Clinical Guideline
South Australian Perinatal Practice Guidelines – Neonatal Hypoglycaemia

Policy developed by:  SA Maternal and Neonatal Clinical Network
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Summary  Guideline for the management of the neonate with hypoglycaemia

Keywords  morbidity, hypoglycaemia, jitteriness, ketogenesis, caesarean, diabetes, hypothermia, breast feed, seizures, respiratory, erythoblastosis fetalis, prematurity, Perinatal Practice Guidelines, Neonatal Hypoglycaemia, clinical guideline

Policy history  Is this a new policy?  N
Does this policy amend or update an existing policy?  Y
Does this policy replace an existing policy?  Y
If so, which policies? Neonatal Hypoglycaemia

Applies to  All SA Health Portfolio
All Department for Health and Ageing Divisions
All Health Networks
CALHN, SALHN, NALHN, CHSALHN, WCHN, SAAS
Other

Staff impact  All Clinical, Medical, Nursing, Allied Health, Emergency, Dental, Mental Health, Pathology

PDS reference  CG116

Version control and change history

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<tr>
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<th>Date from</th>
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Note

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient’s medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing 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,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements
Management of hypoglycaemia in the newly born and neonatal periods

- Newly born who are well but identified as ‘at risk’
  - Prem >32 weeks
  - BW <10th centile
  - Maternal diabetes
  - TTN
  - temp <36°C
  - Suspected asphyxia requiring simple resuscitation
  - Maternal beta blockers, valproate

- Screening PGL at 1 and 4 hours of age
  - Breast feed, or give formula if mother’s intent is to artificially feed, as soon as practicable if there is no clinical contraindication
  - If significantly premature, consider the need for gavage feeds
  - Correct hypothermia

- PGL >2.0 at both 1 and 4 hours. Normal.
  - No further PGLs if baby is well
  - Consider supplemental feeds for term babies with IUGR or who are breast fed

- Postnatal ward baby
  - Disinterest in feeding for 8 hours or more from birth or the last feed.
  - Hypothermia (temp <36°C)
  - Jitteriness
  - PGL at time of assessment

- Baby at any age with a major illness
  - Seizures
  - Unwell baby
  - On-going or evolving respiratory distress
  - Suspected infection with clinical instability
  - Suspected heart problem with cyanosis or poor perfusion
  - Suspected asphyxia with advanced resuscitation (intubation or cardiac massage)
  - Erythroblastosis fetalis
  - Gestation <32 weeks

- PGL 1.5-2.0 at either 1 or 4 hours
  - Offer breast feed or EBM, or formula if intent is to artificially feed, or 10% glucose by means agreeable to mother in a quantity equivalent to a 1 or 2 hourly aliquot of a standard starting volume (~2-4mL/kg)
  - Give 10% glucose infusion at 60 mL/kg/day if respiratory distress
  - Repeat PGL in 1 hour. Therapeutic goal PGL >2.5mmol/L (enteral); >3.5mmol/L (IV)

- PGL >2.5. Normal.
  - Consider causes of poor feeding other than hypoglycaemia
  - Correct hypothermia
  - Consider other causes of jitteriness (hypocalcaemia, medication or drug withdrawal, normal)
  - Seek advice where appropriate

- PGL 1.5-2.5
  - Offer breast feed or EBM, or formula if intent is to artificially feed, or 10% glucose by means agreeable to mother
  - Manage an identified problem
  - Repeat PGL in 30 to 60 minutes; consider 10% glucose infusion @ 60mL/kg/day if goal not achieved
  - Therapeutic goal PGL >2.5mmol/L
  - Seek advice

- PGL <1.5
  - Obtain IV access without delay
  - Immediate PGL required

- PGL <2.5
  - Continue IV 10% glucose infusion with therapeutic goal PGL >3.5mmol/L
  - Hypoglycaemia unlikely to be the cause of seizures
  - Seek advice

- PGL >2.5
  - Continue IV 10% glucose infusion with therapeutic goal PGL >3.5mmol/L
  - Hypoglycaemia unlikely to be the cause of seizures
  - Seek advice

- PGL <1.5 at any time
  - Urgent action required
  - Give IV 10% glucose bolus (2mL/kg) and start infusion initially at 90mL/kg/day
  - If IV access is delayed, give IM glucagon while continued IV access is pursued
  - Repeat PGL in 30 minutes
  - Therapeutic goal PGL >3.5mmol/L for all babies on IV fluids; adjust fluids down if goal achieved
  - Aim to achieve therapeutic goal within 30-60 mins
  - Seek advice
Important points

Key physiological principles

> In the newly born, glucose levels are maintained in blood by the release of liver glycogen reserves in the first few hours, by gluconeogenesis, and by sparing of glucose consumption through the oxidation of fat reserves and the utilisation of ketone bodies and lactic acid as energy substrates by the brain.

