British Association of Perinatal Medicine

Identification and Management of Neonatal Hypoglycaemia in the Full-Term Infant (Birth – 72 hours)

A BAPM Framework for Practice

January 2024

Contents

Document updates

Date	Page	Changes made
20/06/2024	Page 10, point 8.	Clarification added “A repeat glucose measurement is indicated only if recommended by the hypoglycaemia guidance.”
16/09/2024	Page 29	Correction made to glucose infusion rate. “**Glucose infusion rate (mg/kg/min) =** [infusion rate (ml/kg/day) / 144] x glucose concentration (%)”

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Language

The British Association of Perinatal Medicine is committed to continuously fostering a diverse environment. We acknowledge the effect language can have on individuals and populations. This guideline makes recommendations for women and people who are pregnant and or breastfeeding. For simplicity of language, the guideline uses the terms women and mothers throughout, but this should be taken to also include people who do not identify as women but who are pregnant, in labour and in the postnatal period. The term breastfeeding is also used but should be taken to include those who term this method of feeding as chest or body feeding. When discussing with a person who does not identify as a woman, please ask them their preferred pronouns and terminology.

This framework/document is specific to the UK context and to aid the creation and review of documents designed for the healthcare professional audience. Therefore, it may not be relevant in other settings. We also acknowledge that we may not get the language right every time, and welcome feedback on our work.

Abbreviations

BAPM	The British Association of Perinatal Medicine
BG	Blood glucose
CHI	Congenital Hyperinsulinism
FfP	Framework for Practice
FGR	Fetal growth restriction
IUGR	Intrauterine growth restriction
IV	intravenous
LGA	Large for gestational age
NEWTT	Newborn Early Warning Trigger and Track
OFC	Occipitofrontal circumference
PCV	Packed Cell Volume
POCT	Point of care testing

Executive Summary of Recommendations

1. Full Term infants (born at or after 37+0 weeks' gestation) at risk of hypoglycaemia and impaired metabolic adaptation (the process of transition from a constant transplacental energy supply in the form of glucose to a variable fuel supply from milk-feeding and utilization of adipose and glycogen stores) include infants of mothers with diabetes, infants whose mothers have taken beta-blockers, and infants with fetal growth restriction (FGR). FGR should be defined using gestational age and sex specific 2nd centile values (i.e. babies who are small for gestational age), and / or clinical wasting (e.g. >2 centiles discrepancy between occipital frontal circumference (OFC) and weight using age and sex normalised charts).
2. Infants at risk of impaired metabolic adaptation and hypoglycaemia should be identified at birth and placed on a care pathway that includes early provision of energy, regular assessment of feeding and clinical condition, and blood glucose (BG) monitoring.
3. Breast milk is the ideal source of energy during postnatal metabolic adaptation. Women should be supported to establish effective breastfeeding.
4. Parents are partners in the care of infants at risk of impaired metabolic adaptation and hypoglycaemia. Parents should be given verbal and written information that describes why their baby is receiving extra support and BG monitoring; how to reduce the likelihood of hypoglycaemia; the signs that indicate when a baby is becoming unwell; and how to raise concerns about their baby's well-being or feeding pattern. A parent information sheet is provided (Appendix 1).
5. Ward based blood gas analysers provide accurate and rapid measurement of neonatal BG concentration, which supports real-time clinical decision making. Many handheld glucose meters are not sufficiently accurate in the range of 0 - 2.0mmol/L. These should be used in consultation with and approval of the local point of care test (POCT) team. Further information on point of care testing (POCT) devices is given in Appendix 5.
6. An operational threshold approach should be used to guide interventions intended to raise BG:
    - A value <1.0mmol/L at any time
    - A single value <2.5mmol/L in a neonate with abnormal clinical signs
    - More than two measurements <2.0mmol/L in a baby with a risk factor for impaired metabolic adaptation and hypoglycaemia but without abnormal clinical signs
7. Buccal administration of glucose 40% oral gel may be used in conjunction with a feeding plan when the BG is 1.0 to 1.9mmol/L.
8. Severe (BG <1.0mmol/L) or persistent hypoglycaemia (>2 measurements < 2.0mmol/L in the first 48 hours after birth) requires urgent medical review and investigation.
9. Practitioners need skills to distinguish between infants with abnormal feeding behaviours that can occur with other signs to suggest illness, and infants who are well but reluctant to feed. A plan for supporting reluctant feeders and their mothers is given in Appendix 2, Flowchart D

Introduction

Background and purpose of the framework

Hypoglycaemia is a leading cause of term admission to neonatal units. In 2016, NHS Improvement and British Association of Perinatal Medicine (BAPM) convened a working group to develop a Framework for Practice (FfP) to address variation in practices in the definition of hypoglycaemia[1], the identification, management and admission thresholds[2] of babies admitted to neonatal units for hypoglycaemia; and to promote safer practices that avoid unnecessary separation of mother and baby.

In rare circumstances neonatal hypoglycaemia is sufficiently severe to cause brain injury and long-term neurodevelopmental impairment, with considerable costs to individuals, families, and the NHS[3]. Therefore, it is incumbent upon clinicians to implement practices that prevent harm that can result from unrecognised or untreated hypoglycaemia, whilst minimising unnecessary interventions and admissions to neonatal units.

This document was revised from the 2017 version. The purpose of the revision was to update the framework to ensure alignment of recommended clinical practice with the most up-to-date scientific evidence.

Target users

All healthcare professionals involved in the care of infants born at term during the first 72 hours after birth. The framework should be delivered in partnership with parents.

Target population

Newborn full-term babies in the first 72 hours after birth during the period of metabolic transition. After 72 hours from birth babies should be managed as per local paediatric guidelines for the management of hypoglycaemia. **Babies born preterm or who are unwell and receiving intensive care are excluded** and should be managed according to relevant national and local neonatal guidelines.

Process

The original Framework for Practice included recommendations based on:

- Literature review including existing guidelines.
- Data analysis of litigation themes.
- Data analysis of admissions for hypoglycaemia.
- National audit of practice including admission and thresholds for intervention.
- Clinical experience.

Members of the revision group met to discuss any necessary changes to key areas of practice concerning the identification and management of term neonates with hypoglycaemia. Members undertook an update to previous literature searches around specified topic areas. This included searches of Medline and PubMed 2016-2022. Further online meetings were held to discuss each area and agree updates or changes to practice points when new evidence was available.

The group met to respond to comments raised during consultation and to agree the final version of the revised Framework.

Framework for Practice Section A: Practice Points

A synopsis of supporting evidence is given for each practice point in Section B.

Identification of infants at risk of impaired metabolic adaptation and recognition of clinical signs

1. 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 BG concentration*:
    - Fetal growth restriction: as indicated by birth weight <2nd centile (small for gestational, Table 1) or clinically wasted (e.g. >2 centiles discrepancy between occipital frontal circumference (OFC) and weight using age and sex normalised charts).
    - Infants of mothers with diabetes.
    - Infants of mothers taking beta-blockers in the third trimester and / or at time of birth.

*Moderate to late preterm infants are at risk of hypoglycaemia. Energy provision and BG monitoring should be planned as part of the care pathway for this group of infants. Care of the moderate to late preterm infant in the postnatal ward setting is beyond the scope of this document and can be found within the BAPM Framework for Practice for early postnatal care of moderate to late preterm infants.

Table 1. Second centile birth weights for boys and girls by week of gestation (from BAPM Newborn Early Warning Trigger and Track Framework for Practice[4])

Gestational age at birth (completed weeks)	Birth weight (kilograms)	
	Boys	Girls
37	2.10	2.00
38	2.30	2.20
39	2.50	2.45
40	2.65	2.60
41	2.80	2.75
42	2.90	2.85

2. Measurement of BG concentration should be performed for any infant who has one or more of the following diagnoses or clinical signs:
    - Perinatal acidosis (cord arterial or infant pH <7.1 and base deficit ≥ -12mmol/L)
    - Hypothermia (<36.5°C) not attributed to environmental factors
    - Suspected / confirmed early onset neonatal infection
    - Central cyanosis
    - Apnoea
    - Altered level of consciousness
    - Seizures
    - Hypotonia
    - Lethargy
    - High pitched cry
    - Abnormal feeding behaviour especially *after a period of feeding well* may be indicative of hypoglycaemia and should prompt a full clinical assessment and consideration of BG measurement. Use BAPM NEWTT2 chart BAPM Newborn Early Warning Trigger and Track Framework.

Signs of abnormal feeding behaviour include:

- Not waking for feeds: *babies may only wake for feeds 3-5 times in the first 24 hours; after the first 24 hours babies should feed at least 8 times in 24 hours.*
- Very frequent feeding: *Babies who breastfeed frequently without appearing satisfied, frequent breastfeeds where baby tires rapidly or stops feeding within the first five minutes.*
- Not sucking effectively: *weak suck or inability to suck.*

Jitteriness, defined as excessive repetitive movements of one or more limbs, which are unprovoked and not in response to a stimulus, is common and is not by itself an indication to measure BG.

