Title: Screening and Management of Neonatal Hypoglycaemia
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Target audience: Staff of the Nottingham Neonatal Service, Delivery Suites and Postnatal Wards
Patients to whom this applies: Patients of the Nottingham Neonatal Service and newborn infants on the Postnatal Wards and Labour Suites of the Nottingham University Hospitals NHS Trust who fit the inclusion criteria of the guideline below
Key Words: Neonatal hypoglycaemia
Risk Managed: Neonatal hypoglycaemia and its complications
Evidence used: The contemporary evidence base has been used to develop this guideline. References to studies utilised in the preparation of this guideline are given at its end.

Clinical guidelines are guidelines only. The interpretation and application of clinical guidelines remain the responsibility of the individual clinician. If in doubt, contact a senior colleague. Caution is advised when using guidelines after the review date. This guideline has been registered with the Nottingham University Hospitals NHS Trust.
The Hypoglycaemia Guideline will be monitored in conjunction with the NUH Maternity Services Clinical and Operational Monitoring Plan.

Key recommendations for blood glucose measurements in newborn infants:

Blood glucose measurement is indicated:
- if the baby is at risk (see Table 3)
- if symptoms suggestive of hypoglycaemia are present
- in the investigation of coma or convulsions during neonatal intensive care

Key practice points:
- An infant who is unarousable for a feed should be screened for hypoglycaemia.
- Jitteriness alone is not a reason to measure blood glucose. Jitteriness is defined as involuntary, symmetrical rhythmical movement that can be stopped by gently flexing or holding the limb.
Newborn infants at risk of hypoglycaemia:

- Preterm (less than 37 weeks gestation)
- Birth weight less than 2\textsuperscript{nd} centile (see Table below)
- Large for gestational age (see Table below)
- Maternal diabetes
- Infants of mothers taking beta-blockers (e.g. Labetalol) in the third trimester and / or at time of delivery
- Severe intrapartum asphyxia, resuscitation at birth
- Ill babies (e.g infection, grunting)
- Babies with a low temperature
- Babies with congenital disorders (Beckwith-Weidemann)

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Intrauterine growth restriction (birth weight 2nd centile or below)</th>
<th>Macrosomic babies (birth weight 98th centile or above)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boys</td>
<td>Girls</td>
</tr>
<tr>
<td>&lt;37</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td>37</td>
<td>&lt;2.10</td>
<td>&lt;2.00</td>
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<tr>
<td>38</td>
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<td>41</td>
<td>&lt;2.80</td>
<td>&lt;2.75</td>
</tr>
<tr>
<td>42</td>
<td>&lt;2.90</td>
<td>&lt;2.85</td>
</tr>
</tbody>
</table>

Healthy term babies have an innate ability to use alternative fuel stored in their bodies for energy if they don’t consume calories via milk. This is called counter regulation.
Healthy term babies are therefore probably not at risk of coming to harm due to hypoglycaemia in the first few days of life.

However, some babies, such as those listed as at risk of hypoglycaemia (see above) may not be able to use these alternative fuels and need to be fed regularly and have their blood sugar levels monitored. It is essential these babies undergo early feeding and skin to skin care is encouraged to keep baby warm. Even a small amount of colostrum can raise the blood glucose level. If parents wish to use formula feed this is also satisfactory.

Currently blood glucose less than 2.6 mmol/l is considered neonatal hypoglycaemia. Infants with two pre feed blood glucose readings equal to or more than 2.6 mmol/l at least 3 hours apart can discontinue blood glucose monitoring.

**Blood sugar levels**

- If the blood glucose is **2.6 mmol/l or above and showing no signs of hypoglycaemia** continue with FLOWCHART 1
- If the blood glucose is **between 1.0 and 2.6 mmol/l and showing no signs of hypoglycaemia**, go to FLOWCHART 2
- If the blood glucose is **between 1.0 – 2.6 mmol/l for more than two measurements** contact a neonatal doctor as the baby may need NICU admission and assessment for causes of persistent hypoglycaemia
- If the blood glucose is under **1 mmol/l or symptomatic**, go to FLOWCHART 3 and refer immediately to a neonatologist.

**Symptomatic hypoglycaemia:**

If a newborn is unwell or shows signs of hypoglycaemia:

- Change in level of consciousness: stupor or lethargy or irritability
- Hypotonia, inactivity
- Seizures
- High-pitched cry, poor feeding
- Hypothermia
- Respiratory depression: cyanosis, apnoea

The neonatal ST1-3 doctor should be informed urgently.

