Prevention and Management of Hypoglycaemia

*Use with the Hypoglycaemia Care Plan for babies on Labour and Postnatal Wards.*

**General Principles**

1) Anticipate hypoglycaemia in high risk infants
   1. consider pre-delivery breast milk harvesting
   2. ensure hypoglycaemia plan known prior to delivery

2) Initiate feeds early and three hourly feeds thereafter for high risk babies

3) Don’t do blood sugar before baby is 2 hours old unless there are clinical signs

4) Give dextrose gel to infants in correct amounts, promptly, according to blood sugar

5) Keep babies warm at all times

6) Avoid separation of mothers and infants.

7) Support establishing breast feeding
   1. Use of dextrose gel as first line treatment for hypoglycaemia
   2. Encourage expression of breast milk for use as feed supplement, only use formula supplements at 60mls/kg/d if no EBM available
   3. Passing of nasogastric tube and admission to SCU (with mother) if more frequent feeds/larger feed volumes required

8) The role of the neonatal SHO/Registrar is to take a history, look for risk factors, examine the baby for signs/symptoms of hypoglycaemia, review the charts, support the parent(s) and midwife, and ensure baby is managed according to the guideline.

9) If enteral feeding insufficient to maintain normal blood sugar levels, to commence IV dextrose
   1. Avoid IV bolus of dextrose if possible
   2. Start IV glucose load at 4-6mg/kg/min and increase in steps of 2mg/kg/min
   3. Use of “5 and 50” glucose regime for independent management of glucose load and flow rate

10) Treat severe hypoglycaemia ≤1.0mmol/L urgently with IV glucose
Blood glucose levels in the neonate

As part of the normal postnatal adaptation, newborn infants' blood glucose levels fall immediately following delivery, reaching the lowest levels within 1-2 hours after birth. After that, in healthy, normally grown term babies the levels then spontaneously recover as feeds are established. The neonatal brain uses lactate as an alternative metabolic fuel whilst feeding is being established in the first 24 - 48 hours. However recent evidence indicates that there is also a hypoketotic state and so babies remain vulnerable until their blood sugar level normalises.

There are some groups of newborns who are at greater risk of symptomatic hypoglycaemia and risk of neuronal damage. **Preterm infants** and **Small for Gestational Age babies (GROW protocol)** may have reduced glycogen stores, impaired gluconeogenesis due to liver immaturity and additional suppression of ketones production (as an alternative substrate). **Large babies** (>4.5kg) or **babies with diabetic mothers** are at risk of hyperinsulinism causing profound hypoglycaemia. Other at-risk groups are defined below.

Definition of hypoglycaemia

We use different levels of blood sugar level (BSL) to define the actions necessary

1. BSL of 2.6mmol/L or more is normal
2. BSL between 1.8 and 2.5mmol/L is usually transitional
3. BSL between 1.5 and 1.8mmol/L may be physiological but may be pathological
4. BSL of 1.5mmol/L or less, if prolonged, may put the baby at risk of neuronal damage
5. BSL of 1.0mmol/L or less is severe hypoglycaemia and requires urgent IV treatment

Symptoms and signs of hypoglycaemia

Neurogenic (sympathetic nervous activity): jitteriness, tachycardia, pallor, hypothermia

Neuroglycopenic (impaired brain function): floppiness, sleepiness (more than 8 hours between feeds), irritability, poor feeding, cyanosis, tachypnoea, apnoeic episodes, weak or high-pitched cry, seizures.

Measurement of blood sugar levels (BSL)

**Do not check a BSL in a baby less than 2 hours old** – low BSL are ‘normal’ before then – unless there are clear clinical signs of hypoglycaemia.

The quickest / most convenient way to measure BSL is with a handheld blood glucose meter. These consistently underestimate the actual sugar level compared to capillary blood gas glucose (CBGS). Thus a low/borderline reading on portable glucose meter should be checked with a CBGS, although treatment (e.g. with dextrose gel) should not be delayed

Jitteriness

Jitteriness is a poorly defined symptom and is not a definitive sign of hypoglycaemia (UNICEF).

Many babies will appear jittery on handling, therefore a definition such as the following is suggested:

“Excessive repetitive movements of one or more limbs, which are unprovoked and usually relatively fast. It is important to be sure that this movement is not simply a response to stimuli.”
Measures for prevention and management of hypoglycaemia

Babies are at LOW or HIGH risk for hypoglycaemia which is often preventable

General measures to PREVENT hypoglycaemia apply to all babies:

**Keep babies warm and dry**

**Offer feeds early (high risk babies within 30 minutes of birth, low risk within 3 hours)**

The risk of hypoglycaemia should be anticipated and assessed on Delivery Suite by the midwife caring for the mother and newborn infant.