Devices for accurate measurement of blood glucose in the newborn

3. Accurate measurement of BG level is essential for diagnosis and management of neonatal hypoglycaemia. Any device used for the measurement of glucose, whether glucose meter or Blood gas machine should be used with the advice and support of pathology Healthcare Scientists, to ensure it is fit for purpose. The quality of results produced by POCT devices on patients, and specifically newborns, must be understood and evidenced prior to the purchase of equipment.
4. All operators of POCT glucose devices should have training on the device which includes pre-analytical sample requirements, quality monitoring of the device, limitations of the device and instructions on how to record the results to ensure a full audit trail. The training content is best constructed with collaboration between the manufacturer, the neonatal education team and Pathology Healthcare scientists. Please see Appendix 5: Point of Care testing for blood glucose in newborn babies for further information.
5. The limitations of any POCT device should be covered in the training on the device. Technology is advancing rapidly, and assumptions should not be made on the technical performance of a device based on historical generalities for example the performance of glucose meters on samples with high packed cell volume is variable.
6. Samples should be taken from a warm well-perfused heel by heel-prick, or from a free flowing venous / arterial sample, using local guidelines for skin asepsis and patient comfort. Air bubbles in capillary tubes should be avoided. Abnormal lipid or protein content in samples may reduce the accuracy of all glucose results. Do not aspirate the sample from a catheter that has had a dextrose infusion running through it.

Management of infants identified to be at risk of impaired metabolic adaptation: general care, feeding support, energy provision and blood glucose monitoring

7. Provide parents with verbal and written information that explains why their baby is receiving extra support and BG monitoring; how the likelihood of hypoglycaemia can be minimised; the signs that could indicate that baby is becoming unwell; and how to raise concerns about their baby's well-being or feeding pattern to staff. An example parent information sheet is provided in Appendix 1. This information may be communicated during the antenatal period or during labour if the risk factors listed in Practice Point 1 are known.
8. Immediately after birth, dry the baby and put a hat on. Place baby in skin-to-skin contact with the mother to provide warmth and to facilitate the initiation of feeding. Ensure that ambient temperature is warm, the room is free from draughts, show the mother safe positioning of the baby, and commence observations using the BAPM Newborn Early Warning Trigger and Track Framework (NEWTT2). Note that NEWTT2 classes BG 2.0 to 2.5mmol/L with a yellow trigger and suggests repeating a set of observations in 1 hour excluding glucose. A repeat glucose measurement is indicated only if recommended by the hypoglycaemia guidance. Begin care

pathway in Flowchart A.

9. Ensure that baby is offered the breast within the first 60 minutes and assess the need for helping the mother with:
    1. breastfeeding support
    2. recognition of early feeding cues (rapid eye movements under the eye lids, mouth and tongue movements, body movements and sounds, sucking on a fist)
    3. signs of effective attachment.
10. Assess and document feeding cues and feeding effectiveness at each feed. Use a tool such as the UNICEF UK Baby Friendly breastfeeding assessment[5].
11. Offer the breast in response to feeding cues but with intervals of no longer than three hours from the beginning of the last feed, until BG measurements have been above 2.0mmol/L on two consecutive occasions. Continue feeding support until mother and midwife are satisfied that effective feeding is established.
12. If the baby is not showing signs of effective feeding, encourage continuous safe skin-to-skin contact and show and support the mother to hand express. Any colostrum expressed should be fed to the baby immediately, using a method that is best suited to the infant's capabilities and parent's preferences and consistent with local policy. Continue to support mother to express at least 8-10 times per 24-hour period until baby is feeding effectively and provide active feeding support until breastfeeding is established. If no colostrum is available and, after discussion with the mother, consider supplementing with infant formula. Formula will be required in larger volumes than colostrum as it is possible that the baby's ability to utilize ketone bodies may be limited by the use of infant formula (40 to 60ml/kg/per day during the first 24 hours; 70 to 90 ml/kg/per day 24-48 hours; 100-120 ml/kg/per day 48 to 72 hours; until colostrum/breastmilk is available). If infant formula is introduced, support the mother to resume breast milk feeds as soon as possible. For the period the mother is expressing she should see increasing volumes of colostrum/ milk expressed day by day. Using a breast pump alongside hand expressing may be helpful.
13. There is a lack of evidence regarding the use of donor breastmilk as part of a hypoglycaemia pathway in the term population hence no recommendation is made.
14. For women who choose to formula feed, offer a feed within the first hour after birth at a volume of 40 to 60 ml/kg/day for the first 24 hours. Implement modified responsive paced feeding by ensuring intervals of no more than three hours from the beginning of one feed to the next. Depending on BG measurement, increase the volume of infant formula if necessary. It is possible that the baby's ability to utilize ketone bodies may be limited by the use of infant formula milk. Feeds should be increased with age to 70 to 90 ml/kg/per day at 24 to 48 hours; 100 to 120 ml/kg/per day 48 to 72 hours. Feed responsively when BG measurements have been above 2.0mmol/L on two consecutive occasions. If the baby does not show feeding cues, i.e., is a reluctant feeder and has no signs of illness, refer to **Practice Points 26 and 27**.
15. Measure the BG level before the second feed (2 to 4 hours after birth). If the baby shows feeding cues before 2 hours do not restrict feeding and allow baby to feed. Measure BG immediately if there are clinical signs suggestive of hypoglycaemia (**Practice Point 2**). Note: babies who feed for very long periods or have long periods of lots of shorter feeds may not have accurate pre-feed BG and may require more prolonged monitoring.
16. Based on the result of the first BG measurement, continue to:
    - **Flowchart A**, if BG >2.0mmol/L
    - **Flowchart B**, if first pre-feed BG is 1.0 to 1.9mmol/L, and no abnormal signs
    - **Flowchart C** if first pre-feed BG <1.0mmol/L, and / or clinical signs consistent with hypoglycaemia at higher BG concentration.
17. All infants at risk of hypoglycaemia including infants of mothers with diabetes, should remain

in hospital for a minimum of 24 hours[16] . Additionally, they should remain in hospital until two consecutive BG measurements are >2.0mmol/L and the mother and staff are satisfied that effective feeding has been established and maintained over several fast-feed cycles. Note: babies who feed for very long periods or have long periods of lots of shorter feeds may not have accurate pre-feed BG and may require more prolonged monitoring.

Consideration of special treatments

18. Infants being managed using the pathway in **Flowchart A** are fed within the first 60 minutes and must have a BG level measured prior to the second feed. If the first BG is 1.0 to 1.9mmol/L or there is a subsequent BG measurement <2.0mmol/L, glucose 40% oral gel (200mg/kg) may be given alongside feeding support (**Flowchart B, Appendix 3**).
19. If BG is <1.0mmol/L, arrange for urgent medical review which will include siting an intravenous (IV) cannula for treatment with IV glucose. If there is a delay in obtaining IV access, consider either glucose 40% oral gel (200mg/kg) (appendix 3) or IM glucagon (200micrograms/kg, maximum 1mg as a single dose).
20. If BG is <1.0mmol/L, glucose 40% oral gel should only be used as an interim measure while arranging for treatment with IV glucose.

Investigations for hypoglycaemia

21. A newborn with persistent (more than 2 BG measurements <2.0mmol/L within the 72 hours of birth) or severe hypoglycaemia (<1.0mmol/L at any time), and infants with signs of acute neurological dysfunction and BG <2.5mmol/L should be referred urgently to a paediatrician / neonatal team for investigation.
    Blood samples for the following investigations should be taken before hypoglycaemia is treated. However, do not delay the treatment to complete investigations and prioritise those marked "*"
    - Glucose*****
    - Insulin and C-peptide*****
    - Free fatty acids*****
    - Beta-hydroxy butyrate (or point of care blood ketones, if available) *
    - Consider investigations for early onset neonatal infection
    - Cortisol
    - Growth hormone
    - Acylcarnitine profile
    - Amino acids
    - Ammonia
    - Lactate

    Urine sample for:
    - Ketones
    - Organic acids

    Investigations marked * should be **prioritised** and treatment of hypoglycaemia should not be delayed if insufficient blood is obtained for the remaining investigations which should then be taken as soon as possible. Consider having local pre-prepared "hypoglycaemia investigation" packs available to send the investigations. Add information on BG levels in the investigations request forms to facilitate appropriate reporting of results. Further investigations should be based on the results of the initial screen and taken following specialist advice.

The Framework does not recommend BG measurement within 1-2 hours of birth. If a BG is measured for a non-indicated reason, e.g., as part of a blood gas read-out and is low, then the clinical team should be alerted to make an urgent assessment about treatment and further testing. Infants with severe hypoglycaemia or abnormal neurological signs should be admitted to the neonatal unit for neurocritical care, investigations, and monitoring.

22. Transient hypoglycaemia defined as one or two measurements of 1.0-1.9mmol/L within the first 72 hours after birth in an infant with no abnormal signs who is feeding effectively does not require the investigations listed in **Practice Point 21**.

