HYPOGLYCAEMIA

DEFINITION
Asymptomatic hypoglycaemia
- Low blood glucose concentrations are common in preterm and small-for-gestational-age infants
- No simple correlation between blood glucose concentration and neuroglycopenia
- Blood glucose ≥ 2.0 mmol/L is safe

Symptomatic hypoglycaemia
- Blood glucose < 2.6 mmol/L and any of the following symptoms, provided these resolve once hypoglycaemia has been corrected:
  - convulsions
  - abnormal neurological behaviour, including hypotonia and poor response to stimulation
  - apnoea

Symptoms cannot be attributed to hypoglycaemia if they persist after adequate treatment. Jitteriness alone does not constitute symptomatic hypoglycaemia

PREVENTION
- Keep all infants warm
- Feed all high risk infants within 2 hr of birth if possible
- In all starved high risk infants, institute IV infusion of glucose 10% (see below)

At risk infants
Perform blood glucose estimation in:
- Small for dates
- Preterm
- Any ill infant
- Infant of diabetic mother
- Beckwith-Wiedemann syndrome
- Haemolytic disease of the newborn
- Severe fluid restriction

Monitor all at risk patients using near-patient monitoring
- First 24 hr, 3-4 hrly
- Second 24 hr, 4-6 hrly
- Then as necessary
- Babies requiring TPN, at least daily
- Babies fed enterally, immediately before feeds

Always verify a low near-patient test result (<2.6 mmol/L) in a symptomatic baby by sending a sample for laboratory blood glucose estimation

MANAGEMENT
Never use concentrated (>20%) glucose solutions in babies

Asymptomatic hypoglycaemia in at-risk infant
- Correct hypothermia (see Hypothermia guideline)
- Increase frequency and/or volume of feeds
- Milk is more beneficial than glucose 10% as it is more energy dense (70 kcal/100 mL v 40 kcal/100 mL) and contains fats that promote ketoneogenesis and glucose uptake
- Repeat glucose measurement after 1 hr. If low, check laboratory blood glucose
- Consider giving IV glucose if:
  - unable to increase/tolerate feed frequency or volume or
  - intensive feeding does not produce normoglycaemia
- Give glucose 6 mg/kg/min (glucose 10% at 90 mL/kg/day) by IV infusion
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- If infant develops symptoms or becomes profoundly hypoglycaemic (<1.1 mmol/L), follow Symptomatic hypoglycaemia protocol (see below) immediately
- Continue enteral feeding during IV infusion

**Step down**
- Once normoglycaemia achieved, wean from infusion as tolerated

**Symptomatic hypoglycaemia**

- Aim for blood glucose ≥2.6 mmol/L
- Give glucose 10% 2.5 mL/kg by IV bolus over 5 min into peripheral vein and follow with an infusion of at least 90 mL/kg/day (~6 mg/kg/min), that may be increased if necessary. Continue enteral feeds
- Record whether symptoms respond to treatment within 30 min: very important for definitive diagnosis of symptomatic hypoglycaemia
- Recheck blood glucose after 30 min. If still low, give another 2.5 mL/kg bolus and increase infusion rate to 120 mL/kg/day (8.3 mg/kg/min) except on day 1 when increase glucose concentration of infusion
- Record response and repeat glucose measurement in 1 hr. If still low, check blood glucose by laboratory estimation and, if hypoglycaemia confirmed, increase delivered glucose content by increasing either volume (to 150 mL/kg/day), or concentration (12.5-20%)

<table>
<thead>
<tr>
<th>Infusion concentration (%)</th>
<th>Volume of 10% glucose (mL)</th>
<th>Volume of 50% glucose (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>47.5</td>
<td>2.5</td>
</tr>
<tr>
<td>15</td>
<td>44.0</td>
<td>6.0</td>
</tr>
<tr>
<td>17</td>
<td>41.0</td>
<td>9.0</td>
</tr>
<tr>
<td>20</td>
<td>37.5</td>
<td>12.5</td>
</tr>
</tbody>
</table>