> Ketogenesis is the adaptive response of principal importance. Utilisation of ketones by the brain allows normal cerebral energy metabolism at lower plasma glucose levels in babies in comparison to older children and adults.

> Newly born babies with impaired adaptive ketogenesis are considered ‘at risk’ of impaired cerebral energy metabolism at low levels of plasma glucose. This includes particularly infants who are preterm, growth restricted, born to mothers with gestational or insulin dependent diabetes, or who have an abnormal transition period due to adverse perinatal circumstances.

Measurement of plasma glucose is required in two broad groups of babies

> Newly born, ‘at risk’ babies who are otherwise well. These babies potentially have impaired adaptive ketogenesis and increased glucose utilisation. They are screened for hypoglycaemia with plasma glucose levels at 1 and 4 hours of age to capture the nadir of plasma glucose.

> Babies who are identified as unwell, who present with neonatal seizures, or who are receiving normal postnatal care and develop symptoms consistent with hypoglycaemia and impaired cerebral energy metabolism. Plasma glucose is measured in these babies immediately at presentation.

Principles and pitfalls in measurement of plasma glucose

> Wide variations in plasma glucose results may occur due to errors in sample collection, processing and assay method. This is particularly important to consider in small hospitals with limited laboratory support.

> Glycolysis by red cells is rapid in newborn samples. Blood samples sent to the laboratories for glucose estimation need to be collected into fluoride containers (preferably), or centrifuged immediately to separate red cells, or kept on ice to avoid inaccuracies due to red cell metabolism.

> Glucose analysis using standard laboratory methods, blood gas machines or ISTAT devices is accurate provided the sample is processed immediately.

> Glucometer and Hemacue machines have utility because they are simple and give immediate bedside results. However, they may have serious inaccuracies at levels of plasma glucose around commonly applied neonatal intervention thresholds. The main danger is a false negative reading where a ‘normal’ result is given while the actual plasma glucose is abnormally low. Therefore, if using these machines, this guideline recommends adjusting the intervention threshold upward to avoid false negatives.

Understanding the definition of hypoglycaemia and how plasma glucose levels are used to guide management
Hypoglycaemia is defined physiologically as that blood glucose level at which cerebral energy needs fail to be met.

However, there is no clear and satisfactory definition of hypoglycaemia based on plasma glucose levels alone, because of the complexities of metabolic and hormonal adaptation to birth, our limited understanding of neonatal cerebral defences in hypoglycaemia, and inadequate long-term data to fully assess the impact of hypoglycaemia on the developing brain\(^1\,^5\,^6\).

Therefore, ‘Operational’ or ‘Intervention’ thresholds are used, which are pragmatic treatment levels for plasma glucose that aim to balance safety with the avoidance of over treatment of healthy babies\(^6\).

Once a decision has been made to treat hypoglycaemia, a ‘Therapeutic’ goal is set that is deliberately higher than the threshold for intervention to allow a safety margin for management.

The intervention threshold is lower for the newly born ‘at risk’ baby than for older or symptomatic babies because plasma glucose normally falls after birth and there is a desire to avoid over-treating normal babies and interfering with breast feeding.
### Summary of plasma glucose intervention thresholds and therapeutic goals

Quoted values are for gold standard laboratory methodology.