"Crash call neonatal team on “2222′ via switchboard"
1 Background

In majority of healthy neonates, the frequently observed low blood glucose concentrations are not related to any significant problem and merely reflect normal processes of metabolic adaptation to extra-uterine life [1]. However, when low blood glucose levels are prolonged or recurrent, they may result in acute systemic effects and other neurologic sequelae. In addition, in a small number of infants, who may have maladaptation of glucose homeostasis, blood glucose monitoring and proactive management is required.

1.1 Extra-uterine adaption of glucose homeostasis

The fetus depends entirely on maternal supply and facilitated diffusion across the placenta to maintain glucose levels and, under normal condition, gluconeogenesis appears only after birth. Following the clamping of the umbilical cord, blood glucose concentration decreases rapidly followed by a gradual stabilisation over the next 6-12 hours. Studies have demonstrated a wide range of glucose concentrations during the first 72 hours, with values ranging from 1.3-2 mmol/l in healthy breast fed infants [2] [3]. Low plasma glucose activates a number of counter-regulatory pathways resulting in increased systemic lipoysis with ketone utilisation by the brain [3]. Other alternative fuels such as pyruvate and lactate are also utilised by the brain and, as a result of these, the healthy newborn infant is probably not at risk of hypoglycaemia associated neuronal injury over the first few days. In contrast, preterm infants and those with altered homeostasis due to hyperinsulinemic states or intrauterine growth restriction may not produce alternative metabolites and are, therefore, at higher risk.

1.2 Definition of hypoglycaemia

Significant hypoglycaemia cannot be defined by a single number that can be applied universally to every infant but may be unique to each individual and vary with their physiologic stage as well as any existent pathology. To deal with such uncertainty, an operational threshold has been suggested as the concentration of plasma or blood glucose at which clinicians should consider intervention, based on the evidence currently available in the literature [1]. Recent guidance from the AAP [4] and NICE [5] have recommended changing practice from a definitive threshold level for treatment of hypoglycaemia to an operational threshold of 2.0 mmol/l with a therapeutic goal of 2.6 mmol/l. Current guidance recommends initiating intervention for hypoglycaemia following two consecutive blood sugars of < 2.0 mmol/l. Furthermore, BAPM guidance [6] has also recommended an operational threshold approach, which advocates using 2.0mmol/l for infants who are at risk of hypoglycaemia but not exhibiting symptoms.

For infants who are at risk of hypoglycaemia, we consider the value for blood glucose at which intervention is warranted to be 2.6 mmol/l but this will be reviewed in light of the above guidance and may be changed in the future.

This recent change in guidance is based on several studies which do not support the original study advocating 2.6 mmol/l as a definitive cut off level for hypoglycaemia. Lucas et al. reported that infants with recurrent episodes of blood glucose levels < 2.6 mmol/l had a significantly reduced developmental score at 18 months corrected age and has a 3.5 times increased incidence of neurodevelopmental impairment (95% confidence interval (CI) 1.3-9.4)[7]. However, the infants included in this study were preterm (mean (standard deviation) gestational age 30.5 (2.7) weeks) and was subjected to both sample and recall bias. Importantly, the authors state that confounding factors, which could contribute to neurodevelopmental impairment were not accounted for in their analysis, therefore, the association between modest hypoglycaemia and poor neurodevelopmental might not be casual but merely a failure to adequately adjust for confounding factors. More recently,
McKinlay et al. demonstrated that neonatal hypoglycaemia, when treated to maintain a blood glucose concentration of at least 2.6 mmol/l (equivalent to 47 mg/dl), was not associated with adverse neurological outcomes [8]. Furthermore, Tin et al followed up 781 preterm infants (< 32 weeks) at both 2yrs and 15 yrs of age, who had recurrent episodes of blood glucose < 2.6 mmol/l and found no difference in neurodevelopmental outcome compared to matched controls [9].

**Recommendation:**
Infants with a single blood sugar < 1.0 mmol/l or symptomatic infants with a blood sugar < 2.6 mmol/l require intervention for hypoglycaemia until two consecutive readings above 2.6 mmol/l are obtained.
2 Measurement of blood glucose

On the NICU, blood glucose measurement should be made using the blood gas machine. If this facility is unavailable, a blood glucose test should be sent to the laboratory. The point of care glucose stick meters may be inaccurate in their estimation of hypoglycaemia, particularly in the presence of conditions such as high haematocrit, high blood oxygen tension and acidosis [10] [11]. These should not be used in the NICU.

On the postnatal wards, where access to a blood gas machine is not immediate, initial blood glucose measurement may be made using a new generation glucose stick test. However, if the result obtained using this method is <2.0 mmol/L, it must always be re-checked immediately by undertaking a repeat measurement from the blood gas machine or a laboratory sample.

