Inadequate clearing of the umbilical venous catheter (UVC) or umbilical arterial catheter (UAC) before collecting blood sample
  - Never take BGL from a venous or arterial line where Glucose is infusing
  - A delay between collection and laboratory analysis may produce a falsely low BGL reading
- Results from arterial, venous and capillary samples may vary by 10-15%
- High haematocrit, especially in preterm neonates, may contribute to low BGL readings in bedside glucometers or when there is a delay in processing samples that are not in a fluoride oxalate tube

4.3.2 Well, asymptomatic babies with risk factors

- Well babies with risk factors do not require routine admission to the neonatal unit\(^18\)
- Asymptomatic hypoglycaemic babies do not require routine admission to the neonatal unit if their BGL can be effectively managed with feeding

There is not a single scientifically derived BGL or range of levels that are associated with clinical signs of hypoglycaemia, and/or adverse sequelae. Despite the controversy surrounding optimal timing and intervals of screening\(^4,11,13,15\), consider individual risk factors.

BGL monitoring should occur:
- Whichever is sooner:
  - Prior to the second feed or within 3 hours of birth if the baby has fed effectively
  - At 2 hours of age if the baby has not fed effectively
  - Every 4-6 hours pre-feeds until monitoring ceases
  - If feeding is unsuccessful, recheck BGL
  - Refer to Section 5.3 Ceasing BGL monitoring

4.3.3 Unwell babies with/without clinical signs of hypoglycaemia

If any baby is unwell:
- A medical review is required [refer to Section 5.2 Unwell babies with/without clinical signs of hypoglycaemia]
- Check BGL immediately
- Repeat BGL at least every 4-6 hours or as indicated [refer to Section 5 Treatment]
5 Treatment
Treat those babies who are hypoglycaemic. The goal is to achieve a BGL of greater than or equal to 2.6 mmol/L prior to routine feeds.

If the glucometer BGL is less than 2 mmol/L, do not wait for confirmation of laboratory or blood gas analyser results before commencing the appropriate treatment.

5.1 Asymptomatic babies with risk factors
BGL 1.5-2.5 mmol/L:
- Notify medical or paediatric staff
- Feed immediately:
  - Give additional expressed breast milk if available
  - If required, supplement with formula
  - Give formula if mother plans to artificially feed
  - Obtain documented informed consent for formula feeds23
  - Guide: 60 mL/kg/day, i.e. 7.5 mL/kg/3 hours
- Recheck BGL after 30-60 minutes
- If BGL does not increase after a feed then commence IV 10% Glucose at 60 mL/kg/day (or age appropriate rate)
- If repeated BGL is less than 2.0 mmol/L – IV therapy is indicated12,24
- Maintain close surveillance4

BGL less than 1.5 mmol/L12 or unrecordable:
- Notify paediatrician
- Urgent treatment with IV therapy is required12
  - Consider drawing diagnostic blood samples prior to commencing IV therapy – treatment should not be delayed if there is difficulty collecting samples
- Do not wait for formal confirmation of low BGL before starting IV therapy
- Commence IV 10% Glucose at 60 mL/kg/day (or age appropriate rate)
- Consider a 2 mL/kg IV bolus of 10% Glucose
  - Beware of severe hyperglycaemia and rebound hypoglycaemia11
  - Due to risk of rebound hypoglycaemia, NEVER give an IV bolus of Glucose without also increasing the background rate11 or concentration of the IV Glucose infusion
- If IV access is delayed, consider IM Glucagon 200 microgram/kg11
- Recheck BGL after 30 minutes
- Adjust IV therapy as required to achieve a BGL greater than or equal to 2.6 mmol/L4,15

5.2 Unwell babies with/without clinical signs of hypoglycaemia
Intervention is required:
- Commence IV 10% Glucose at 60 mL/kg/day (or age appropriate rate)
- Recheck BGL after 30 minutes
- Adjust IV therapy to achieve a therapeutic BGL of greater than or equal to 2.6 mmol/L4,15
- Ensure a neurological assessment
- Refer to Section 4.3.3 Unwell babies with/without clinical signs of hypoglycaemia