**LOW RISK INFANTS**

Normally grown term infants who are well, warm and feeding properly are at low risk of hypoglycaemia and do not require routine BSL testing. Infrequent feeding in a well infant is not an indication for BSL testing – it is usual for a baby to feed as little as 4 times in the first 24 hours of life - but a baby should not go for longer than 8 hours between feeds.

If there are clinical concerns – if baby becomes systemically unwell or there are signs of hypoglycaemia, manage baby according to the “Clinical Concern Pathway” (below)

**HIGH RISK INFANTS**

High risk babies should be identified by their midwife on Delivery Suite and the “Hypoglycaemia Care Plan” should be commenced and placed in the notes. Babies will follow the “Infant at Risk Pathway”.

High risk criteria include any one or more of:

- Prematurity (<37 weeks gestation – including all babies up to and including 36+6 weeks)
- Small for Gestational Age (GROW protocol – less than 10th centile on EFW/BW)*
- Large for dates (≥ 4.5kg birth weight)
- Diabetic mother (all types)

Infants of women with diabetes are also at higher risk of persistent respiratory distress, congenital heart disease, polycythaemia, and severe jaundice. If there are any clinical concerns in these infants, the Neonatal SHO should be called to review the baby.

Other factors may increase the risk of neonatal hypoglycaemia:

- Maternal drug therapy (beta blockers, sodium valproate)
- Infection
- Polycythaemia
- Hypoxic-ischaemic encephalopathy
- Respiratory distress
- Inborn errors of metabolism
- Syndromes such as Beckwith- Wiedemann
- Rebound hypoglycaemia following IV dextrose bolus

* The GROW protocol is used antenatally to identify babies who are SGA based on parental characteristics such as...
height and ethnicity. It is administered by the Perinatal Institute. The use of GROW nationally and by region (e.g. South East Coast can be found here). More information about GROW can be accessed here.
Hypoglycaemia Care Pathway:
Preventing and Managing Hypoglycaemia in Newborns

Most babies at risk of / with hypoglycaemia will be managed by midwives on Delivery Suite/ Postnatal Ward without the need for escalation of medical intervention beyond dextrose gel administration. This approach supports breastfeeding and bonding, reduces the number of heel-pricks for the baby and shortens the length of stay.

BSL of 2.6mmol/L (or more) is the **THERAPEUTIC OBJECTIVE**
BSL of 1.8mmol/L is the **OPERATIONAL THRESHOLD** (neonatal medical team informed)

There are 3 escalations in the pathway for calling the Neonatal SHO. Use the **SBAR** (**S**ituation- **B**ackground- **A**ssessment- **R**ecommendation) framework to ensure clear communication e.g.

Inform Neonatal SHO that:
(S) “Baby X is X hours/days old, has low blood sugar (level, how checked), temperature is X°C
(B) Any risk factors,
(A) Is being managed on pathway and received (X doses of gel) (X blood sugar checks)

AND

**SHO - INFORM** (R) attendance not expected
**SHO - REVIEW** (R) attendance required soon but not urgently
**SHO - URGENT** (R) attendance required urgently”

Dextrose Gel

Dextrose gel is the immediate first-line treatment for any low blood sugar. 0.5mls per kg of 40% dextrose gel should be given to the infant (200mg/kg glucose). 0.5mls is approximately equivalent to the same amount of 40% dextrose gel that can be generously applied to an adult fingertip. Therefore the dose is **one full fingertip per kg** – for example a 3kg baby would require 3 “full fingertips” worth of 40% dextrose gel. A 3.5kg baby would receive 4 full fingertips etc. The gel is applied topically to the buccal mucosa.

**INFANT AT RISK PATHWAY** for those infants who have one (or more) risk factors

- Feed within 30 minutes of birth
  - If first feed is taken within 1 hour of birth, check first BSL prior to the second feed (~3 hours)
  - If first feed more than 1 hour after birth (pathway failure), check BSL at 2 hours of age
  - Feeds should be offered 3 hourly
  - The first (pre-feed) BSL should be checked on the portable blood glucose meter
  - The baby’s temperature should be checked at the time of the BSL
  - If first BSL is ≥2.6 mmol/L then recheck in 9-10 hours (prior to the 4th feed). Observe infant on the postnatal ward for 24hours (general obs, monitor feeding). If there are any further concerns (such as poor feeding or clinical signs of hypoglycaemia), recheck BSL immediately and start a NEW hypoglycaemia care plan. If the first pre-feed BSL is <2.6 mmol/L, the CBGS should be checked (the NICU blood gas machine has a glucose-only profile for this purpose)

If the first pre-feed BSL or CBGS is less than 2.6mmol/L then **give dextrose gel immediately** THEN

- If CBGS between 1.5 and 1.8mmol/L AND no symptoms/signs
  - SHO - REVIEW
  - Ensure feeding plan being followed
  - No formula top ups
- If CBGS between 1.5 and 1.8mmol/L AND symptoms/signs present
  - SHO – ATTEND
- If CBGS ≤1.5mmol/L then for immediate SHO/Registrar attendance
The infant should be fed (breast or formula according to maternal preference.) Every step should be taken to aid and support mothers who wish to breast feed to help with establishment of breastfeeding.

