South Australian Perinatal Practice Guidelines

Hypoglycaemia (Neonatal)

Important points

Key physiological principles[1,2,3]

- 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.[4]
- 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 bed-side 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.

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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.
- There is no clear and satisfactory definition of hypoglycaemia based on plasma glucose levels alone, however, 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 goals6

Table 80.1
Quoted values are for gold standard laboratory methodology.

Clinical setting	Intervention threshold	Therapeutic goal	Main therapeutic intervention
Well infant, not in 'at risk' group	Don't measure glucose unless hypothermic, feeding abnormally, or becomes unwell.		Normal care
'At risk' well infant screened for hypoglycaemia at 1 and 4 hours of age	<2.0mmol/L	>2.5 mmol/L	Feeding
Unwell infant Abnormal feeding or hypothermia beyond the 4 hour transition period Seizures Requiring intravenous fluids (implies an unwell infant)	<2.5 mmol/L	>3.5 mmol/L	IV glucose. Feeds in selected cases.
All infants	<1.5 mmol/L urgent treatment required with IV glucose	>3.5 mmol/L	IV 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.[4,6]
- Plasma glucose levels of <1.5mmol/L require urgent treatment with IV dextrose 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

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fat, loose skin folds, withered appearance) formula supplementation of breast-feeding until breast milk flow is established is recommended. (follow link to Chapter 25 fetal growth restricted)

- 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.
- Large size for gestation (follow link to chapter 24 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.[7,8]
- Jitteriness is common and usually benign, and a PGL>2.5mmol/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 (for further information, refer to male and female intrauterine growth charts)
- Mild prematurity (32-37 weeks gestation)
- Hypothermia (per rectum temperature < 36^0C)
- 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.

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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 2-4ml/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 2mL/kg over 5 minutes followed by an infusion of 60ml/kg/d of 10% dextrose
- Repeat PGL in 1 hour. Therapeutic goal PGL >2.5mmol/L for enteral feeding and >3.5mmo/L on IV fluids.
- Seek advice

If PGL<1.5 mmol/L at any time

- Obtain IV access and give 10% glucose bolus and infusion as above. Consider glucagon 0.1 milligram/kg (=0.1 units/kg) IM, if IV access delayed
- Repeat PGL in 30 minutes. Therapeutic goal PGL>3.5mol/L
- 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 (PR temp <36^{O}C)
- Jitteriness

If PGL≥2.5mmol/L

- Hypoglycaemia is not the cause of symptoms

If PGL 1.5-2.5mmol/L

- Feeding is attempted with a repeat PGL in 1hour
- Therapeutic goal PGL>3.5mmol/L
- Seek advice

If PGL<1.5mmol/L

- Obtain IV access and give an IV 10% glucose bolus and infusion as above. Consider glucagon 0.1milligram/kg (=0.1 units/kg) IM, if IV access delayed.
- Therapeutic goal PGL >3.5mmol/L
- 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

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- 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 60ml/kg/d as part of management of the underlying problem

A PGL is taken immediately at the time of assessment

If PGL<2.5mmol/L

- Give an IV 10% glucose bolus 2mL/kg over 5 minutes and repeat the PGL in 30 minutes
- Consider glucagon 0.1 milligram/kg (=0.1 units/kg) IM, if IV access delayed
- Therapeutic goal PGL >3.5mmol/L
- Paediatric or neonatology advice is required

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