5.3 Ceasing BGL monitoring
For babies who have no obvious underlying cause for their hypoglycaemia, cease monitoring if for 24 hours the:
- BGL has been greater than or equal to 2.6 mmol/L, and
- The baby is feeding effectively [refer to Queensland Clinical Guideline: Breastfeeding initiation], and
- The baby is well and has not required IV therapy
5.4 Intravenous therapy

- IV therapy is indicated for babies who:
  - Have BGLs persistently less than 2.0 mmol/L\textsuperscript{12, 24}
  - BGL less than 1.5 mmol/L
  - Are unwell
  - Are not tolerating enteral feeds as treatment for hypoglycaemia\textsuperscript{13,14,15}
  - Mother refuses treatment with formula
- Admit babies requiring IV therapy to a neonatal unit
- Once treatment with IV 10% Glucose has commenced, monitor BGL:
  - Hourly until greater than or equal to 2.6 mmol/L, then 4-6 hourly
- Inadequate Glucose infusion rates are an important cause of ongoing hypoglycaemia:
  - If receiving an IV Glucose infusion calculate the Glucose in mg/kg/minute [refer to Appendix A]
  - If BGL remains less than 2.6 mmol/L despite an IV Glucose infusion:
    - Increase the concentration of Glucose infused (e.g. from 10% to 12% to 14% to 16% to 18% [refer to Appendix A])
      - Infusions of greater than 12% Glucose should be delivered via a central line or a UVC\textsuperscript{6}
      - Be cautious of only increasing the IV therapy rate, as this will increase the risk of fluid overload and its effects, especially that of dilutional hyponatremia
      - If a rate of 100 mL/kg/day is reached on day one of baby's life, then increase the concentration rather than the rate
  - If the Glucose infusion rate is greater than 10 mg/kg/minute, or baby greater than 72 hours of age:
    - Ensure paediatric endocrinology consult
  - Consider pharmacological intervention for severe, persistent or recurrent hypoglycaemia
  - Resite an infiltrated cannula promptly\textsuperscript{4}
  - The BGL goal for babies with severe, recurrent or persistent hyperinsulinaemic hypoglycaemia is greater than or equal to 2.6 mmol/L\textsuperscript{16}
  - If there is no contraindication to oral feeding:
    - Support the mother who wishes to breastfeed while her baby receives IV therapy\textsuperscript{15} [refer to the Queensland Clinical Guideline: Breastfeeding initiation]\textsuperscript{19}
    - Decrease IV therapy once BGL has been stable for 12 hours:
      - Do not decrease Glucose infusions abruptly\textsuperscript{13}
      - Reduce IV rate gradually as volume of enteral feed increases\textsuperscript{13,15}
  - Check BGL:
    - 30 minutes after commencing IV therapy
    - 30 minutes after any change is made to rate or concentration of IV therapy
    - In the event of pharmacological intervention
    - Pre-feed as IV therapy reduces\textsuperscript{15}
    - If feeding changes (e.g. transitioning from supplementation with formula to exclusively breastfeeding)
## 6 Severe, persistent, recurrent or atypical hypoglycaemia

- Babies with severe, persistent or recurrent hypoglycaemia are at risk of developing neurological morbidity\(^{11,14}\)

Transient hypoglycaemia does not require further investigation.\(^{12}\) However, to exclude/identify underlying pathology, infection, metabolic or endocrine disease in babies where the hypoglycaemic presentation is severe, persistent, recurrent or atypical, specialist management and further investigation (i.e. a hypoglycaemia screen) is required.\(^{12}\)

Investigate hypoglycaemia that is:

- Symptomatic including seizures or altered level of consciousness\(^{11}\)
- Severe:
  - BGL less than 1.5 mmol/L or unexpectedly low for the clinical situation
  - Baby requiring greater than 10 mg/kg/min of Glucose at any time\(^{11}\)
- Persistent or recurrent\(^{11}\):
  - Early onset hypoglycaemia that is persisting/recurring after 72 hours
- Associated with other abnormalities such as\(^{11}\):
  - Midline defects
  - Micropenis
  - Exomphalos
  - Erratic temperature control
- Unusual in presentation and/or no maternal or neonatal risk factors present
- Family history of Sudden Infant Death Syndrome, MCAD deficiency, Reye’s syndrome or developmental delay\(^{11}\)

- Admit to neonatal unit (special care nursery/intensive care nursery)
- Level 1-3 neonatal units:
  - Consider service capability and consult with a higher level neonatal service\(^{25}\)
  - Transfer to a higher level neonatal service may be required for ongoing management
    - Refer to Section 6.2 and Queensland Clinical Guideline: Neonatal stabilisation\(^{26}\)

### 6.1 Hypoglycaemia screen and further investigations

Perform a hypoglycaemia screen:

- At the time the baby is hypoglycaemic\(^{6,11,14}\) – some results cannot be interpreted when the BGL is normal
- Before giving a feed if a feed is due
- Before additional treatment (e.g. IV Glucose)
- Without stopping current treatment e.g. continuous feeds or IV Glucose
- Referring to local HSS guidelines for recommended sample collection and testing requirements
  - Prepare a ‘hypoglycaemia kit’ with instructions and appropriate sample containers to avoid delay in obtaining critical samples\(^{6,11,14}\)
- All Level 1-3 neonatal units\(^{25}\) – discuss with a neonatologist

Ensure a neonatologist and/or paediatric endocrinologist is involved in further investigations and management\(^{11}\)
### 6.1.1 Investigations

Table 1. Hypoglycaemic screen and other investigations

<table>
<thead>
<tr>
<th>Tests†</th>
<th>Amount†</th>
<th>Sample†</th>
<th>Container guide^</th>
<th>Specimen collection†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Routine investigations to be taken when the baby is hypoglycaemic (BGL &lt; 2.6 mmol/L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Insulin (±C-peptide) Cortisol Growth hormone | 900 µL | Serum gel or lithium heparin | red cap x2 or green cap x2 | • If haematocrit is high (> 0.55%), collect more blood then suggested  
• If sampling is difficult and minimal blood is obtained, label request: ‘Attention: endocrine section’ |
| Ketones# (3 OH butyrate) | 200 µL | Serum gel | red cap | – |
| Adrenocorticotrophic hormone | 400 µL | EDTA | pink cap | – |
| Free fatty acids | 100 µL | Serum gel | red cap | – |
| **Other routine investigations** |
| Acyl-carnitine profile | 1-2 full spots or 150 µL | Newborn screening test card or Lithium heparin | – | • Label with ‘acyl-carnitine profile’  
• In addition to the routine Day 2-5 screen to be sent separately at the usual time |
| Blood gas analysis (includes electrolytes, glucose, Hb, Hct, lactate) | As per local analyser | Blood gas syringe or capillary tube | Blood | • Specimen on ice if sent to laboratory |
| Urinary metabolic profile | 10 mL | Urine | Yellow specimen | • First urine sample passed after the hypoglycaemic episode but does not need to be collected before treatment is started  
• Send to laboratory immediately after collection |

**Consider further investigations for inborn errors of metabolism including**: 3

<table>
<thead>
<tr>
<th>Tests†</th>
<th>Amount†</th>
<th>Sample†</th>
<th>Container guide^</th>
<th>Specimen collection†</th>
</tr>
</thead>
</table>
| Plasma amino acid profile | 100 µL | Lithium heparin preferred | Green cap | • 2nd preference: EDTA  
• 3rd preference: Serum gel |
| Ammonia# | 500 µL | EDTA | Pink cap | – |
| Pyruvate | 1000 µL | – | – | Specialist collection – contact local laboratory |