Ensure the infant is warm and dry.

BSL should be repeated prior to the next feed (3 hourly). There is no need to take post-feed BSL.

Provided that the blood sugars are stable or improving and that the infant remains well, treatments with dextrose gel can be used up to three times whilst ensuring warmth and 3 hourly feeding.

After 3 ‘rounds’ of dextrose gel, if the blood sugar is still low then offer top-up milk supplements (EBM if available, formula if not) at 10mls/kg per feed (this equates to approximately 60mls/kg/day).

If this is the baby’s first low glucose reading (i.e. it was normal after the first feed but on retesting prior to the fourth feed is now low) use dextrose gel.

In line with the UK Baby Friendly Initiative we aim to promote and support breast feeding mothers, whilst ensuring the safety of all infants at risk of hypoglycaemia. Moderate hypoglycaemia (i.e. BSL 1.8-2.5mmol/L) in an otherwise well infant is not a contraindication to breast feeding, and establishment of breast feeding should be supported at all stages of the care pathway, even when supplemental formula is required. Expressed breast milk should be used first as a supplement (if available), and parents should be informed as to why infant formula is being used if this becomes necessary.

**These guidelines are intended for the management of otherwise well babies on the Postnatal Ward and Delivery Suite. They are not intended to replace clinical judgement, and if there are concerns at any point the Neonatal SHO or Registrar should be contacted, although they are expected to follow the guideline under normal circumstances.**

Supplements (EBM or formula) may sometimes be required at “day ahead” volumes: 90mls/kg/day on first day, 120mls/kg/day on second day, 150mls/kg/day on third day onwards.

If a baby is vomiting consider other causes (structural obstruction, sepsis) or consider a change to more frequent smaller volume feeds.

**CLINICAL CONCERN PATHWAY**

Normally grown term infants may be started on the Hypoglycaemia Care Plan if there is clinical concern: if the baby becomes systemically unwell or there are signs of hypoglycaemia such as poor tone, excessive sleepiness (>8 hours between feeds), irritability, apnoea, jitteriness or seizure activity.

In these cases the baby should have a first blood sugar level as per the above pathway. Once the baby has had two consecutive blood sugar levels at 2.6mmol/L or more, monitoring can be stopped. With these infants there is no need to complete a further 24 hours observation as per the high risk infants.
Persistent Hypoglycaemia

If, despite the above measures infants remain persistently hypoglycaemic or are profoundly hypoglycaemic at any stage, further measures will need to be taken. If BSL are 1.8-2.5 mmol/L and infants remain systematically well, the commencement of “day ahead” volumes of EBM/formula supplements (see above) and/or feeding more frequently may be adequate as the next step after dextrose gel (three ‘rounds’ can be used – see pathway).

Where possible, it is preferable to use enteral feeding/supplementation to IV dextrose. If an infant requires two hourly feeding, a nasogastric tube can be passed and the baby admitted to SCU so that mothers and babies can be kept together where possible.

Management of persistent hypoglycaemia requiring IV dextrose

Any infant who has persistent symptoms, is not tolerating enteral feeds, or is unable to maintain normoglycaemia with appropriate enteral feeds alone should be commenced on an intravenous infusion of 10% dextrose. This will involve admission. Blood tests required will depend on the clinical scenario