Persistent low blood glucose measurement

23. Persistent hypoglycaemia (more than two measurements <2.0mmol/L within the first 72 hours after birth) can be the first sign of hyperinsulinism or another metabolic disorder characterized by neonatal hypoglycaemia. It is important to refer to a paediatrician and screen such infants (see **Practice Point 21** for list) to identify hyperinsulinism or another disorder that requires specific therapy.
24. Hyperinsulinism should be considered if BG concentration remains low (<2.0mmol/L on >2 occasions in first 72 hours despite adequate energy provision and a feeding plan), or if a glucose dose greater than 8mg/kg/min is required. Check blood insulin to C-peptide molar ratio to exclude the possibility of exogenous insulin administration.
25. In cases of suspected or confirmed hyperinsulinism, aim to maintain BG concentration >3.0mmol/L in the first 48 hours and >3.5mmol/L after 48 hours from birth. Liaise with specialists as soon as possible. Whilst awaiting specialist input take into consideration that metabolic transition occurs over several days; healthy babies have BG levels which increase over the first 18 hours and remain stable to 48 hours before increasing to values normal for the paediatric population by day 4 when they will have completed their metabolic transition[61]. This document is aimed at babies from birth to 72 hours only, after which local guidance on the management of babies and children with hypoglycaemia should be followed (pending specialist input).

Management of the reluctant feeder with no risk factors for impaired adaptation

26. A thorough clinical assessment should be made and documented within six hours after birth, at which time practitioners should differentiate between a well-baby who is reluctant to feed versus a baby whose feeding pattern suggests an abnormal clinical state due to illness. Signs of reluctant feeding include not waking for feeds, not latching at the breast, not sucking effectively, and appearing unsettled. Skin-to-skin contact and laid-back nursing will stimulate the baby to use innate abilities and help the mother recognize feeding cues. Feeding support should be provided to reluctant feeders using **Flowchart D** and **Appendix 2,** and medical review should be prompt if there are concerns that feeding behaviours may reflect an abnormal clinical state.
27. BG should be measured if reluctant / non-effective feeding follows a period of effective feeding or if there are any abnormal clinical signs in addition to reluctant feeding.

Framework for Practice Section B: Synopsis of supporting evidence

Identification of infants at risk of impaired metabolic transition and recognition of clinical signs clinical signs: Practice Points 1 and 2.

Infants with fetal growth restriction (FGR) are at risk of hypoglycaemia due to low glycogen stores, increased peripheral insulin sensitivity, impaired gluconeogenesis due to a poorly coordinated response to hypoglycaemia by counter-regulatory hormones, and increased insulin secretion[6-13].

Pragmatically, FGR should be defined as birth weight ≤2nd centile using the gestation and sex specific values listed in Table 1. Use of an arbitrary weight threshold (e.g., 2.5kg) fails to detect growth restriction in infants born at >40 weeks' gestation, and this practice was identified as a contributory factor in litigation. Be aware that FGR can manifest as low subcutaneous fat stores (so called 'wasted' or 'scrawny' appearance) despite birth weight above 2nd centile. At present there is insufficient evidence to recommend the use of customised growth charts for detection of infants at risk of hypoglycaemia[14, 15], and clinical assessment of FGR at birth remains important[3].

Diabetes is the most common medical disorder of pregnancy in the UK, affecting 2-5% of pregnancies[16]. Infants of mothers with diabetes are at increased risk of hypoglycaemia due to transient hyperinsulinism[17]; the risk is reduced but not completely ameliorated by good glycaemic control[18,19]. Therefore, all infants of mothers with diabetes, irrespective of the type of diabetes, should be monitored for hypoglycaemia[16].

Exposure to beta-blockers used to treat maternal disease is associated with hypoglycaemia due to transplacental transfer of drug and interruption of glycogenolysis in the offspring[10, 20].

The clinical signs associated with hypoglycaemia are non-specific so BG measurement should be undertaken in any infant who presents with one or more of the abnormal signs listed in **Practice Point 2**[21,22].

BG should be monitored in infants with diseases associated with:

- Low energy availability, e.g. moderate to severe perinatal hypoxia-ischaemia.
- Impaired hormone / enzyme responses, e.g. moderate to severe perinatal hypoxia-ischaemia, clinically suspected or confirmed early onset neonatal infection (but not babies who have undergone infection screens for risk factors only), pituitary / adrenal insufficiency, inborn errors of metabolism.
- Hyperinsulinism, e.g. congenital hyperinsulinism, Beckwith- Wiedemann syndrome.

It is controversial whether infants who are large-for-gestational age (LGA, birth weight >90th centile) are at risk of hypoglycaemia. Data from a registry and a case series have been interpreted by some to suggest that LGA is a risk factor for hypoglycaemia[23,24] but features of study design including retrospective data collection, inconsistent measurement devices, variations in timing of sampling, and limited clinical phenotyping of study groups, leave doubt about causation. The working group considers that if there is no evidence of maternal diabetes and the baby does not have features suggestive of Beckwith-Wiedemann syndrome, then routine screening of LGA infants for hypoglycaemia is not indicated.

Occasionally, it will be appropriate to screen infants based on history of first degree relative with a heritable disorder associated with neonatal hypoglycaemia. Where possible, this should be planned before birth so that parents and staff are prepared.

Devices for accurate measurement of blood glucose in the newborn: Practice Points 3-6

POCT blood gas analysers should be considered the reference standard for measuring blood glucose based on accuracy and speed of result availability. Blood gas analysers produce glucose results as a calculated 'plasma glucose equivalent' concentration that should agree with laboratory plasma glucose results in the majority of cases[25], and they have the advantage of accessibility and speed in most maternity and newborn facilities. Blood gas analysers may be configured to give a 'glucose only' reading on a small sample.

Central laboratory measurement of glucose from samples sent in fluoride oxalate tubes is inconsistent due to variable inhibition of glycolysis in the first 30 to 90 minutes, and variability in time taken to reach the laboratory for processing. Processing time may lead to impractical delays in obtaining results and guiding clinical management.

Some cot side technology or handheld glucose meters are still prone to significant limitations especially in the range of 0-2.0mmol/L[26-28]. The International Organisation for Standardisation (ISO) standard 15197:2013 was implemented on 1st June 2016. Although the ISO standard is not intended to apply to BG meters for professional use, it is the only standard available and is therefore used as a benchmark for performance by glucose meter manufacturers and their products are awarded Œmarks based upon compliance with the standard. The standard specifies that 95%of the measured glucose values shall fall within +/-0.83mmol/L of the average measured values of the reference measurement procedure at glucose concentrations <5.55mmol/L. Although handheld glucose meters are available that meet the ISO standard the user must understand the limits of their accuracy.

In centres where handheld devices are used to screen for low BG, please refer to Appendix 5: Point of Care testing for blood glucose in newborn babies for further information on understanding how POCTs perform in newborn infants.

Glucose biosensors, which might permit non-invasive and accurate continuous measurement of transdermal glucose, are currently under development with the potential for enormous impact[29]. It is essential that blood samples are collected in an optimal manner that includes skin asepsis, measures for patient comfort according to local policy, and that samples are taken from a warm well-perfused heel (or venous / arterial blood). Avoid air bubbles if collecting in a capillary tube.

In summary, analysis of plasma glucose equivalent using a blood gas machine provides a rapid and accurate measurement of neonatal BG to support real-time clinical decisions. Consideration should be given to providing access to this ward-based technology in all clinical settings where newborn infants are looked after. See Appendix 5: Point of Care testing for blood glucose in newborn babies.

Management of infants identified to be at risk: general care, feeding support, energy provision and blood glucose monitoring: Practice Points 7-16

The principles of management for antenatal or immediate postpartum identification of infants at risk of impaired metabolic adaptation are thermal care, early energy provision and feeding support, monitoring of BG concentration with an accurate device that provides results in real time, and listening and responding to parents' views about infant feeding and well-being.[3,22, 30, 31]

Be aware that maternal obesity is associated with lower breastfeeding rates, which may be mediated in

part by impaired lactogenesis[32-34]. These women may require additional support to establish breastfeeding successfully.

Cold stress is associated with hypoglycaemia and should be avoided by looking after mother and baby in a warm environment free from drafts with safe skin-to-skin contact, and placement of a hat[31].

There should be regular assessment of the baby when awake, including colour, tone, respiratory rate, heart rate, temperature, level of consciousness, and signs associated with hypoglycaemia (listed in **Practice Point 2**). This should include assessment of feeding behaviours, which may be a presenting sign of significant hypoglycaemia[3]. Thorough clinical assessment cannot be made effectively during sleep. The BAPM NEWTT2 chart is recommended for documenting clinical information[4].

If a baby has abnormal clinical signs suggestive of hypoglycaemia, BG should be measured immediately and urgent review by a paediatrician or advanced neonatal nurse practitioner should be sought.
The aim should be to ensure that needs are met as far as possible by breastfeeding, or by the use of expressed colostrum / breast milk (EBM) because exclusive breastfeeding optimises health outcomes for mother and infant.[35] Breast milk feeds may optimize the metabolic adaptation by improving availability of alternative cerebral fuels,[36,37] and type of milk feed has modifying effects on the pioneering microbiota[38, 39] which may have implications for life long immune and metabolic health[40-42]. If the baby is unable to breastfeed effectively, the mother should be encouraged to express her milk to feed colostrum to her baby and to maximise future lactation. For mothers who intend to formula feed, the aim should be to ensure frequent, effective feeding. Exclusive infant formula feeding has been associated with lower availability of alternative cerebral fuel. Babies will therefore require larger volumes of formula than breastmilk: 40 to 60ml/kg/per day during the first 24 hours, increasing volumes if required; 70 to 90ml/kg/per day 24 to 48 hours; 100 to 120 ml/kg/per day 48 to 72 hours.