**Give glucose 20% centrally as extremely hypertonic.**

*If UVC used, ensure tip not near liver*

**Failure to respond**
- If >12 mg/kg/min of glucose required to achieve normoglycaemia, hyperinsulinaemic state is very likely. Obtain blood sample at time of hypoglycaemia for simultaneous measurement of:
  - blood glucose
  - plasma insulin and serum C-peptide
  - free fatty acids
  - ketones
  - cortisol
  - growth hormone
  - acylcarnitines
  - collect next passed urine for organic acid analysis
- Administer glucagon 200 microgram/kg (maximum 1 mg) IM, SC, or IV. Check blood glucose within 30 min of glucagon administration, and hrly thereafter until stable
- If persistent hyperinsulism suspected, seek advice from paediatric endocrinologist/metabolic paediatrician, and consider early transfer to a unit specialising in the management of such infants

**Routine addition of glucose polymers (e.g. Maxijul) not recommended.**

*If a decision made to use Maxijul, discuss with paediatric dietitian. Beware risk of necrotising enterocolitis*

**Prescription to make up 50 mL of varying concentrations of glucose solution**

**Step down**
- Once blood glucose normal, wean infant on to milk feeds either continuously or by hrly boluses

**MONITORING**
- Hypoglycaemic patients:
  - if symptomatic, every 30 min
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- if asymptomatic, every hr
- continue until normoglycaemic
- Once normoglycaemic, 3-4 hrly until 24 hr has elapsed since last hypoglycaemic episode

SEVERE PERSISTENT OR RECURRENT HYPOGLYCAEMIA

Causes of recurrent, persistent neonatal hypoglycaemia

- Hyperinsulinism
- Endocrine deficiency, especially panhypopituitarism
- Disorder of fatty acid metabolism
- Disorder of carbohydrate metabolism
- Disorder of amino acid metabolism
- Rate of glucose infusion required is good guide to likely cause

<table>
<thead>
<tr>
<th>Substrate or endocrine deficiency</th>
<th>&lt;5 mL/kg/hr of glucose 10% required (&lt;8 mg/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperinsulinism</td>
<td>&gt;6 mL/kg/hr of glucose 10% required (&gt;10 mg/kg/min)</td>
</tr>
</tbody>
</table>

When to investigate further

- Persistent recurrent hypoglycaemia, especially in ‘low risk’ baby
- Unexpectedly profound hypoglycaemia in a well baby
- Hypoglycaemia in association with metabolic acidosis
- Hypoglycaemia in association with other abnormalities:
  - midline defects
  - micropenis
  - exomphalos
  - erratic temperature control
- Family history of SIDS, Reye’s syndrome, or developmental delay

Investigations

- Paired insulin and glucose estimations while hypoglycaemic (hyperinsulinism confirmed if insulin >10 picomol/L when glucose <2 mmol/L or glucose:insulin ratio <0.3)
- Urinary ketones and organic acids
- Serum C-peptide
- Plasma cortisol and growth hormone
- Plasma amino acids
- Plasma acylcarnitine
- Free and total carnitines
- Free fatty acids and betahydroxybuturate
- Galactosaemia screen
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Management of glycaemic status in at risk infants

Cord blood glucose not available

- Check cord blood glucose

>2.6 mmol/L

NO and symptomatic

- Admit to neonatal unit
- Start IV glucose (10%) 90 mL/kg/day

>2.60 mmol/L

- Check blood glucose 1 hr later

>2.0 mmol/L

Symptomatic

- Increase volume and/or concentration of IV glucose
- Consider glucagon after senior advice
- Investigate

NO

Asymptomatic

- Increase volume and frequency of feeds
- Check blood glucose before 4th feed

>2.6 mmol/L

NO

- Continue feeding
- Check blood glucose before 4th feed

YES

- Continue feeding
- No more blood glucose monitoring necessary unless symptomatic

>2.0 mmol/L

YES

- Continue feeding
- Check blood glucose before 4th feed

>2.6 mmol/L

YES

- Check blood glucose 1 hr later

- Continue IV fluids
- Commence and increase enteral feeds as tolerated
- Monitor pre-feed blood glucose and decrease IV fluids gradually

YES or No and asymptomatic

- Do not admit to neonatal unit unless otherwise indicated
- Initiate feeding as soon as possible
- Breastfeeding recommended but support mother’s choice
- Check blood glucose before 2nd feed

>2.0 mmol/L

YES

- Continue feeding
- Check blood glucose before 4th feed

>2.6 mmol/L

YES

- Continue feeding
- No more blood glucose monitoring necessary unless symptomatic