Recommendation:
- In NICU and on Labour Suite: all samples taken for blood glucose levels should be measured on a blood gas machine
- On postnatal wards: blood glucose levels may be measured with bedside glucose sticks but values < 2.0 mmol/l should be confirmed by the gas machine or a laboratory sample

3 Symptoms of hypoglycaemia

Infants may manifest neuroglycopenic signs and symptoms when blood glucose level is low. These can be subtle and are often non-specific such as those given in Table 1. However, it is vital that infants with signs/symptoms of neuroglycopenia are treated as these infants are generally considered at risk of poor neurological outcome. If truly caused by hypoglycaemia, such signs are relatively easily and quickly reversed by normalisation of glucose levels.

Table 1. Features of neuroglycopenia in newborn infants

| Change in level of consciousness: stupor or lethargy or irritability |
|-------------------------|--------------------------|
| Hypotonia, inactivity    |
| Seizures                |
| High-pitched cry, poor feeding |
| Hypothermia             |
| Respiratory depression: cyanosis, apnoea |

4 Causes of hypoglycaemia in newborn infants

Neonatal hypoglycaemia may occur due to conditions that interrupt the normal extra-uterine adaptation of glucose metabolism or may be a consequence of a co-existing pathology. Some of the conditions that pre-dispose a newborn infant to low blood glucose levels are listed below.

Table 2. Some conditions that predispose to hypoglycaemia

<table>
<thead>
<tr>
<th>Prematurity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-uterine growth restriction and low birth weight</td>
</tr>
<tr>
<td>Sepsis</td>
</tr>
<tr>
<td>Perinatal stress such as hypoxia-ischemia, respiratory distress, meconium aspiration</td>
</tr>
<tr>
<td>Hypothermia</td>
</tr>
<tr>
<td>Maternal drugs such as Tolbutamide and beta blockers, e.g. Labetalol, Polycythaemia</td>
</tr>
</tbody>
</table>
Congenital disorders such as Beckwith-Weidemann, presence of midline defects
Hyperinsulinaemic states such as in infants of diabetic mothers, congenital hyperinsulinemia
Inborn errors of metabolism such as galactosaemia, beta oxidation defects, glycogen storage diseases

5 Infants who require blood glucose monitoring

Normal term infants (> 37 weeks gestation) who are bottle / breast feeding do not require blood glucose monitoring unless they have a predisposing factor (Table 2) or are unwell. As discussed in Section 1.1, term healthy infants may have low blood glucose levels which are normal and safe.

Infants at risk of maladaptation of glucose homeostasis should be proactively identified and treated. **Infants who require screening and proactive management of neonatal hypoglycaemia are listed in Table 3.** These infants are at increased risk of hypoglycaemia and require regular blood glucose monitoring until it is established that they have made a successful transition to extra-uterine glucose homeostasis.

Blood glucose must also be tested in any infant who has symptoms of neuroglycopenia (Table 1).

**Recommendation:**
Infants in the at-risk groups require regular blood glucose monitoring and proactive management to maintain blood glucose levels above a level of 2.6 mmol/l (Table 3)

5.1 Infants of diabetic mothers

The following recommendations are adapted from the NICE guidelines for management of diabetes in pregnancy [5]

- Infants of women with diabetes should stay with their mothers unless there is a clinical complication or there are abnormal signs that warrant admission for intensive or special care
- Blood glucose testing should be carried out routinely 2-4 hours after birth
- Infants of women with diabetes should not be transferred to community care until they are at least 24 hours old and not before it is ensured that the infant is maintaining blood glucose levels and is feeding well.

5.2 Clinical macrosomia

Infants with birth weight 4.5kg are considered macrosomic irrespective of gestational age. However, many infants can have features of fetal overgrowth even when they may not have reached this weight cut off for macrosomia. Such babies may appear ‘fat’ i.e. excess subcutaneous fat such as “chubby cheeks.”

Infants born to women with gestational diabetes, overweight or obese mothers or women with excess gestational weight gain may be at risk of the macrosomic phenotype. Despite being <4.5kg, these infants may be at increased risk of hypoglycaemia. Infants who are greater than 98th centile in weight for their gestational age (Table 3 or use individualised growth chart) are more likely to have excess fetal growth and may also be considered at risk for hypoglycaemia.
Table 3 Infants who require screening and proactive management of neonatal hypoglycaemia

The following groups are at risk of neurological sequelae of neonatal hypoglycaemia, and measures should be in place to identify them at birth for early milk / energy provision and monitoring of blood glucose concentration:

- Infants of all diabetic mothers
- Infants of mothers taking beta-blockers (e.g. Labetalol) in the third trimester and / or at time of delivery
- Intrauterine growth restriction (birth weight 2\textsuperscript{nd} centile or below) or clinically wasted
- Macrosomic babies (birth weight 98\textsuperscript{th} centile or above)

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Boys</th>
<th>Girls</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>42</td>
<td>&lt;2.90</td>
<td>&lt;2.85</td>
<td>&gt;4.8</td>
<td>&gt;4.55</td>
</tr>
</tbody>
</table>

6 Prevention and management of hypoglycaemia

Women should be encouraged to have skin to skin contact with their baby as soon as possible after birth, which will help maintain normothermia and encourage breastfeeding. Babies should not be separated from their mothers for management of hypoglycaemia wherever possible.