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Intervention threshold</th>
<th>Therapeutic goal</th>
<th>Main therapeutic intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well infant, not in ‘at risk’ group</td>
<td>Don’t measure glucose unless hypothermic, feeding abnormally, or becomes unwell.</td>
<td></td>
<td>Normal care</td>
</tr>
<tr>
<td>‘At risk’ well infant screened for hypoglycaemia at 1 and 4 hours of age</td>
<td>&lt; 2.0 mmol / L</td>
<td>&gt; 2.5 mmol / L</td>
<td>Feeding</td>
</tr>
<tr>
<td>Unwell infant</td>
<td>&lt; 2.5 mmol / L</td>
<td>&gt; 2.5-3.5 mmol / L</td>
<td>IV 10 % glucose. Feeds in selected cases.</td>
</tr>
<tr>
<td>All infants</td>
<td>&lt; 1.5 mmol / L (urgent treatment required with IV 10 % glucose)</td>
<td>&gt; 3.5 mmol / L</td>
<td>IV 10 % glucose</td>
</tr>
</tbody>
</table>

**Important points of emphasis are:**

- Healthy term babies who are not ‘at risk’ should not have plasma glucose levels measured because the result will have little meaning[^4,6].
- Plasma glucose levels of < 1.5 mmol / L require urgent treatment with IV 10 % glucose to avoid cerebral energy deficiency and potential brain injury.
- In utero growth restriction is an important cause of hypoglycaemia and other morbidity. For babies who are significantly clinically malnourished (little subcutaneous fat, loose skin folds, withered appearance) formula supplementation of breast-feeding until breast milk flow is established is recommended (see PPG: Fetal growth restricted).[^1]
- Disinterest in, or poor feeding for more than 8 hours after birth, or after previous feed, (particularly when previous feeding has been good) requires medical assessment and a plasma glucose measurement.
- All babies born to mothers with diabetes are at risk of hypoglycaemia regardless of size at birth or the tightness of glycaemic control in pregnancy, and all such babies should be screened with plasma glucose levels.[^1] Mothers with diabetes should be encouraged to express colostrum / breast milk and store frozen for later use.

[^1]: References are not specifically cited in the text but are likely to be included in the full version of the guidelines.
> Large size for gestation (see PPG: accelerated fetal growth) is not a risk factor for hypoglycaemia where glucose challenge or tolerance tests have been documented to be normal, and such babies do not require routine screening\textsuperscript{7,8}

> Jitteriness is common and usually benign, and a PGL $> 2.5$ mmol / L excludes hypoglycaemia as a cause

> Where a baby is ‘at risk’ or has symptoms consistent with hypoglycaemia and a plasma glucose level can’t be obtained or the result will be delayed, appropriate treatment with feeding or IV fluids should be instituted and not deferred until the glucose result is known

> In most cases of documented hypoglycaemia, paediatric or neonatology advice should be sought due to the many considerations in management both of the hypoglycaemia and associated conditions

> Unusual or persistent hypoglycaemia will require further investigation for metabolic or endocrine causes, and such babies should not be discharged without further evaluation
Guidelines for screening, detection and management of hypoglycaemia in the newly born and neonatal periods

1. Newly born who are well but identified as ‘at risk’

Well, transitional babies are at risk of hypoglycaemia if there are perinatal factors that impair adaptive ketogenesis and/or increase glucose consumption

- Respiratory distress post elective caesarean birth at term with a low level oxygen requirement ($FIO_2 < 0.3$) and suspected transient tachypnoea of the newborn
- Maternal diabetes
- Birth weight $< 10^{th}$ percentile for gestation
- Mild prematurity (32-37 weeks gestation)
- Hypothermia (temperature $< 36^\circ C$)
- Suspected perinatal asphyxia where there has been a need for simple resuscitation measures (includes positive pressure with face mask where there is a rapid response to resuscitation but a need for transitional observation)
- Maternal treatment with drugs that interfere with glucose homeostasis, most importantly beta-blockers and valproic acid

These babies have screening plasma glucose levels at 1 and 4 hours of age

If there is no respiratory distress the baby should be offered the breast as soon as practicable, or if the mother wishes to artificially feed offered a bottle of formula

If there is low level respiratory distress, feeding is not required in the first 4 hours provided PGLs remain normal

**If both the 1 hour and 4 hour PGL ≥ 2.0 mmol / L (normal)**

- These babies should be treated as normally as possible
- Seek advice if further clinical concerns