The optimal time to measure BG concentration is just prior to the second feed[10, 22]. In practice,for the infant who is well, this will be within four hours of birth. If the infant is not showing any feeding cues within four hours, then this should be considered a sign of possible hypoglycaemia and should prompt BG measurement.

There is no evidence to support routine supplementation of feeds with energy supplements[43,44]. The hPOD trial concluded there is no evidence for the use of prophylactic dextrose gel for babies at risk of hypoglycaemia to prevent neonatal unit admission or treatment for hypoglycaemia[45].

The Diabetes and Antenatal Milk Expression (DAME) trial concluded that there is no harm in women with diabetes with an otherwise low risk pregnancy, expressing colostrum from 36 weeks' gestation. Babies in the trial were more likely to receive only breast milk during their hospital stay, however, there was no reduction in hypoglycaemia or neonatal unit admission with hypoglycaemia[46, 47].

All infants at risk of hypoglycaemia including infants of mothers with diabetes, should remain in hospital for a minimum of 24 hours[16]. They should remain in hospital until two consecutive BG measurements are >2.0mmol/L and the mother and staff are satisfied that effective feeding has been established and maintained over several fast-feed cycles.

Thresholds for intervention

The level of BG concentration that leads to cerebral injury in newborns and adverse neurodevelopmental outcome is unknown[48]. Although attempts have been made to identify a single 'safe' BG value[49-51], studies have been confounded by inclusion of infants with independent risk factors for adverse neurodevelopmental outcome such as perinatal asphyxia, have not taken account of

different risk profiles for impaired metabolic transition, have seldom documented duration of hypoglycaemia, have been uncontrolled, and follow-up has not been sufficiently long and complete. There is some consensus based on the literature that BG levels below 1.0mmol/L that are persistent beyond 1 to 2 hours (or are recurrent) *and* are associated with acute neurological dysfunction present the greatest risk for cerebral injury, and that brief episodes of hypoglycaemia in the absence of acute neurological dysfunction or an associated disorder are less likely to lead to cerebral injury and poor outcome[52].

A detailed description of the metabolic transition from fetal to neonatal life is beyond the scope of this document and is reviewed elsewhere[10,53]. In summary, the fetal brain is exposed to glucose concentrations that are around 0.5mmol/L lower than those of maternal plasma[54]. The lower limit of fetal glucose concentration is around 3.0mmol/L[55]. Following separation from the placental circulation there is a physiological decline in BG concentration to a nadir at 1 to 2 hours, and in healthy neonates levels begin to increase 2 to 3 hours after birth, largely driven by endogenous glucose production rather than by feeding. Levels that are typical of infants, children and adults (3.5 to 5.5mmol/L) are not reached until 3 to 4 days after birth[56-61]. The GLOW study results showed that the period of postnatal hypoglycemia in the cohort of mostly breast-fed babies resolved by day 4 from birth.[61] It is not unusual for healthy, breast fed newborn infants to have BG values of less than 2mmol/L in the first 24 hours after birth[36, 59, 60], without apparent adverse consequence, and in a well-phenotyped group of infants (35 to 42 weeks' gestational age) with risk factors for hypoglycaemia, concentrations <2.6mmol/L and <2.0mmol/L occurred in 51% and 19% respectively, but very few had abnormal clinical signs[62].

Given the uncertainties of defining a 'safe' lower limit of BG and the need to take account of differences in availability and mobilisation of alternative cerebral fuels between patient groups, an 'operational threshold' approach to the management of neonates with hypoglycaemia was developed by expert consensus in 2000[30]. This defines "the concentration of plasma or whole BG at which clinicians should intervene based on evidence currently available in the literature." In this model, infants at risk of impaired metabolic adaptation and neurological sequelae from hypoglycaemia are identified, and interventions to raise the BG are recommended at specified thresholds. There are two caveats: first, acute neurological dysfunction in association with low BG at any level should prompt urgent investigation and treatment; and second, there are special circumstances such as hyperinsulinism and perinatal asphyxia when the threshold should be raised.

The operational threshold model has been adopted widely, but controversy remains about threshold values for diagnosis and intervention. For example, the 2011 American Academy of Pediatrics guidance recommends screening high risk infants (defined as late preterm [34 to 36 weeks' gestation], SGA, infants of mothers with diabetes and LGA) 30 minutes after the first feed and intervene with feed or IV glucose for values 25 to 40mg/dl (1.4 to 2.2mmol/L). The threshold range for intervention increases to 35 to 45mg/dl (1.9 to 2.5mmol/L) between 4 and 24 hours after birth. Once hypoglycaemia has been diagnosed the guideline recommends targeting glucose concentrations > 45mg/dl (2.5mmol/L)[63]. The 2015 Pediatric Endocrine Society guideline recommends that in the first 48 hours after birth, the target BG concentration should be 50mg/dl (2.8mmol/L), stating that "neurogenic and neuroglycopenic symptoms usually occur when the plasma glucose concentration decreases to 50 to 70mg/dl (2.8 to 3.9 mmol/L)"[64]. We did not find evidence to support this statement for healthy neonates born at term.

The variation in recommended thresholds in published guidance is reflected in practice in English Neonatal Units, which define hypoglycaemia between 2.0 and 4.0mmol/L[2].

The HypoEXIT study[65], a multicentre randomized noninferiority trial of healthy asymptomatic babies at

risk of hypoglycaemia, compared threshold values for hypoglycaemia of 2.0 and 2.6mmol/L, and reported neurodevelopmental outcome at 18 months. They concluded the lower threshold was noninferior to the higher threshold in terms of cognitive and motor development at 18 months of age. Although there were fewer severe hypoglycaemic episodes in the higher threshold group, they also received more treatment interventions, but duration of hospital stay was similar.

The Children with Hypoglycaemia and Their Later Development (CHYLD) study group reported 2-year outcomes of infants born at 35 weeks or more with risk factors for hypoglycaemia defined as maternal diabetes, birth at <37 weeks, and birth weight that was low (<10th percentile or <2500 g) or high (>90th percentile or >4500 g). Hypoglycaemia was defined as <2.6mmol/L, and according to this definition over half of participants experienced hypoglycaemia. A treatment strategy was in place to maintain BG >2.6mmol/L. The study[66] reports the following important observations about at-risk infants who receive treatment aimed at targeting BG of at least 2.6mmol/L. The first is that hypoglycaemia was not associated with an increased risk of neurosensory impairment (RR 0.95, 95% CI 0.75-1.20, p=0.67) or processing difficulty, defined as an executive-function score or motion coherence threshold that was more than 1.5 SD from the mean (RR 0.92, 95% CI 0.56-1.51, p=0.74). The second is that the mean difference in BG concentration between those who did and those who did not have a poor outcome was only 0.16mmol/L. These observations raise the possibility that adverse outcomes that were prevalent in this study group may be a function of the underlying risk profile rather than BG concentration per se. A follow-up study at 4.5 years reported that neonatal hypoglycaemia was not associated with increased risk of neurosensory impairment although among secondary outcomes it was associated with increased risk of poor executive function and visual motor function in children who had experienced lower BG concentrations[67].

In summary, no study has shown that treatment of asymptomatic hypoglycaemia in 'at risk' groups improves neurodevelopmental outcome, and no randomised trial comparing different treatment thresholds with sufficiently long and complete follow-up has been carried out. In the absence of these forms of evidence the group considered that there is no new argument to support a change in the operational threshold approach proposed by Cornblath et al in 2000[30] , reviewed on several occasions since[48, 51,52]

1. A value <1.0mmol/L at anytime.
2. Baby with abnormal clinical signs: single value <2.5mmol/L.
3. Baby at risk of impaired metabolic adaptation but without abnormal clinical signs: <2.0mmol/L and remaining <2.0mmol/L at next measurement.

In infants who have suspected hyperinsulinism, investigations (if not already done) should be performed if the BG is <3.0mmol/L. The treatment threshold should be 3.0mmol/L in neonates with suspected hyperinsulinism in the first 48 hours after birth and 3.5mmol/L after 72 hours of age[68, 69]. The operational threshold should be increased to at least 2.5mmol/L in infants with moderate-severe hypoxic-ischaemic encephalopathy (for review see[70]). Higher BG concentration may confer benefit in this patient group, however hyperglycaemia is also harmful and should be avoided[71-73].

Consideration of special treatments: Practice Points 17-19

Treatment with glucose 40% oral gel (dextrose gel) by buccal administration is a simple and safe treatment for initial care of infants with low BG[74]. Buccal glucose gel can be used as first-line treatment to manage hypoglycaemia in late preterm and term babies in the first 48 hours after birth, enabling babies to remain with their mothers, avoid NICU admission and increase likelihood ofbreastfeeding after discharge. It is important to use glucose gel in conjunction with an infant feeding plan to enable establishment of oral feeds. Buccal glucose gel can be a useful adjunct to Baby Friendly approaches for managing low BG soon after birth[75].