6.1 At-risk babies on postnatal ward, labour suite or the neonatal unit:

Flowchart 1 describes the initial management of all infants who fall in at-risk categories listed in Table 3.

6.2 Infants of diabetic mothers

The following recommendations are adapted from the NICE guidelines for management of diabetes in pregnancy [5]

- Infants of women with diabetes should stay with their mothers unless there is a clinical complication or there are abnormal signs that warrant admission for intensive or special care.
- Blood glucose testing should be carried out routinely 2-4 hours after birth
- Infants of women with diabetes should not be transferred to community care until they are at least 24 hours old and not before it is ensured that the infant is maintaining blood glucose levels and is feeding well.

6.3 Clinical macrosomia

Infants with birth weight >98th centile considered macrosomic. However, many infants can have features of fetal overgrowth even when they may not have reached this weight cut off for macrosomia. Such babies may appear ‘fat’ i.e. excess subcutaneous fat such as “chubby cheeks.”

Infants born to women with gestational diabetes, overweight or obese mothers or women with excess gestational weight gain may be at risk of the macrosomic phenotype. Despite being <4.5kg, these infants may be at increased risk of hypoglycaemia. Infants who are greater than 98th centile in weight for their gestational age (Table 3 or use individualised growth chart) are more likely to have excess fetal growth and may also be considered at risk for hypoglycaemia.

6.4 Management of hypoglycaemia in babies on postnatal ward, labour suite or the neonatal unit:

Flowchart 2 describes the management of all infants whose blood glucose is between 1.0mmol/l to 2.6mmol/l and have no abnormal clinical signs.

6.5 Management of infants with persistent low blood glucose, symptomatic infants and those with blood glucose <1mmol/l

A summary of management of this group of infants is given in Flowchart 3. The information in Flowchart 3 should be used in conjunction with the following:

6.5.1 Continue milk feeds

- Milk feeds (breastmilk) should be continued whenever possible and safe to do so. Galactose derived from hydrolysis of lactose in the gut increases hepatic glycogen production and allows for sustained between-feeding hepatic glucose release [12]. Feeds also induce production of intestinal peptides such as incretins that promote insulin secretion at a steadier pace than the spikes seen with intravenous bolus of glucose. Milk feeds also increase levels of alternative fuels such as ketones derived from fatty acids in milk and amino acids which are substrates for gluconeogenesis.
- Feed volumes may be increased to at least a “day ahead” of usual fluid requirement (refer to Guidelines D2 and D3) and may even be increased further, as tolerated.

6.5.2 Intravenous 10% glucose bolus and use of oral glucose gel

- Infants with very low blood glucose (<1mmol/l) or signs / symptoms of neuroglycopenia should receive a bolus of 10% glucose (2.5ml/kg) as soon as intravenous access is obtained and blood samples taken for tests for hypoglycaemia. Any intravenous bolus of glucose must be followed by increasing the amount of carbohydrate delivered to avoid the risk of rebound hypoglycaemia.
- Only 10% glucose should be used for intravenous boluses of glucose – greater concentrations of glucose must never be given as boluses.
- If intravenous access is not readily obtainable, 200 mg/kg of oral glucose gel (0.5ml/kg of 40% glucose gel) may be administered in to the oral mucosa while intravenous access is established. A feed should be given after this bolus. A randomised controlled trial of glucose gel (200 mg/kg) vs. placebo for management of hypoglycaemia in 35-42 weeks in the first 48 hours of life demonstrated that
treatment with 40% glucose gel was effective in reversal of hypoglycaemia without increasing the risk of rebound hypoglycaemia and was not associated with adverse effects [13].

- Infants who require IV or oral bolus of glucose should be admitted to the NICU and adequate blood glucose levels with milk feeds must be established prior to discharge.

6.5.3 Monitor fluid electrolyte balance

- A combination of IV glucose with the continuation of enteral feeding can result in large volumes of fluid being administered to infants with hypoglycaemia. A careful assessment of fluid and electrolyte balance with monitoring of urinary output and serum electrolytes is required.
- Large fluid volumes may be administered inadvertently. This may be avoided by using higher concentration of glucose to limit the volume delivered.
- Large volume of IV fluids without adequate electrolytes may cause dangerous electrolyte imbalances. Serum electrolytes must be monitored regularly and electrolytes should be added to IV fluids as required.