**If either the 1 hour or 4 hour PGL is 1.5 - 2.0 mmol / L**

- If no respiratory distress, these babies should be fed
- Breast feed if mother available, or if mother wishes to breast feed but is unavailable, give EBM or 10 % glucose orally in the quantity equivalent to a one or two hourly aliquot of a standard starting volume (around 2-4 mL/kg) by a means agreeable to mother and staff. A similar formula volume can be given with mother’s consent or if her intent is to artificially feed
- If respiratory distress, give intravenous 10 % glucose bolus (2 mL / kg) over 5 minutes followed by an infusion of 60 mL/kg/day of 10 % glucose
- Repeat PGL in 30 to 60 minutes. Therapeutic goal PGL $> 2.5 \text{mmol} / \text{L}$ for enteral feeding and $> 3.5 \text{mmol} / \text{L}$ if on IV fluids
- Seek advice

**If PGL< 1.5 mmol / L at any time**

- Obtain IV access and give 10 % glucose bolus (as above) and 10 % glucose infusion initially at 90 mL/kg/day above. Consider glucagon 0.1 milligram / kg ($= 0.1 \text{ units} / \text{kg}$) IM, if IV access delayed
> Repeat PGL in 30 minutes
> Therapeutic goal PGL > 3.5 mmol / L. Consider adjusting 10 % glucose infusion rate down if threshold achieved
> Seek advice

2. Postnatal ward babies

A PGL and medical assessment is immediately advised for postnatal ward babies with:
> Disinterest in feeding for 8 hours or more from birth or the last feed
> Hypothermia (temp < 36°C)
> Jitteriness

**If PGL ≥ 2.5 mmol / L**
> Hypoglycaemia is not the cause of symptoms

**If PGL 1.5-2.5 mmol / L**
> Feeding is attempted with a repeat PGL in 30-60 minutes
> Therapeutic goal PGL > 2.5 mmol / L; consider 10 % glucose infusion at 60 mL/kg/day if goal not achieved
> Seek advice

**If PGL < 1.5 mmol / L**
> Obtain IV access and give an IV 10 % glucose bolus (as above) and 10 % glucose infusion initially at 90 mL/kg/day. Consider glucagon 0.1 milligram / kg (= 0.1 units / kg) IM, if IV access delayed
> Repeat PGL in 30 minutes.
> Therapeutic goal PGL > 3.5 mmol / L. Consider adjusting 10 % glucose infusion rate down if threshold achieved
> Seek advice

3. Babies at any age with a major illness

Immediate IV access and plasma glucose measurement are performed at any age in specific clinical contexts where an illness has become apparent since birth or there are neurological symptoms consistent with impaired neuronal metabolism

> Seizures
> Unwell baby

> Ongoing or evolving respiratory illness
> Suspected or proven infection with clinical instability
> Suspected congenital heart disease presenting with cyanosis or poor perfusion
> Suspected perinatal asphyxia where there has been a need for intubation or cardiac massage during resuscitation
> Erythroblastosis fetalis
> Significant prematurity (< 32 weeks gestation)

All such babies will require an intravenous 10 % glucose infusion commencing at 60 mL/kg/day as part of management of the underlying problem

A PGL is taken immediately at the time of assessment
If PGL < 2.5 mmol / L

- Give an IV 10 % glucose bolus 2 mL / kg (as above) and 10 % glucose infusion initially at 90 mL/kg/day. Consider glucagon 0.1milligram / kg (= 0.1 units / kg) IM, if IV access delayed
- Repeat the PGL in 30 minutes
- Therapeutic goal PGL > 3.5 mmol / L. Consider adjusting 10 % glucose infusion rate down if threshold achieved
- Ongoing paediatric or neonatology advice is required
South Australian Perinatal Practice Guidelines

Neonatal hypoglycaemia

References


Abbreviations

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<thead>
<tr>
<th>BW</th>
<th>Birth weight</th>
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<tr>
<td>C</td>
<td>Celsius</td>
</tr>
<tr>
<td>EBM</td>
<td>Expressed breast milk</td>
</tr>
<tr>
<td>et al</td>
<td>And others</td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>IUGR</td>
<td>Intrauterine growth restriction</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>kg</td>
<td>Kilogram(s)</td>
</tr>
<tr>
<td>mL</td>
<td>Millilitre(s)</td>
</tr>
<tr>
<td>mmol/L</td>
<td>Millimols per litre</td>
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<tr>
<td>PR</td>
<td>Per rectum</td>
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<tr>
<td>PGL</td>
<td>Plasma glucose level</td>
</tr>
<tr>
<td>Prem</td>
<td>Premature</td>
</tr>
<tr>
<td>TTN</td>
<td>Transient tachypnoea of the newborn</td>
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