* Refer to local health service guidelines for recommended sample collection and testing requirements  
^ Coloured caps, referring to small volume blood tubes, are a guide, and may vary between services  
# Specimens that need to go on ice  

**Documentation: Pathology specimen request slip**

- To enable prioritisation of tests according to initial results, volume of blood available and the clinical scenario include:
  - Birth weight
  - Gestational age
  - Symptoms if present
  - Primary and/or provisional clinical diagnosis and indication for investigation
  - As well as requesting each individual test, mark ‘Neonatal hypoglycaemia screen’
6.1.2 Interpretation of results

- A hypoglycaemic screen may indicate a metabolic or endocrine disorder. If further investigation and management required, seek advice from:
  - Biochemical pathologist, and/or
  - Paediatric endocrinologist or metabolic physician

- Generally, detectable insulin in the presence of hypoglycaemia implies a hyperinsulinaemic state:
  - The result is confirmed by absence of free fatty acids and 3 OH butyrate (ketogenesis and FFA mobilisation are suppressed by insulin)
  - Hyperinsulinism is often transient but can be persistent and require long term treatment

- Cortisol > 200 nmol/l and Growth Hormone > 20 mU/mL represents a normal response to hypoglycaemia (although this response is blunted in the newborn)\(^2^7\):
  - Consider less response as suggestive of hypothalamic, pituitary or adrenal dysfunction:
    - Seek prompt paediatric endocrine consultation

- If ammonia > 50 micromol/L:
  - Consider a metabolic disorder:
    - Seek consultation
6.2 Pharmacological intervention

If the Glucose infusion rate is greater than 10 mg/kg/minute:

- Consider pharmacological intervention for severe, persistent or recurrent hypoglycaemia\(^3\)
  - Refer for specialist management (e.g. paediatric endocrinologist/metabolic physician) where required as this is almost certainly hyperinsulinaemia
  - Ensure diagnostic samples have been collected prior to using specific medication [refer to Section 6.1 Hypoglycaemia screen and further investigations]

The BGL goal for babies with severe, recurrent or persistent hyperinsulinaemic hypoglycaemia is greater than or equal to 2.6 mmol/L.\(^16\) If the blood glucose does not normalise, consider in order of preference*:

- **Glucagon**\(^{26,*}\)
  - 200 microgram/kg bolus IV or IM
    - Rise in BGL lasts approximately 2 hours – monitor for rebound hypoglycaemia
    - Maximum dose: 1mg
  - 10-20 microgram/kg/hour IV infusion
    (10 microgram/kg/hour = 0.5 mL/hour of 1 mg/kg Glucagon in 50 mL Water for Injection or 5% Glucose)
    - Rise in blood glucose should occur within one hour of starting infusion – adjust rate according to response
    - Maximum rate: 50 microgram/kg/hour\(^{29}\)

- **Hydrocortisone**\(^*\)
  - 1-2 mg/kg/dose 6 hourly IV or oral\(^{30}\)
  - Add after 24-48 hours of IV therapy but only for temporary treatment for 1-2 days\(^{31}\), then slowly reduce dose
  - Monitor: BP & BGL\(^{28}\)

- **Diazoxide**\(^{29,*}\)
  - In consultation with a paediatric endocrinologist
  - Initially 5 mg/kg/dose twice daily IV or orally
    - Pharmacy department may prepare an oral mixture
  - Adjust dose according to response:
    - Usual maintenance: 1.5-3 mg/kg/dose, 2-3 times daily
    - Maximum: 7 mg/kg/dose, 3 times daily
  - Avoid IV route if able – extravasation can cause tissue necrosis
  - Monitor: BP – sodium and fluid retention is a common side-effect\(^{28}\)
  - Prolonged use – white cell and platelet count; regularly assess growth and bone development
  - Administer with:
    - **Hydrochlorothiazide**\(^*\) 1-2 mg/kg/dose bd oral\(^{28}\)
      - Pharmacy department may prepare an oral mixture