6.6 Infants with signs / symptoms of neuroglycopenia

- Establish IV access
- Obtain blood samples for hypoglycaemia screen (ensure minimal delay in treatment to obtain blood samples)
- Give a bolus of IV glucose (2.5ml/kg) followed by continuous glucose infusion at 90-120 ml/kg/d
- Check blood glucose 30 min after and monitor regularly. If blood glucose remains low, increase glucose delivery as given in Section 6.8.

In the absence of clearly identifiable risk factors (as in Table 3 or if the infant has hypoglycaemic encephalopathy, investigation of the underlying cause of hypoglycaemia is mandatory (consider the conditions listed in Table 2 or other possible differential diagnoses). Investigations should be undertaken as soon as possible after the low blood glucose result (Appendix 12.1).

6.7 Following intervention, if the blood glucose improves to ≥ 2.6 mmol/l

- Rate of glucose delivery can be reduced if the blood glucose remains stable (i.e. ≥ 2.6 mmol/l) on two consecutive measurements.
- Intravenous glucose should be gradually reduced and enteral feeding continued with monitoring of pre-feed blood glucose with each blood glucose level >2.6 mmol/l.
- When the infant is on full enteral feeds the feed interval can then be gradually increased until 3-4 hourly.
- Blood glucose monitoring can be discontinued following two consecutive levels >2.6mmol/l whilst on 3-4 hourly feeds.

6.8 Following intervention, if the blood glucose remains between 1.0 to 2.5 mmol/l and there are no abnormal clinical signs

Consider the following:

- Increase feed volume if tolerated and appropriate
- Decrease feed intervals to hourly feeds
- If / when the feed interval is hourly and the feed volume cannot be increased any further (e.g. infant is unable to tolerate larger volume of milk such as due to vomiting/ large gastric aspirates):
- Increase volume of intravenous glucose infusion, if fluid electrolyte balance allows (note caution in Section 6.5.3)

**Increase concentration of glucose infusion to deliver more glucose at same or smaller volume of infusion**

- Table 4). Central venous access will be required for delivering glucose solutions over 12.5% concentration.

### 6.9 Choice of enteral feed

Enteral feeds should be continued whenever possible. This should preferably be as breast feeds or cup or gastric tube feeds with expressed breast milk (EBM). Appropriate formula for gestational age or birth weight may be given if not breast feeding (see Guideline D4).

If feed volume cannot be increased further, or is not being tolerated, then a glucose polymer, such as Maxijul, can be added to EBM or formula milk. Changing to a high energy milk or preterm formula is not recommended as these formulae have higher concentrations of non-glucose components which are not required by infants with hypoglycaemia. The use of glucose polymer and any change from of milk should be discussed with the neonatal consultant. Maxijul can be added to EBM or formula milk to increase the glucose and energy in the same volume of milk (Appendix 12.2).

### Table 4. Rates of glucose delivery

<table>
<thead>
<tr>
<th>Strength of IV glucose solution</th>
<th>Rate of glucose delivery (mg/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10%</td>
</tr>
<tr>
<td>Fluid infusion rate (ml/kg/d)</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>4.2</td>
</tr>
<tr>
<td>90</td>
<td>6.3</td>
</tr>
<tr>
<td>100</td>
<td>6.9</td>
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<td>120</td>
<td>8.3</td>
</tr>
<tr>
<td>150</td>
<td>10</td>
</tr>
</tbody>
</table>

*15% and 20% glucose solutions must be delivered via a central line
Glucose delivery rates in white (in black boxes) indicate the need for investigating for hyperinsulinaemia, particularly when required at > 48 hours of age

### 7 Glucose utilisation rates

If hypoglycaemia persists and/or there is difficulty weaning the IV glucose, glucose utilisation rates should be calculated and IV fluids weaned slowly so that the increase in enteral volume maintains or increases the glucose delivery (See table 7 for enteral feed glucose content).
Normal glucose utilisation rates are 4-6 mg/kg/min. Infants in the high-risk groups or those with other pathologies frequently require 6-10 mg/kg/min. The rate of glucose delivery to an infant can be calculated by the formula given below.

\[
\frac{(%\text{glucose}\times10)\times\text{ml/kg/day}}{24\times60} = \frac{\%\text{glucose}\times\text{ml/kg/day}}{144} = \text{glucose infusion rate (mg/kg/min)}
\]

**Infants who require >10 mg/kg/min, particularly beyond the first 48 hours of life usually have a pathological basis for their hypoglycaemia.** These cases must be discussed with the Duty Neonatal Consultant and a referral to the Paediatric Endocrinology team considered.

