South Australian Perinatal Practice Guideline

Neonatal Hypoglycaemia

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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

Explanation of the aboriginal artwork:
The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the Aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectfully manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Purpose and Scope of Perinatal Practice Guideline (PPG)

The purpose of this PPG is to provide nursing/midwifery and medical staff with guidance on managing neonatal hypoglycaemia. The guideline is primarily intended for use in term / late preterm infants during the first 48 hours of life who constitute the vast majority of infants diagnosed with hypoglycaemia. Its use in extremely unwell / premature infants, infants with underlying metabolic / endocrine conditions or prolonged hypoglycaemia, although safe, might be individualised by the attending senior clinician.

Flowchart: 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 & >97th centile
- Maternal diabetes
- TTN
- Temp <36°C
- Suspected asphyxia requiring IPPV or APGAR <6 at 5 min
- Maternal beta blockers, valproate

Screening PGL at 1 and 4 hours of age
- Breast feed within 30-60 min, or give formula as soon as practical if mother's intent is to artificially feed, if there is no clinical contraindication
- If 32-35 weeks gavage feeds with EBM or formula or IV 10% glucose 60ml/kg/d will be required
- Correct hypothermia

PGL>2.0 mmol/L at both 1 and 4 hours. Normal.
- No further PGLs if baby is well, unless indicated
- Consider supplemental feeds for late preterm or IUGR babies who are breast fed

PGL 1.5-2.0 mmol/L at either 1 or 4 hours
- Buccal Glucose gel 40% at 0.5mL/kg/dose, followed by breast feed and EBM (if available) by means agreeable to mother, if baby is asymptomatic, ≥35 weeks and clinically stable
- If intent is to artificially feed, give formula 30mL/kg/day in a 3 hourly aliquot
- If respiratory distress or other indication for IV fluids, give 2mL/kg bolus of 10% glucose followed by infusion at 60 mL/kg/day
- If 32-35 weeks, gavage feed or use IV glucose
- Repeat PGL in 1 hour.
- Therapeutic goal PGL≥2.6mmol/L
- If more than 2 doses of glucose gel are required or if persistent hypoglycaemia, seek consultant advice

PGL < 1.5 mmol/L at any time

Postnatal ward baby
- 8 hours or more without feed
- Hypothermia (temp <36°C)
- Jitteriness

PGL at time of assessment

PGL ≥2.6 mmol/L- 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 mmol/L
- Buccal Glucose gel 40% at 0.5mL/kg/dose (*Note: glucose gel is not recommended after 48 hours of age*)
- Followed by breast feed and EBM if available, by means agreeable to mother, if baby is asymptomatic and physiologically stable
- If intent is to artificially feed, give formula 30mL/kg/day in a 3 hourly aliquot
- Repeat PGL in 30 to 60 minutes
- Therapeutic goal PGL ≥2.6mmol/L; consider 10% glucose infusion at 60mL/kg/day if goal not achieved
- If more than 2 doses of glucose gel are required or if persistent hypoglycaemia, seek consultant advice

Urgent action required
- Buccal Glucose gel 40% at 0.5ml/kg/dose (if no major illness) AND
- 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 ≥ 2.6mmol/L if maternal diabetes or no major illness OR ≥3.5mmol/L if major illness
- Aim to achieve therapeutic goal within 30-60 mins
- Seek consultant advice

Baby at any age with a major illness
- Seizures
- Critically unwell baby
- Severe respiratory distress
- Suspected infection with clinical instability
- Suspected heart problem with cyanosis or poor perfusion
- Suspected asphyxia with advanced resuscitation (intubation or cardiac massage)

Gestation <32 weeks

Immediate PGL required
Obtain IV access without delay

PGL < 2.6 mmol/L at any time

PGL≥2.6
- Continue IV 10% glucose infusion with therapeutic goal PGL ≥3.5mmol/L
- Hypoglycaemia unlikely to be the cause of seizures
- Seek consultant advice

If persistent or unexplained hypoglycaemia OR PGL<2.6mmol/L after 48 hours of age, consider:
- *Immediate Hypoglycaemia screening bloods (provided treatment is not delayed) AND*
- *A controlled fasting study for 6 hours prior to discharge*

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Summary of Practice Recommendations

Healthy term infants with no risk factors should not have their plasma glucose levels (PGL) measured on a routine basis.

The PGL treatment thresholds and therapeutic aims in this protocol refer to laboratory analysed plasma samples or ABL gas machine values. The lower accuracy of point of care blood glucose measurements using hand-held devices for detecting hypoglycaemia at laboratory levels <2.6mmol/L should be recognised, especially in the context of hypoglycaemic symptoms (sleepiness, poor feeding, poorly responsive to examination).

For 'at risk' infants, PGL level of >2.0mmol/L is considered normal in the first 4 hours of life in the absence of symptoms of hypoglycaemia.