The use of glucose 40% oral gel in neonates is not new, it was recommended over 20 years ago[76], but a previous randomised trial that was designed to assess intermittent BG concentrations did not show differences between gel and placebo[77]. More recently the'Sugar Babies' trial assessed whether treatment with dextrose gel was more effective than feeding alone for reversal of neonatal hypoglycaemia in at-risk babies[78]. This study showed that infants randomised to dextrose gel (glucose 40% oral gel) had significantly less treatment failure, defined as glucose <2.6mmol/L after two treatment attempts with dextrose gel versus placebo (relative risk 0.57, 95% CI 0.33 – 0.98). Treatment with dextrose gel also lowered rates of neonatal intensive care unit (NICU) admission for hypoglycaemia compared with placebo (16 [14%] *vs* 30 [25%]), with a number needed to treat of 8. In addition, fewer infants were formula feeding at 2 weeks of age in the dextrose gel group compared with placebo group (5 [4%] *vs* 15 [13%]). Despite treatment with dextrose gel 12% of infants treated hadat least one rebound episode of hypoglycaemia (within 6 hours), and 24% had at least one recurrent episode of hypoglycaemia (within 48 hours of birth). So, although the gel decreased the need, it did not completely eliminate the use of intravenous dextrose.

Finally, a two-year follow-up study of the 'Sugar Babies' trial reported that rates of neurosensory impairment, processing difficulties, and multiple secondary growth and developmental outcomes were equivalent between the dextrose gel and placebo groups[79].

Although rebound hypoglycaemia and recurrent hypoglycaemia were similar between groups in the original study and there was reassuring continuous glucose monitoring sensor data, a theoretical concern remained that the dextrose gel treatment might have delayed definitive treatment with intravenous dextrose and adversely impacted long-term neurodevelopmental outcomes. The 2-year follow-up data is reassuring that the early benefits seen with dextrose gel do not come at a cost of worse neurodevelopmental outcomes at two years of age. However, dextrose gel treatment was targeted to infants at-risk for hypoglycaemia who were otherwise asymptomatic, therefore the results do not apply to infants with symptomatic, severe, prolonged, or recurrent hypoglycaemia (i.e. the infant with severe hyperinsulinism), and should not be used in these circumstances except as an emergency measure if there is a delay in gaining IV access and IM glucagon is unavailable.

In a dose finding study, glucose 40% oral gel given at one hour after birth to neonates with risk factors for hypoglycaemia reduced the number of infants with BG less than 2.6mmol/L during the following 48 hours with a number needed to treat of 10, but 95% confidence intervals were wide (5 - 115) and the study was not designed to evaluate the effect of prophylaxis on clinical outcomes[80]. A randomised trial of prophylactic oral glucose 40% oral gel for prevention of neonatal hypoglycaemia did not show a benefit in terms of either preventing NICU admission or reducing treatment for hypoglycaemia[81]. The working group does not recommend use of prophylactic glucose 40% oral gel.

Investigations for hypoglycaemia: Practice Points 20-21

Transient hypoglycaemia (BG 1.0 to 1.9mmol/L observed on one or two occasions over the first 48 hours after birth), in the absence of abnormal clinical signs, does not require additional investigations[20].

A newborn with persistent (BG 1.0 to 1.9mmol/L on >2 occasions) or severe hypoglycaemia (<1.0mmol/L on one occasion) should have investigations listed in **Practice Point 20** to look for the cause *during the period of hypoglycaemia*[22,82]. The results of these investigations and the possible need for additional tests should be discussed with a specialist in paediatric metabolic medicine and / or paediatric endocrinology.

Infants with abnormal neurological signs and hypoglycaemia should have neurocritical care monitoring

in a neonatal unit[83], and brain MRI with long-term follow-up is recommended because of the risk of brain tissue injury and neurodevelopmental impairment in this group[84].

Persistent or recurrent low blood glucose measurement: Practice Points 22-24

Persistent or recurrent hypoglycaemia (>2 measurements 1.0 to 1.9mmol/L during the first 48 hours after birth) can be the first presentation of an underlying disorder of glucose metabolism[82,85]. Early detection of this group of infants is important because specific interventions designed to reduce the risk of brain injury may be required[68].

Detailed clinical assessment and screening investigations should be performed urgently. Congenital Hyperinsulinism (CHI) is one of the most frequent causes of persistent or recurrent low BG. It is a heterogeneous condition caused by dysregulation of insulin secretion from pancreatic beta cells. If CHI is suspected, diagnosis should be made promptly by confirming high plasma insulin levels and BG levels should be maintained >3.0mmol/L during the first 48 hours; increasing to an operational threshold of 3.5mmol/L from 48 hours[68]. Treatment should be initiated before results from other components of the screening tests (**Practice Point 20**) have been processed.

Although most infants with CHI have no other abnormal clinical signs, CHI and other conditions associated with neonatal hypoglycaemia may be recognisable syndromes so careful clinical assessment can be informative for guiding subsequent tests[86-89]. Some of the more common are:

- Beckwith Wiedemann syndrome.
- Turners syndrome.
- Costello syndrome.
- Kabuki syndrome.

Non-syndromic genetic disorders of congenital CHI[68] and other rare disorders that cause persistent hypoglycaemia may require specific long-term treatment and management. These include metabolic disorders of glycogen storage, fatty acid oxidation and gluconeogenesis, hypopituitarism and adrenal insufficiency leading to deficiencies in growth hormone and cortisol[9]. Sometimes there may be diagnostic clues such as features of Prader-Willi syndrome[90], hyperpigmentation of the skin suggesting the diagnosis of familial glucocorticoid deficiency (FGD)[91], or midline defects, undescended testes or micropenis in hypopituitarism, but typically no other signs are present and extensive laboratory evaluation is required, guided by specialist advice.

In summary, the approach to babies with persistent or recurrent low BG is: early detection by ensuring relevant appropriate screening investigations are collected; admit to neonatal unit to ensure that management with adequate energy provision; keep BG > 3.0mmol/L in the first 48 hours after birth until insulin levels are known; and seek early specialist advice about additional investigations and management.

Parent information: why baby is being monitored, how to tell if your baby may be unwell, and how to escalate concern (Practice Point 25, appendix 1)

To empower parents of babies at risk of hypoglycaemia to serve as informed partners in their baby's care, they should be provided with information that explains why their baby is being monitored, how to assess their baby's general condition, and how to assess feeding cues and effective feeding. Parents should be provided with a clear method for escalating concerns to the healthcare team[92]. A recurrent theme in litigation cases concerning neonatal hypoglycaemia is failure of the healthcare team to record

and take heed of maternal concerns about infant well-being[3]. The working group endorses the recommendation from the paper that "maternal concerns should not be discounted and should be followed by a detailed and documented history and assessment of the baby's condition."
See **Appendix 1** for suggested parent information sheet**.**

Management of the reluctant feeder with no risk factors for impaired transition: Practice Points 26-27

We recommend pro-active support of feeding in the immediate post-partum period for all term infants[31]. This should be followed by an assessment within 6 hours to identify whether initiation of feeding has been effective, or whether the infant is a reluctant feeder (does not show feeding cues). Practitioners need to be skilled in the clinical assessment of *effective* feeding and *reluctant* feeding and be able to interpret feeding behaviour in the context of a general assessment of well-being. Infants with no risk factors (**Practice Point 2**) and no abnormal clinical signs but who are reluctant to feed should be given an active feeding plan (**Appendix 2**).

Infants who are not feeding effectively, especially after a period of effective feeding, or have one or more abnormal clinical signs should have BG measured.

Appendix 1. Parent Information Sheet: Protecting your baby from low blood glucose

What is low blood glucose?

You have been given this leaflet because your baby is at increased risk of having low blood glucose (also called low blood sugar or hypoglycaemia).

Babies who are small, premature, unwell at birth, or whose mothers have diabetes or have taken certain medication (beta-blockers), may have low blood glucose in the first few hours and days after birth, and it is especially important for these babies to keep warm and feed as often as possible to maintain normal blood glucose levels.

If your baby is in one of these 'at risk' groups, it is recommended that they have some blood tests to check their blood glucose level. Extremely low blood glucose, if not treated, can cause brain injury resulting in developmental problems. If low blood glucose is identified quickly, it can be treated to avoid harm to your baby.

Blood glucose testing

Your baby's blood glucose is tested by a heel-prick blood test. A very small amount of blood is needed, and it can be taken with your baby in skin-to-skin contact. The first blood test should be done before the second feed (2-4 hours after birth) and repeated until the blood glucose levels are stable.
You and your baby will need to stay in hospital for the blood tests.You will know the result of the test straight away.

How to avoid low blood glucose

- **Skin-to-skin contact**
  Skin-to-skin contact with your baby on your chest helps keep your baby calm and warm and helps establish breastfeeding. Lie in a position where your head and shoulders are raised (not flat on your back). Have baby in a position where you can look into their eyes, and you can check that baby is well in this position.
- **Keep your baby warm**
  During skin-to-skin contact your baby should wear a hat and be kept warm with a blanket or towel. Once you go home from hospital your baby will no longer need to wear a hat indoors. If your baby is in a cot, keep baby warm with blankets.
- **Feed as soon as possible after birth**
  Ask a member of staff to support you with feeding until you are confident, and make sure you know how to tell if breastfeeding is going well, or how much formula to give your baby.
- **Feed as often as your baby wants, but do not leave more than 3 hours between feeds**
  Feed your baby whenever you notice "feeding cues" which include rapid eye movements under the eyelids, mouth and tongue movements, body movements and sounds, sucking on a fist. Don't wait for your baby to cry – this can be a late sign of hunger. Let your baby feed for as long as they want and offer both breasts if you are breastfeeding. If your baby is not showing any feeding cues yet, hold baby in skin-to-skin and offer a feed. To reduce the risk of low blood glucose your baby should have a feed within three hours of the beginning of the last feed. Your midwife will talk to you about when you can move to responsive feeding.