### 8 Special investigations

These are required if:

- glucose infusion rates to prevent hypoglycaemia are persistently >12 mg/kg/min in a well grown or large for gestational age baby (small for gestational age babies quite often need high glucose infusion rates for several days)
- there is evidence of hypothalamic dysfunction such as unstable temperature or, in a boy, small or abnormal genitalia
- profound hypoglycaemia occurs unexpectedly in a well-grown term baby
- hypoglycaemia is associated with other abnormalities (e.g. exomphalos, coloboma)
- there is a family history of sudden infant death, Reye syndrome, severe developmental delay, poorly defined neuropathy or myopathy, or other evidence suggestive of an inborn error of metabolism.

In children, circulating insulin concentrations are usually undetectable (<1 microU/l) when the blood glucose concentration is <4.5 mmol/l. In the newborn infant, up to 48 hours old, it can be normal to have circulating insulin concentrations up to 10 microU/l even when the blood glucose is 3 mmol/l or less. However, after this, low blood sugars with detectable insulin levels must be investigated further, in discussion with the consultant and in liaison with the Paediatric Endocrinology team.

A list of suggested initial investigations is given in Appendix 12.1. Ensure that these results have been reviewed and noted prior to discharge. If any result is pending at the time of discharge, this must be mentioned in the discharge summary and communicated to the infant’s named Neonatal Consultant.

### 9 Management of hyperinsulinism

Infants who are suspected or confirmed to have hyperinsulinism must be managed in consultation with the Paediatric Endocrinology team and the investigations given in Appendix 12.1 should be augmented, if required, on their advice. A provocative fasting test may be required for identifying the aetiology of hypoglycaemia [11]. This may be performed under supervision of the Paediatric Endocrinologist.

Adequate carbohydrate intake at appropriate intervals must be determined prior to discharge and any pharmacological treatment required to decrease insulin secretion should be considered after discussion with Duty Neonatal Consultant and the Paediatric Endocrinologist. These may include such as diazoxide (Proglycem) (starting dose 5 mg/kg/day in 3 divided doses) with chlorothiazide (5 mg/kg twice a day) or somatostatin (as octreotide, 1 microgram/kg subcutaneously every 4 hours or as a continuous subcutaneous infusion 0.25 micrograms/kg/hour) with glucagon by continuous IV infusion (5 – 10 micrograms/kg/hour). Diazoxide can cause both sodium and water retention causing a
potential risk of both hyponatraemia or hypernatraemia and pulmonary hypertension. Chlorthiazide is given alongside diazoxide to reduce the risk of retention, as well as potentiating its glycaemic effect. Referral by the Paediatric Endocrinologist to a centre skilled in the management of these conditions may be required.

10 Going home with Blood Sugar Monitoring

A small number of babies may need to go home with blood sugar monitoring. To do so, is a decision made jointly by the Duty Consultant Neonatologist and the Consultant Paediatric Endocrinologist. Infants who have unstable blood glucose and / or require blood sugar monitoring at home should not be discharge unless they are term gestation.

Liaison with the Paediatric Endocrinology Nurses is required and parents must receive appropriate training and have follow-up arrangements as per the Children’s Hospital guidelines for going home with blood sugar monitoring.

11 Audit points

- Appropriate screening of infants at risk of neonatal hypoglycaemia
- Appropriate management of infants with neonatal hypoglycaemia
## 12 Appendix

### 12.1 Laboratory investigations

**Table 5. Laboratory investigations required in significant hypoglycaemia**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sample type</th>
<th>Volume</th>
<th>Turnaround time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>Blood</td>
<td>0.5ml</td>
<td>60 minutes</td>
</tr>
<tr>
<td>Lactate</td>
<td>Fluoride oxalate</td>
<td>0.5ml</td>
<td>60 minutes</td>
</tr>
<tr>
<td>Free fatty acids</td>
<td>Fluoride oxalate</td>
<td>0.5ml</td>
<td>One week</td>
</tr>
<tr>
<td>3-hydroxybutyrate</td>
<td>(Grey top)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ammonia</td>
<td></td>
<td></td>
<td>60 minutes</td>
</tr>
<tr>
<td>Liver Function Tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid Function Tests</td>
<td>Blood</td>
<td>2 ml</td>
<td></td>
</tr>
<tr>
<td>Serum amino acids</td>
<td>Lithium heparin</td>
<td></td>
<td>One week</td>
</tr>
<tr>
<td></td>
<td>(Green top)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acylcarnitine</td>
<td></td>
<td>1 ml</td>
<td></td>
</tr>
<tr>
<td>Serum cortisol</td>
<td>Blood</td>
<td>1ml</td>
<td>One day</td>
</tr>
<tr>
<td>Insulin</td>
<td>Serum</td>
<td>2 ml</td>
<td>One week</td>
</tr>
<tr>
<td>C peptide</td>
<td>(Yellow top)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Growth hormone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine organic acids</td>
<td>Urine</td>
<td>10 ml</td>
<td>One week</td>
</tr>
<tr>
<td>Urine amino acids</td>
<td>Universal pot</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine ketones</td>
<td>Bedside stick</td>
<td>1 drop</td>
<td>immediate</td>
</tr>
</tbody>
</table>
12.2 Addition of glucose polymer

If feed volume cannot be increased further or is not being tolerated, the glucose polymer, Maxijul, can be added to EBM or formula milk to increase the glucose and energy in the same volume of milk. Changing to enriched formula milk which increases all nutrition is not recommended.