- Infants receiving IV dextrose should also receive enteral feeds IF there are no contraindications
- Normal neonatal hepatic glucose production rate is 4-6 mg/kg/min – start IV 10% dextrose at this rate
  - For BSL 1.5 - 2.5 mmol/L despite attempts at enteral management, starting 10% dextrose at 90mls/kg/day will give 6.25mg/kg/min. A bolus is not normally required unless the baby is symptomatic, as boluses can provoke rebound hyperinsulinism.
  - For BSL <1.5 mmol/L (on CBGS) despite treatment (dextrose gel/feed) and/or with symptoms (e.g. fitting), give IV bolus of 3mls/kg of 10% dextrose AND increase the glucose load being given (either increasing rate or concentration of IV dextrose). Do not give an IV bolus without also using glucose infusion. The aim is to rapidly increase BSL to >2.0 mmol/L.
  - Glucose load should be increased in steps of 2mg/kg/min. Use the glucose infusion calculator
  - Check BSL 30 minutes after initiation of treatment and then at 2 hours. Frequency of testing can be reduced if there has been an adequate response.
  - If BSL is still low, the glucose load needs to be increased. This can be done by increasing either volume of 10% dextrose given or increasing the concentration of the dextrose. It is important not to increase the volume of fluid given beyond 120mls/kg/day on the first day of postnatal life as there is a risk of hyponatraemia.
  - To increase the concentration of dextrose use the “5 and 50” regime and online calculator
  - If the concentration of dextrose required >12.5% this must be given through a central line (UVC/long line)
  - At all stages document the amount of glucose being given in mg/kg/min
  - Further boluses can be given if there are further episodes of severe or symptomatic hypoglycaemia but this should not be done in isolation: glucose load should also be increased AND cause for the drop should be searched for (tissued IV line, possible metabolic condition etc.)
  - The attending/on call consultant should be informed of all infants with persistently severely hypoglycaemia and of infants requiring >12mg/kg/minute IV glucose
  - Once BSL >2.6 mmol/L for 24 hours, reduce IV fluids and increase enteral fluids as appropriate every 6 hours, checking blood sugars 4 hourly. On full enteral feeds check BSL every 6 hours for 24 hours, then 12 hourly for 24 hours, then cease testing if BSL consistently >2.6mmol/L
“5 & 50” glucose regime

- By running 5% and 50% dextrose as simultaneous infusions, glucose load (mg/kg/min) and flow rate (mls/hr) can be independently adjusted.
- If final glucose concentration is >12.5%, run infusion through a central line (UVC or long line).
- Electrolytes can be added to these infusions – the total desired amount (in mmol/kg/day) added to both infusions, calculated for both as if run at the full total daily volume (mls/kg/day). For example, 4mmol/kg/day NaCl desired at 120mls/kg/day would need 16.6mmol NaCl to be added to one 500ml bag of fluid. Therefore add 16.6mmol NaCl to BOTH the 5% dextrose and 50% dextrose bag (as if each would run at 120mls/kg/day). 120mls/kg/day will be delivered by a combination of the 5% and 50% dextrose depending on the glucose load required but regardless of the final glucose concentration 4mmol/kg/day of NaCl will be delivered).

Glucagon for severe hypoglycaemia

- Glucagon (100mcg/kg IM) may be required in the following situations:
  - Unable to gain IV access in newly admitted infant with symptomatic hypoglycaemia
  - Loss of IV access in presence of significant/symptomatic hypoglycaemia
  - Persistence of hypoglycaemia despite increasing glucose infusion rate
  - Presence of seizures and hypoglycaemia
- Rarely an IV bolus or infusion of glucagon might be needed. Rates of 15-30 mcg/kg/hr can be given IV or subcutaneously

Further Management of Persistent Hypoglycaemia

If infant remains hypoglycaemic despite glucose load of 12mg/kg/min take bloods (preferably when baby is hypoglycaemic but do NOT delay treatment) for:

**FIRST LINE**
- Laboratory Glucose
- FBC, LFTs, TFTs
- Blood gas with lactate
- Insulin level [send to RSCH – speak to biochemist, emphasise urgent sample, same day result needed]
- Cortisol
- Growth hormone
- Urine dip test for ketones

**SECOND LINE**
- Ammonia (speak to biochemist, needs to go to lab immediately on ice)
- Lactate
- Fatty acids
- Ketone bodies
- Carnitine and acetylcarnitine (on blood spot form)
- Urine organic acids
Further testing such as lumbar puncture for CSF glucose depends on the clinical scenario / history.

- High insulin levels with hypoglycaemia and no urinary ketones indicates hyperinsulinism. In hyperinsulinism it is not unusual to have a glucose requirement of 15-20mg/kg/min

- Some babies may benefit from Infatrini formula for extra glucose intake. This should be discussed with the attending Consultant and (if possible) the Dietician first. The Nutritional Calculator can be used to work out glucose delivery rates.

- Treatment with diazoxide / chlorthiazide should be considered (by the attending Consultant). Total fluids should be reduced to 120mls/kg/day as diazoxide may cause fluid retention. Dr Bahl will advise on management and Dr Khalid Hussein at GOSH may be contacted if advice/transfer if required for refractory cases.

**Follow up**

All *significantly* symptomatic babies and those who have required more than 12mg/kg/min of glucose infusion should be followed up as outpatients. Please discuss with the attending Consultant.
References


Diwaker et al. Plasma glucose levels in term infants who are appropriate size for gestation and exclusively breast fed. Arch Dis Child Fetal Neonatal Ed 2002; 87: F46-48


Guidelines prepared by Dr. Matthews, Dr. Sage, Dr. Reynolds March 2014
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