- **Express your milk (colostrum)**
  If you are reading this leaflet whilst you are pregnant you may wish to hand express some colostrum before your baby is born. We suggest you talk to your midwife to discuss if this is the right thing for you and they can talk to you about how to express milk antenatally.
  If you are breastfeeding and your baby struggles to feed, try to give some expressed breast milk. A member of staff will show you how to hand express your milk or watchthe UNICEF hand expression video (search "UNICEF hand expression"). You may also consider using a breast pump alongside hand expressing. If possible, it is good to have a small amount of expressed milk saved in case you need it later, so try to express a little extra breast milk in between feeds. Ask your midwife how to store your expressed milk and for support with using a breast pump if you still need to express milk after the first couple of days.

Don't hesitate to tell staff if you are worried about your baby

If your baby appears to be unwell, this could be a sign that they have low blood glucose. As well as doing blood tests, staff will observe your baby to check he / she is well, but your observations are also important, as you are with your baby all the time and know your baby best. **It is important that you tell staff if you are worried** that something is wrong with your baby. Parents' instincts are often correct.

Signs that your baby may be unwell

- **Your baby is not feeding well**
  In the first few days your baby should feed effectively at least every 3 hours, until their blood glucose is stable, and then at least 8 times in 24 hours. Ask a member of staff how to tell if your baby is attached and feeding effectively at the breast, or how much formula your baby needs.
  If your baby becomes less interested in feeding than before, this may be a sign they are unwell, and you should raise this with a member of staff.
- **Is your baby warm enough?**
  Your baby should feel slightly warm to touch, although hands and feet can sometimes feel a little cooler. If you use a thermometer the temperature should be 36.5^0C and 37.5^0C inclusive.
  If your baby is cold this can lead to low blood sugar. If they are too hot this can be a sign of infection which can also lead to low blood sugar.
- **Is your baby alert and responding to you?**
  When your baby is awake, he/she will look at you and pay attention to your voice and gestures.
  If you try to wake your baby, he/she should respond to you in some way.
- **Is your baby's muscle tone normal?**
  A sleeping baby is very relaxed but should still have some muscle tone in their body, arms, and legs and should respond to your touch. It can be normal to make brief, light, jerky movements. Ask a member of the team if you are not sure about your baby's movements.
  If your baby feels completely floppy, with no muscle tone when you lift their arms or legs, or if your baby is making strong repeated jerky movements, this is a sign they may be unwell.
- **Is your baby's colour normal?**
  Look at the colour inside your baby's lips and tongue – they should be pink.
- **Is your baby having difficulty with breathing?**
  Babies' breathing can be quite irregular, sometimes pausing for a few seconds and then breathing very fast for a few seconds.
  If you notice your baby is breathing very fast for a longer, continuous period, or seems to be struggling to breathe with very deep chest movements, nostrils flaring or making noises with each breath out – this is not normal. Call the emergency number given to you by your midwife.

Who to call if you are worried

- In hospital, inform any member of the clinical staff.
- At home, call the emergency number given to you by your midwife.
- Out of hours, call NHS 111 or [local number for urgent assessment]
- If you are really worried, take your baby to your nearest Paediatric A&E or dial 999. [Insert local information]

What happens if your baby's blood glucose is low?

If the blood glucose test result is low, your baby should feed as soon as possible and provide skin-to-skin contact. If the blood glucose level is very low the neonatal team may advise urgent treatment to raise the blood glucose and this could require immediate transfer to the Neonatal Unit.

Another blood glucose test will be done before the next feed or within 2-4 hours.

If you are breastfeeding and your baby does not breastfeed straight away, a member of staff will review your baby to work out why. If they are happy that your baby is well, they will support you to hand express your milk and give it by oral syringe / finger / cup / spoon.

If your baby has not breastfed, and you have been unable to express any of your milk, you will be advised to offer infant formula.

In some hospitals the team may prescribe a dose of dextrose (sugar) gel as part of the feeding plan because this can be an effective way to bring your baby's glucose level up.

If you are breastfeeding and advised to give some infant formula, this is most likely to be forone or a few feeds only. You should continue to offer breastfeeds and try to express milk asoften as possible to ensure your milk supply is stimulated.

Very occasionally, if babies are too sleepy or unwell to feed, or if the blood glucose is still lowafter feeding, he / she may need to go to the Neonatal Unit / Special Care Baby Unit. Staff will explain any treatment that might be needed. In most cases, low blood glucose quickly improves within 24-48 hours and your baby will have no further problems.

Going home with baby

It is recommended that your baby stays in hospital for 24 hours after birth. After that, if your baby's blood glucose stable and your baby is feeding well, you will be able to go home.

Before you go home, make sure you know how to tell if your baby is getting enough milk. A member of staff will explain the normal pattern of wet and dirty nappies and changes in the colour of dirty nappies. For further information, if you are breastfeeding, see 'How you and your midwife can recognise that your baby is feeding well' (Search 'UNICEF Baby Friendly assessment tool').

It is important to make sure that your baby feeds well **at least 8 times every 24 hours** and most babies feed more often than this. There is no need to continue waking your baby to feed every 2–3 hours as long as your baby has had at least 8 feeds over 24 hours unless this has been recommended for a particular reason. You can now start to feed your baby responsively. Your midwife will explain this.

If you are bottle feeding, make sure you are not overfeeding your baby. Offer the bottle when baby shows feeding cues and observe for signs that baby wants a break. Don't necessarily expect your baby to finish a bottle – let them take as much milk as they want.

Once you are home, as with all newborn babies, you should continue to look for signs that your baby is well and seek medical advice if you are worried about your baby.

Appendix 2. Management of reluctant feeding in healthy term infants

See Flowchart D.

Managing breastfed healthy term infants

Healthy term babies may feed enthusiastically at birth and then sleep for many hours. To prevent a potential negative effect on a baby's wellbeing, establishment of feeding and the stimulation of lactation follow the flow chart overleaf from birth for all well, term babies.

Feeding Cues

Feeding cues indicate the beginning of feeding readiness when babies are more likely to latch on and suck and can occur during periods of light sleep as well as when a baby is awake. Cues include rapid eye movements under the eyelids, mouth and tongue movements, body movements and sounds, sucking on a fist. Crying can be a way of indicating that the feeding cues have been missed. If this doesn't occur, support should be provided and documented until effective feeding is established.

Assisted feeding (cup, spoon, oral syringe)

Occasionally it may be helpful to give a baby small amount of colostrum using a cup, spoon or oral syringe.

To give a cup feed safely, hold baby in an upright position, ensuring that baby's neck and shoulders are well supported. Make sure baby is fully awake, calm and alert. Half-fill the cup and hold it so that it just touches baby's mouth. It should reach the corners of the baby's mouth and rest lightly on the bottom lip. Allow the baby to take a small sip, to encourage drinking – do not pour the milk into the baby's mouth. Tip the cup just enough so that the baby can lap the milk. Keep the cup in this tilted position and allow the baby to start again when ready.

To give a syringe feed safely, the calm and alert baby should be held in the mother's arms slightly upright, not flat. The oral syringe is gently placed in between the gum and cheek and a little colostrum gently instilled, no more than 0.2ml at a time. Allow the baby time to taste and enjoy the milk. Stop if the baby starts sucking, allow time to swallow, then give a little more. Move onto cup or paced bottle feeding depending on local policy and parental choice once you have more than 5ml to give. If there is a clinical indication to provide formula or a mother makes an informed choice to provide formula this can also be given in a cup depending on local policy. A nasogastric tube may be required if the baby shows no cues in response to assisted feeding methods.

Boosting confidence

You can help and support the mother and boost her confidence by teaching her to hand express. Give her a supply of oral feeding syringes and feeding cups, encourage skin contact, especially in the laid-back position and help her to recognize her baby's feeding cues. Encourage the mother to offer her breast to her baby when ready, and to feed her baby expressed breast milk until baby is breastfeeding actively and effectively.

If baby does not establish breastfeeding, support the mother to continue expressing. Ensure increasing volumes of colostrum/ expressed milk day by day to meet baby's nutritional requirement. We suggest expressing at least 8-10 times in 24 hours, including at night with no long intervals. Some mothers can

find it helpful to use an electric breast pump alongside hand expressing.

If the mother cannot or chooses not to express colostrum

The length of labour and the type of birth may influence the mother's feelings about hand expressing and giving colostrum intensively for the first few hours. The mother may ask to give formula instead. If the mother cannot or chooses not to express her colostrum it is the responsibility of the midwife to ensure this is an informed decision based on awareness of the benefits of breastfeeding and the risks of formula. This will be documented by the midwife in the woman's notes. Infant formula can be given by cup or by pacing bottle feeds depending on local policy and parental choice. Volumes should be offered appropriate to the baby's age i.e. 0 to 24 hours 40 to 60 ml/kg/ per day.