The use of glucose supplements to EBM or formula milk should be discussed with the Attending Neonatal Consultant. Addition of 2 x 2.5ml scoops to either EBM or term formula milk gives approximately 10% concentration of carbohydrate, so increasing milk and decreasing IV 10% dextrose will ensure an equivalent carbohydrate intake (see table 7 below).

If Maxijul needs to be added to EBM or formula milk, the possible cause of the hypoglycaemia must be re-evaluated and a hypoglycaemia screen initiated and the Neonatal Dietitian consulted. No scoop other than a small 2.5ml scoop as shown below should be used.

![Image of a 2.5ml scoop]

### Table 6. Protein, Carbohydrate and Energy Profile of Milks and Supplements

<table>
<thead>
<tr>
<th>Per 100ml or as stated</th>
<th>Protein g</th>
<th>Carbohydrate g</th>
<th>Energy kcal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast milk/C&amp;G First</td>
<td>1.3</td>
<td>7.4</td>
<td>67</td>
</tr>
<tr>
<td>Maxijul per100g</td>
<td>nil</td>
<td>100</td>
<td>400</td>
</tr>
<tr>
<td>1x2.5ml dark blue scoop = 1.3g</td>
<td>nil</td>
<td>1.3</td>
<td>5</td>
</tr>
<tr>
<td>2x2.5ml dark blue scoop = 2.6g</td>
<td>nil</td>
<td>2.6</td>
<td>10</td>
</tr>
<tr>
<td>100ml EBM/term formula + Maxijul</td>
<td>1.4</td>
<td>10</td>
<td>77</td>
</tr>
</tbody>
</table>

*A small supply of Maxijul in 200g tins + separate 2.5ml scoops are kept on both NICUs. Further supplies are available from the Paediatric Dietitians (ext 63170) at QMC and are ordered by the purchasing team via the Dietetic Dept (ext 57639/8) at City.

Out of hours there is an emergency supply on D34, Children’s Hospital, QMC, ext 69034.

There is no scoop in the tin so separate 2.5ml scoops are available on request from the neonatal or children’s dietitians. These require washing in hot soapy water and drying with a paper towel before use and then storing in the tin for future use. Tin and scoop should be discarded 1 month after opening.
13 References


Flowchart 1. Management of infants at risk of neonatal hypoglycaemia: infants who are clinically well and have blood glucose level ≥ 2.6 mmol/l

**At risk infants who require screening**

- Infants of all diabetic mothers
- Severe intrapartum asphyxia, resuscitation at birth, signs of encephalopathy
- Infants of mothers taking beta-blockers (e.g. Labetalol) in the third trimester and/or at time of delivery
- Intrauterine growth restriction (birth weight 2nd centile or below) or clinically wasted
- Macrosomic babies (birth weight 98th centile or above)

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Boys</th>
<th>Girls</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;37</td>
<td>All</td>
<td>All</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td>37</td>
<td>&lt;2.10</td>
<td>&lt;2.00</td>
<td>&gt;3.8</td>
<td>&gt;3.6</td>
</tr>
<tr>
<td>38</td>
<td>&lt;2.30</td>
<td>&lt;2.20</td>
<td>&gt;4.1</td>
<td>&gt;3.9</td>
</tr>
<tr>
<td>39</td>
<td>&lt;2.50</td>
<td>&lt;2.45</td>
<td>&gt;4.3</td>
<td>&gt;4.2</td>
</tr>
<tr>
<td>40</td>
<td>&lt;2.65</td>
<td>&lt;2.60</td>
<td>&gt;4.6</td>
<td>&gt;4.3</td>
</tr>
<tr>
<td>41</td>
<td>&lt;2.80</td>
<td>&lt;2.75</td>
<td>&gt;4.7</td>
<td>&gt;4.4</td>
</tr>
<tr>
<td>42</td>
<td>&lt;2.90</td>
<td>&lt;2.85</td>
<td>&gt;4.8</td>
<td>&gt;4.55</td>
</tr>
</tbody>
</table>

Keep warm – check infant’s temperature, encourage skin to skin
Start feeding early (within one hour of birth) and feed regularly (at least every 3 hours)
If the infant is unable to feed from the breast, give colostrum by syringe/cup or formula milk at 10-15 ml/kg by cup/syringe/bottle (as per Guideline D4 & parental choice)
Check blood glucose level prior to second feed:

**Is the blood glucose level greater than 2.6 mmol/l?**

**Support breastfeeding 3 hrly or formula feed every 3 hours, as per parental choice at 10-15ml/kg.**
Recheck blood glucose before next feed.