The therapeutic goal for treatment of hypoglycaemia is ≥2.6mmol/L except in babies with a major illness as defined in this protocol receiving IV fluids, where the therapeutic goal is ≥3.5mmol/L.

Glucose gel followed by breast feeding is an effective intervention for a PGL between 1.5-2.0mmol/L in the first 4 hours, and for PGLs between 1.5-2.5mmol/L in the first 48 hours of life, in infants who are ≥35 weeks gestation with no symptoms of neuroglycopaenia.

Infants with severe hypoglycaemia of <1.5mmol/L will require intravenous fluids.

Abbreviations

BW	Birth weight
C	Celsius
EBM	Expressed breast milk
IM	Intramuscular
IPPV	Intermittent positive pressure ventilation
IUGR	Intrauterine growth restriction
IV	Intravenous
kg	Kilogram(s)
mL	Millilitre(s)
mmol/L	Millimols per litre
PGL	Plasma glucose level
PPG	Perinatal Practice Guideline
PR	Per rectum
Prem	Premature
TTN	Transient tachypnoea of the newborn

Definitions

Hypoglycaemia	Defined physiologically as that blood glucose level at which cerebral energy needs fail to be met

Important points

Key physiological principles[1-5]

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 and lactate production are the adaptive responses 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 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 and rural 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 and blood gas machines is accurate provided the sample is processed immediately.

In hospitals where blood gas analyser or iSTAT is not readily available, Point of Care devices where the product information states a performance range that includes a PGL < 2.6 mmol/L (e.g. Medisense glucometer 1.1-33.3 mmol/L) have utility because they are simple and give immediate bed-side results. However, data suggest that falsely low values under 2.6 mmol/L are frequent (may lead to over intervention), while false negative values under 2.0mmol/L (missed hypoglycaemia in the first 4 hours) are less likely (unpublished data, personal communication Dr S Morris). '**Normal' results in a symptomatic or unwell infant should be treated cautiously and confirmed by alternate means including laboratory plasma glucose, iSTAT or blood gas analyser where possible.**

Understanding the definition of hypoglycaemia and how plasma glucose levels are used to guide management [4,7,8,10,11]

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.

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.

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[4,9,10]

Quoted values are for gold standard laboratory methodology

Clinical setting	Intervention threshold (PGL)	Therapeutic goal (PGL)	Main therapeutic intervention
Well infant, not in 'at risk' group	Do not measure glucose unless hypothermic, feeding abnormally or becomes unwell		Feeding
'At risk' well infant screened for hypoglycaemia at 1 and 4 hours of age	1.5-2.0 mmol/L	≥ 2.6 mmol/L	Glucose gel 40% Feeding
Hypoglycaemia after the 4 hour transition period in asymptomatic infant	< 2.6 mmol/L	≥ 2.6 mmol/L	Glucose gel 40% Feeding IV 10 % glucose
Any infant with severe hypoglycaemia who is not critically unwell (includes infants of diabetic mothers)	< 1.5 mmol/L	≥ 2.6 mmol/L	Urgent treatment with IV 10 % glucose (bolus and infusion)
Any infant with major illness or critically unwell	< 3.5 mmol/L	≥ 3.5 mmol/L	IV 10% glucose

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
- PGL of 1.5 – 2.0 mmol/L require treatment with 40% glucose gel 0.5mL/kg/dose, followed by breast feed and EBM if available, provided the baby is ≥ 35 weeks gestation, less than 48 hours of age, has no symptoms of hypoglycaemia, and is physiologically stable. Where there is intent to formula feed, give formula of 30mL/kg/day in a 3 hourly aliquot after the glucose gel.
- PGL 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 *Fetal growth (restricted)* PPG available at www.sahealth.sa.gov.au/perinatal)
- Large size for gestation in the absence of maternal diabetes is a risk factor for hypoglycaemia, and most guidelines recommend hypoglycaemia screening for these infants.[6,10,13] To strike a pragmatic balance between the risk of hypoglycaemia and that of over-intervention, a threshold of >97th centile is recommended for PGL monitoring.
- Birth weight must be plotted on a percentile chart to ensure that babies with a birth weight <10th centile or > 97th centile are appropriately screened for hypoglycaemia at 1 and 4 hours of age
- 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.[12] Mothers with diabetes should be encouraged to express colostrum / breast milk and store frozen for later use (see *Breastfeeding* PPG available at www.sahealth.sa.gov.au/perinatal)
- Jitteriness is common and usually benign, and a PGL ≥ 2.6 mmol/L excludes hypoglycaemia as a cause
- Where a baby is 'at risk' or has symptoms consistent with hypoglycaemia and a PGL 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 of both 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 [4, 7-11]

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. These include:

- Moderate and late preterm infants (32-37 weeks gestation)
- Maternal diabetes
- Birth weight < 10th percentile for gestation
- Birth weight > 97th centile for gestation
- Hypothermia (temperature < 36°C)
- 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
- Suspected perinatal asphyxia where there has been a need for positive pressure ventilation, Apgar score <6 at 5 minutes of age or abnormal cord gas pH <7.1
- Maternal treatment with drugs that interfere with glucose homeostasis, most importantly beta-blockers and valproic acid

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

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

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

- Glucose gel 40% at 0.5ml/kg/dose, if no respiratory distress
- This is followed immediately by a breast feed and EBM if available by means agreeable to the mother, provided baby is asymptomatic, ≥ 35 weeks gestation and physiologically stable
- If intent is to artificially feed, give formula 30mL/kg/day in a 3 hourly aliquot
- 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 is PGL ≥2.6mmol / L for enteral feeding and IV fluids
- If more than 2 doses of glucose gel are required or for persistent hypoglycaemia, seek consultant advice

If PGL<1.5 mmol/L at any time

- Glucose gel 40% at 0.5ml/kg/dose AND
- Obtain IV access and give 10 % glucose bolus (2mL/kg over 5 min) and 10 % glucose infusion initially at 90 mL/kg/day
- Consider glucagon 200microgram / kg (= 0.2 units / kg) IM, if IV access delayed
- Repeat PGL in 30 minutes. Therapeutic goal is PGL ≥2.6mmol / L if infant does not have any major illness. Aim to achieve therapeutic goal in 30-60 minutes
- Seek consultant advice

2. Postnatal ward babies

A PGL and medical assessment is immediately advised for postnatal ward babies with:

- 8 hours or more without feed
- Hypothermia (temp < 36°C)
- Jitteriness

If PGL ≥ 2.6mmol/L

- Hypoglycaemia is not the cause of symptoms

If PGL 1.5-2.5 mmol/L

- Buccal Glucose gel 40% at 0.5mL/kg/dose
- Followed immediately by breast feed and EBM if available, by means agreeable to mother if baby is asymptomatic and physiologically stable. Glucose gel is not recommended after 48 hours of age.
- If intent is to artificially feed, give formula 30mL/kg/day in a 3 hourly aliquot
- Manage an identified problem
- Therapeutic goal is PGL ≥2.6mmol/L
- Repeat PGL in 30 to 60 minutes; consider 10% glucose infusion at 60mL/kg/day if goal not achieved
- If more than 2 doses of glucose gel are required or for persistent hypoglycaemia, seek consultant advice

If PGL <1.5 mmol/L

- Glucose gel 40% at 0.5ml/kg/dose AND
- Obtain IV access and give 10 % glucose bolus (2mL/kg over 5 min) and 10 % glucose infusion initially at 90 mL/kg/day
- Consider glucagon 200microgram / kg (= 0.2 units/kg) IM, if IV access delayed
- Repeat PGL in 30 minutes. Therapeutic goal is PGL ≥2.6mmol/L if infant does not have any major illness. Aim to achieve therapeutic goal in 30-60 minutes.
- Seek consultant 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. These include:

- Seizures
- Critically unwell baby
- Severe 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
- 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 and managed accordingly in conjunction with the underlying problem.

If PGL <2.6mmol/L

- Give IV 10% glucose bolus (2mL/kg) and start infusion initially at 90mL/kg/day. If fluid restriction is required, consider the need for concentrated glucose solution
- If IV access is delayed, give IM glucagon 200microgram / kg (= 0.2 units / kg) while continued IV access is pursued
- Repeat PGL in 30 minutes
- Therapeutic goal PGL ≥ 3.5mmol/L. Aim to achieve therapeutic goal within 30-60 mins
- Seek consultant advice

If PGL ≥2.6mmol/L

- Continue IV 10% glucose infusion at 60ml/kg/d with therapeutic goal PGL ≥3.5mmol/L
- Hypoglycaemia unlikely to be the cause of seizures
- Seek consultant advice

4. Babies with unexplained or persistent hypoglycaemia, or hypoglycaemia beyond the first 48 hours

Consider hypoglycaemia screen provided the treatment of hypoglycaemia is not delayed. Further testing for underlying metabolic/ endocrine causes may be necessary in liaison with the endocrine team.

A controlled fasting study for 6 hours is recommended prior to discharge home.

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Write Group Lead

Dr Jojy Varghese

Write Group Members

A/Prof Andy McPhee
Dr Scott Morris
Dr Nigel Stewart

SAPPG Management Group Members

Sonia Angus
Lyn Bastian
Dr Elizabeth Beare
Elizabeth Bennett
Dr Feisal Chenia
John Coomblas
Dr Danielle Crosby
Dr Vanessa Ellison
Jackie Kitschke
Dr Kritesh Kumar
Catherine Leggett
Dr Anupam Parange
Rebecca Smith
A/Prof Chris Wilkinson

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Developed by: SA Maternal, Neonatal & Gynaecology Community of Practice
Contact: HealthCYWHSPerinatalProtocol@sa.gov.au
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