- **Octreotide**\(^*\)
  - Initially 2-5 microgram/kg/dose every 6-8 hours subcutaneous injection
  - Adjust dose according to response:
    - Up to 7 microgram/kg every 4 hours may rarely be required
  - For persistent hyperinsulinaemic hypoglycaemia unresponsive to Diazoxide and Glucose
  - Monitor closely when initiating treatment and changing doses
  - Avoid abrupt withdrawal
  - Has been associated with necrotising enterocolitis\(^{32}\)

*Refer to Australian pharmacopoeia for further information. Useful reference sources also include [refer to latest editions]:
- BNF for children, Neofax, Paediatric pharmacopoeia/AMH Children’s Dosing Companion
7 Inter-hospital transfer

Once the decision has been made to transfer the baby to a higher level facility, this will be coordinated by Retrieval Services Queensland (RSQ) and a neonatal medical coordinator, by calling 1300 799 127. Refer to Queensland Clinical Guideline: Neonatal stabilisation for retrieval.26

8 Discharge and follow up

Follow up depends on the severity, duration and the underlying cause of the hypoglycaemia.

As a guide for discharge and follow-up:
- Monitor the asymptomatic newborn for the suggested BGL screening time [refer to Section 4.3.2 Well, asymptomatic babies with risk factors]
  - Ensure the newborn is able to maintain BGL greater than or equal to 2.6 for at least three consecutive normal feeds2
- For severe, symptomatic, recurrent or atypical neonatal hypoglycaemia:
  - Discuss with a neonatologist/paediatrician and as required an endocrinologist or metabolic specialist
  - Consider early MRI imaging – this may assist in predicting neurodevelopmental outcome33
  - Ensure long term follow-up
  - For babies discharged on Diazoxide – ensure ability to maintain euglycaemia for 6 hours fasting
- Other follow-up will be cause dependent
References


Appendix A: Glucose infusion calculation and conversion

Glucose infusions greater than 12% should be delivered via a central line.6

Method to increase Glucose concentration

<table>
<thead>
<tr>
<th>Desired Glucose concentration</th>
<th>Volume of 10% Glucose</th>
<th>Volume of 50% Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>12%</td>
<td>95 mL</td>
<td>5 mL</td>
</tr>
<tr>
<td>14%</td>
<td>90 mL</td>
<td>10 mL</td>
</tr>
<tr>
<td>16%</td>
<td>85 mL</td>
<td>15 mL</td>
</tr>
<tr>
<td>18%</td>
<td>80 mL</td>
<td>20 mL</td>
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</tbody>
</table>

Glucose infusion rate in mg/kg/min of 10% Glucose in mL/kg/day

<table>
<thead>
<tr>
<th>10% Glucose</th>
<th>Glucose infusion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg/kg/min</td>
<td>mL/kg/day</td>
</tr>
<tr>
<td>4.2</td>
<td>60</td>
</tr>
<tr>
<td>4.9</td>
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<td>5.6</td>
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<td>6.3</td>
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<tr>
<td>10.4</td>
<td>150</td>
</tr>
<tr>
<td>11.1</td>
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</tbody>
</table>

Glucose infusion rate in mg/kg/min with different Glucose concentration in mL/kg/day

<table>
<thead>
<tr>
<th>Glucose mg/kg/min</th>
<th>10%</th>
<th>12%</th>
<th>14%</th>
<th>16%</th>
<th>18%</th>
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<tr>
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<td>180</td>
<td>154</td>
<td>135</td>
<td>120</td>
</tr>
</tbody>
</table>

Formula for calculating Glucose infusion rate in mg/kg/min

\[
\text{mg/kg/min} = \frac{\text{Glucose concentration} \% \times \text{volume infused in mL/kg/day}}{144}
\]
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