**Is the blood glucose level ≥ 2.6 mmol/l?**

- **Yes**
  - Continue to support breast feeding and/or feed at least 3-4 hourly*
  - No further blood glucose monitoring required unless there are clinical signs / symptoms of hypoglycaemia*

- **No**
  - See Flowchart 2

---

*Infants with two blood consecutive blood glucose values ≥ 2.6 mmol/l do not require further blood glucose monitoring

*Every infant with signs / symptoms of neuroglycopenia must be managed according to Flowchart 3.
Flowchart 2. Management of infants with moderately low (1 - 2.5 mmol/l) blood glucose level who are otherwise well *

**The infant’s blood glucose level is < 2.6 mmol/l**

Does the infant have any clinical signs/symptoms of hypoglycaemia (see Table 1)?

- **No**
  - Is the blood glucose < 1 mmol/l
    - **No**
      - Keep warm, consider skin to skin
      - Give feed: breast feed and/or offer expressed breast milk/formula by cup/syringe (60-90 ml/kg/day)
      - Recheck blood glucose after before next feed
      - Is the blood glucose level > 2.6 mmol/l?*
    - **Yes**
      - See Flowchart 3
  - **Yes**

- **Yes**

**Give feed: breast feed and / or offer expressed breast milk / formula by cup / syringe**

**Recheck blood glucose before next feed**

**Is the blood glucose level > 2.6 mmol/l?***

- **Yes**
  - *Continue to support feeding at least 3-4 hourly*
  - *No further blood glucose monitoring required unless there are clinical signs/symptoms of hypoglycaemia*
- **No**

**Give feed: breast feed and / or offer expressed breast milk / formula at 90-120 ml/kg/day by cup / syringe or NG tube**

**Recheck blood glucose after 1 hour**

**Is the blood glucose level > 2.6 mmol/l?***

- **Yes**
  - *Give next feed by cup / syringe or NG tube*
  - *If more than 2 measurements <2.6 Contact NICU team: consider admission to NICU, two hourly feeds and / or IV glucose.*
- **No**

---

Well babies with moderate hypoglycaemia should not be separated from their mother unless admission to NICU is required for other reasons.

*Every infant with blood glucose level < 1 mmol/l or signs / symptoms of neuroglycopenia must be managed as per Flowchart 3.*
Flowchart 3: Management of infants with persistent low blood glucose, those with blood glucose < 1mmol/l and / or signs / symptoms of neuroglycopenia

1. Obtain intravenous (IV) access
   Take blood sample for laboratory confirmation of blood glucose
   Collect blood samples for hypoglycaemia screen (see Table 6)

2. The infant's blood glucose level is < 1 mmol/l
   AND / OR
   Infant has clinical signs/symptoms of hypoglycaemia (see Table 1)

3. If safe, continue feeding. Consider syringe or nasogastric tube feeding, if otherwise well & unable to breast or bottle feed at 60ml/kg/day two hourly
   Recheck blood glucose after 1 hour
   Is the blood glucose level > 2.6 mmol/l?

   a. No
      Increase IV infusion to 90 ml/kg/day
      Continue to feed and consider changing to hourly feeds, if able and safe to do so

   b. Yes
      Recheck blood glucose at 1 hour
      Is the blood glucose level > 2.6 mmol/l?

      i. No
         Give IV 10% glucose 2.5ml/kg
         Increase glucose delivery rate by increasing concentration of glucose solution or volume of infusion. See Section 6.3.1.3 of Guideline D1. Fluid electrolyte balance must be monitored carefully to avoid electrolyte imbalances when delivering equal to or greater than a day ahead fluid requirements.

      ii. Yes
         Increase IV 10% glucose infusion
         Continue feeding breast / EBM / formula top-ups 2 hourly at a higher volume*

4. Oral glucose gel 200mg/kg massaged into the buccal mucosa can be given while IV access is obtained

5. Delay in IV access

*IV glucose can be reduced gradually (e.g. by 10ml/kg/d after every normal blood glucose level) while enteral feeds are increased by 20-30 ml/kg/day (as tolerated and if required), to ensure blood glucose remains stable
When the infant is on full enteral feeds, is otherwise well, and has had two blood glucose values of > 2.6 mmol/l, blood glucose monitoring can be discontinued