Once lactation is established infant formula top ups should be replaced with expressed breastmilk, if the mother wants to. Parents should be supported to recognise effective breastfeeding, so they can identify when a top up is or is not required. Avoid giving large volumes of infant formula once lactation is established, we suggest not exceeding 20ml of formula per feed in addition to breastfeed, if needed.

Recognising effective feeding

The baby should be alert, actively sucking but settled at the breast; the baby should end breastfeeding spontaneously and remain settled for a short period until the next feed. The feed should be pain free and the baby should demonstrate adequate wet and dirty nappies appropriate to age. For further information see the Baby Friendly Breastfeeding assessment tool[5].

Appendix 3: Use of glucose 40% oral gel

Indications

- Blood glucose 1.0 to 1.9mmol/L in infant with no abnormal clinical signs.
- Severe hypoglycaemia (BG <1.0mmol/L) where there is no intravenous access.

Notes

- Must be given by buccal route.
- Must be used in conjunction with a feeding plan.
- For babies with severe hypoglycaemia (BG <1.0mmol/L) should be only used as an interim measure while arranging for urgent medical review and treatment with IV glucose.

Dose

- Use glucose 40% oral gel 200mg/kg, up to two doses given 30 minutes apart per episode of hypoglycaemia and a maximum of six doses of buccal gel in 48 hours.
- Glucose 40% oral gel contains approximately 400mg/ml of glucose. A dose of 200mg/kg is approximately equivalent to 0.5ml/kg. Practitioners may decide that variations in glucose content per 1 ml glucose 40% oral gel are unlikely to be clinically significant; advice from the local pharmacist can be sought.
- Table 2 provides a practical volume to administer the 200mg/kg/dose for babies within specific weight bands.

Table 2. Volume and dose of glucose 40% oral gel by baby's weight bands

Weight of baby	Volume of glucose 40% oral gel	Dose of glucose
1.5 to 1.99 kg	1 ml	400 mg
2.0 to 2.99 kg	1.5 ml	600 mg
3.0 to 3.99 kg	2 ml	800 mg
4.0 to 4.99 kg	2.5 ml	1000 mg
5.0 to 5.99 kg	3 ml	1200 mg
6.0 to 6.99 kg	3.5 ml	1400 mg

Method of administration

- Draw up correct volume of glucose 40% oral gel using a 2.5 or 5ml oral / enteral syringe.
- Dry oral mucosa with gauze, gently squirt gel with syringe (no needle) onto the innercheek and massage gel into the mucosa using latex-free gloves.
- Offer a feed, preferably breast milk, immediately after administering glucose gel.
- Repeat oral glucose gel if baby remains hypoglycaemic according to flow chart B.

Up to six doses can be given over a 48-hour period but any more than one dose should be discussed with the neonatal team, and it is advisable for the baby to be examined before the third dose is administered.

Appendix 4: Intravenous dextrose concentration

Table 3 gives the glucose infusion rate (in mg/kg/min) provided by IV glucose infusions at different rates.

Table 3. Glucose delivery rate provided by IV glucose infusion

Flow rate of 10% dextrose (ml/kg/day)	Infusion rate (mg/kg/min)
40	2.77
60	4.16
80	5.55
100	6.94
120	8.33
130	9.03
140	9.72
150	10.42

How to calculate mg/kg/min from ml/kg/day for any concentration of glucose

Glucose delivery rate for any concentration of glucose solution and infusion rate can be calculated using the following formula:
Glucose infusion rate (mg/kg/min) = [infusion rate (ml/kg/day) / 144] x glucose concentration (%)

How to make up any concentration of glucose in any volume:

If preprepared glucose solution is not available in the desired concentration, the desired concentration can be prepared using the following calculations:

- Desired concentration of glucose = D%
- Volume of desired concentration of glucose = V ml
- Available lower concentration of glucose = L%
- Volume of lower concentration of glucose to add = LV ml
- Available higher concentration of glucose = H%
- Volume of higher concentration of glucose to add = HV ml

Step 1: calculate the volume of higher concentration of glucose to add (HV)

- HV (ml) = V(ml) X (D% - L%) / (H% - L%)

Step 2: calculate the volume of lower concentration of glucose to add (LV)

- LV (ml) = V (ml) – HV (ml)

Step 3: Add HV and LV to get the volume of desired concentration of glucose (V)

- V (ml) = HV (ml) + LV (ml)

When producing local guidance, neonatal units may find it useful to include tables of volumes required for preparation of standard glucose concentrations and worked examples according to local practice.

Appendix 5: Point of Care testing for blood glucose in newborn babies

Point of care testing (POCT) is defined as an analytical test performed outside of the laboratory setting, by a healthcare professional. Critical to this guidance is the understanding of how POCT devices perform in newborns.

Recommendations

- To fully understand the performance of any POCT, clinical staff are strongly encouraged to engage with their pathology department, and specifically POCT leads.
- No POCT equipment should be used, or purchased for use in the neonatal unit, without engagement between pathology Healthcare Scientists and neonatal leads, to ensure it is fit for purpose. The quality of results produced by POCT devices on patients, and specifically newborns, must be understood and evidenced.
- POCT devices should be regularly subjected to internal quality control and registered on an external quality assessment scheme. The results of which should be monitored by a Health and Care Professions Council-registered pathology Healthcare Scientist.
- Staff using POCT equipment must have training on the device. The content of training is best supported by Pathology POCT Healthcare Scientists. Training must cover the following:
    - Pre-analytical sample requirements.
    - Quality monitoring of the device.
    - Limitations of the device.
    - Recording of the results.
- The results of a POCT test are critically dependent on the quality of the sample tested. The pre-analytical requirements for blood samples must be fully understood to produce high quality results.
- Historically glucose meters were not able to demonstrate good performance in the neonatal population due to the patient's high haematocrit levels and the devices poor precision at low glucose levels. However, there is now good evidence that some capillary blood glucose meters are suitable for the neonatal population and are precise and accurate at low glucose levels. They bring the benefits of using a very small blood volume, producing results in seconds and not producing incidental results for other parameters that are not clinically requested. Pathology Healthcare scientists can support in the understanding of performance from published literature, manufacturer supplied information and by performing local studies.
- Blood gas analysers are regularly used in neonatal units and can provide accurate results at low blood glucose levels. It is noted that they can be set to only report glucose levels, thus preventing the reporting of results not clinically requested. POCT pathology staff can be engaged to support this formatting within departments.
- Caution should be taken when using multiple methods for the testing of blood glucose in newborns. It is preferred practice to monitor glucose levels using the same method, to ensure changes in results reflect change in the patient as opposed to analytical method differences. Results must be recorded in the patient's record including the date and time of the test, the operators name and the device used to do the test. The aim should be for POCT devices to be electronically integrated into the patients record to ensure all results are recorded with a full audit trail.

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Flowchart A. Management from birth - 24 hours of term infants at risk of hypoglycaemia (Box 1)

Dry and place baby skin-to-skin care in a warm, draught free room.

Put hat on baby, and cover with a warm blanket. Encourage and support early breastfeeding within the first hour after birth.

For women who chose to formula feed, feed within the first hour after birth and give a volume appropriate for 40 to 60ml/kg /day.

Provide verbal and written information to parents that explains how to prevent hypoglycaemia, why their baby needs blood glucose monitoring, lists signs that may indicate hypoglycaemia (Box 2), and advises parents to inform a member of the healthcare team if they are concerned about their baby's well-being (Appendix 1).

↓

Check pre-feed blood glucose level prior to second feed (2-4 hours after birth):
Is the blood glucose level ≥2.0mmol/l?

YES ↓

NO → See Flowchart B

Encourage frequent feeding and ensure no longer than 3 hours between feeds.

Assess the need for helping the mother with: ongoing feeding; hand expression; recognition of early feeding cues; and signs of effective attachment and feeding.

For women who chose to formula feed, give 40 to 60ml/kg/day 3 hourly over the first 24 hours after birth

Check blood glucose level prior to third feed (no longer than 8 hours after birth):

Is the blood glucose level ≥2.0mmol/l?

NO → See Flowchart B

YES ↓

No further blood glucose monitoring required unless there are clinical signs of hypoglycaemia (**Box 2**).

Observe feeding in hospital for at least 24 hours.

Continue to support responsive breastfeeding and ensure that mother understands how to assess effective feeding and knows how to escalate concerns.

Complete at least one recorded breastfeeding assessment using local / BFI tool prior to transfer home.

If formula fed give 40 to 60ml/kg/day 3 hourly over the first 24 hours after birth. Increase volumes thereafter.

Box 1. Infants who require routine blood glucose monitoring

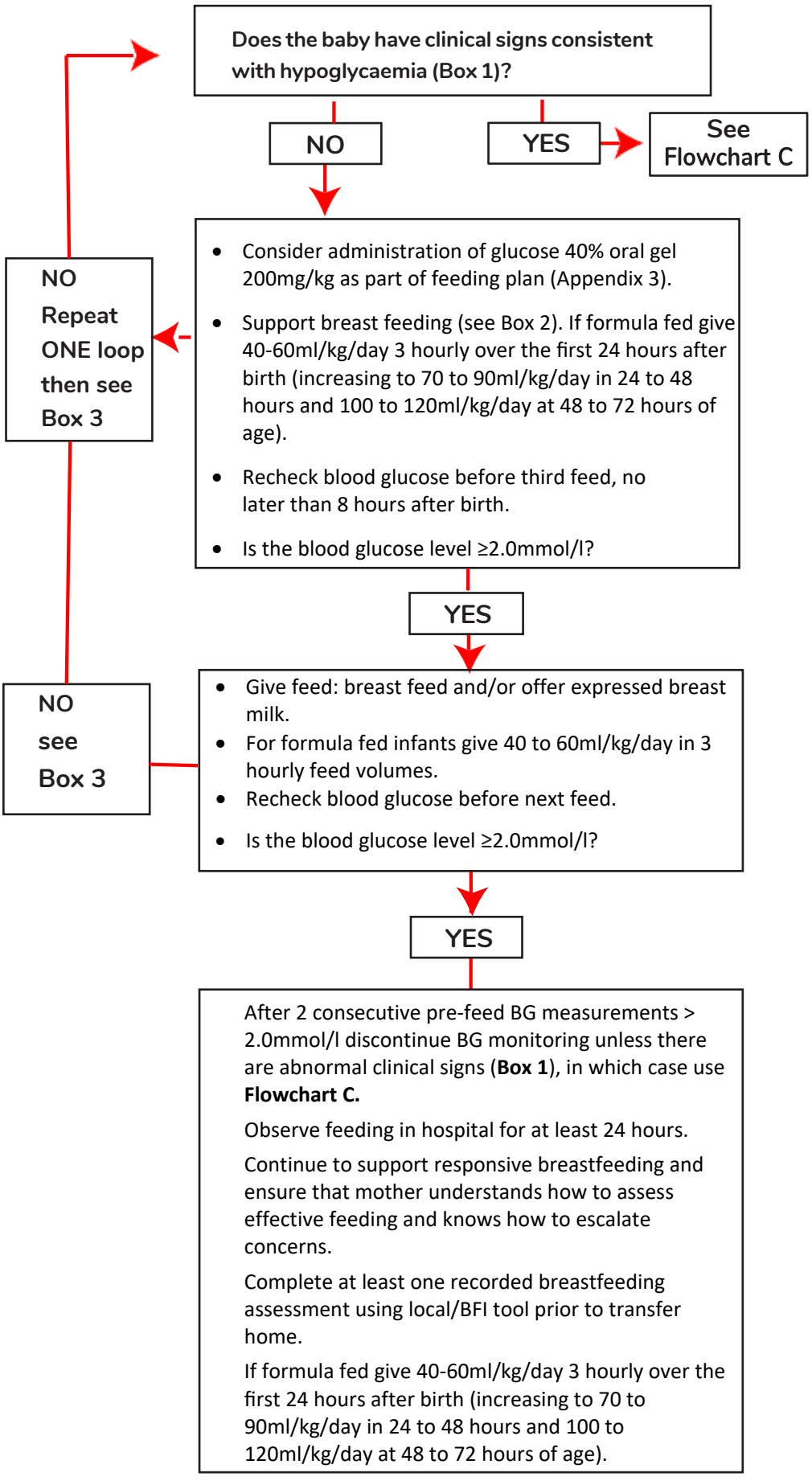
- Fetal growth restriction: as indicated by birth weight <2nd centile (small for gestational age, refer to Table 1) or clinically wasted.
- Infants of mothers with diabetes.
- Infants of mothers taking beta-blockers in the third trimester and / or at time of birth.

Box 2. Signs that may indicate hypoglycaemia

- Lethargy
- Abnormal feeding behaviour especially after a period of feeding well
- High pitched cry
- Altered level of consciousness
- Hypotonia
- Seizures
- Hypothermia (<36.5°C)
- Cyanosis
- Apnoea

Identification and Management of Neonatal Hypoglycaemia in the Full-Term Infant: A Framework for Practice. British Association of Perinatal Medicine, 2023

Flowchart B. Pre-feed BG 1.0 to 1.9mmol/l and no abnormal clinical signs (birth to 72 hours)



Box 1. Signs that may indicate hypoglycaemia

- Lethargy
- Abnormal feeding behaviour especially after a period of feeding well
- High pitched cry
- Altered level of consciousness
- Hypotonia
- Seizures
- Hypothermia (<36.5°C)
- Cyanosis
- Apnoea

Box 2. Supporting breast feeding

Encourage skin-to-skin contact.

Offer breast feed and if not feeding effectively teach mother to hand express.

Give colostrum obtained to baby by the method suitable toparents.

Continue to encourage hand expression at least 8-10 times in 24 hours and support feeding on the breast until infant is feeding effectively.

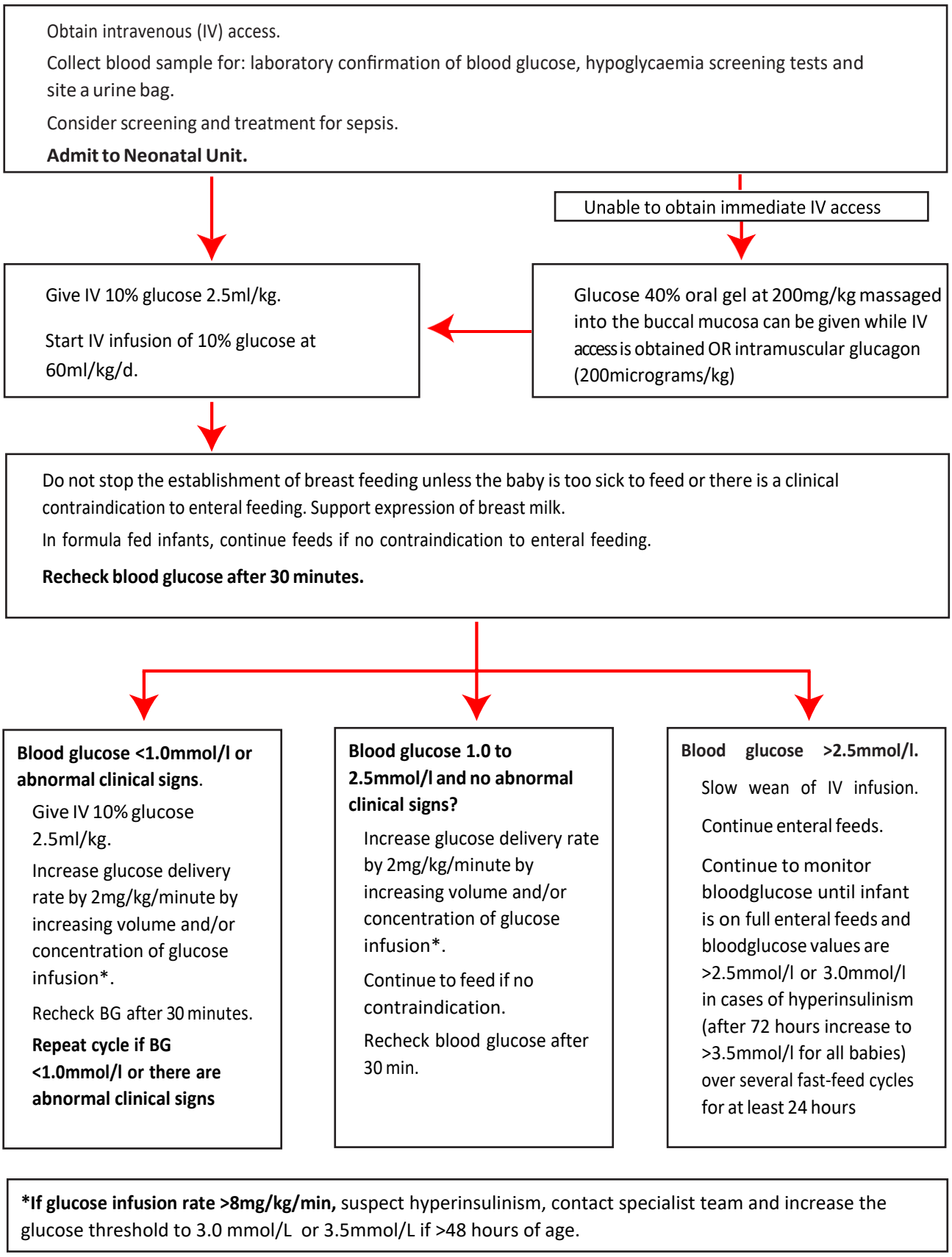
Box 3. If more than 2 measurements 1.0-1.9mmol/l, inform neonatal team.

Investigate for causes of hypoglycaemia, consider sepsis.

Consider increased feed frequency, nasogastric tube insertion or IV infusion of 10% glucose.

Identification and Management of Neonatal Hypoglycaemia in the Full-Term Infant: A Framework for Practice. British Association of Perinatal Medicine, 2023.

Flowchart C. Blood glucose < 1.0mmol/l and / or clinical signs consistent with hypoglycaemia



***If glucose infusion rate >8mg/kg/min,** suspect hyperinsulinism, contact specialist team and increase the glucose threshold to 3.0 mmol/L or 3.5mmol/L if >48 hours of age.

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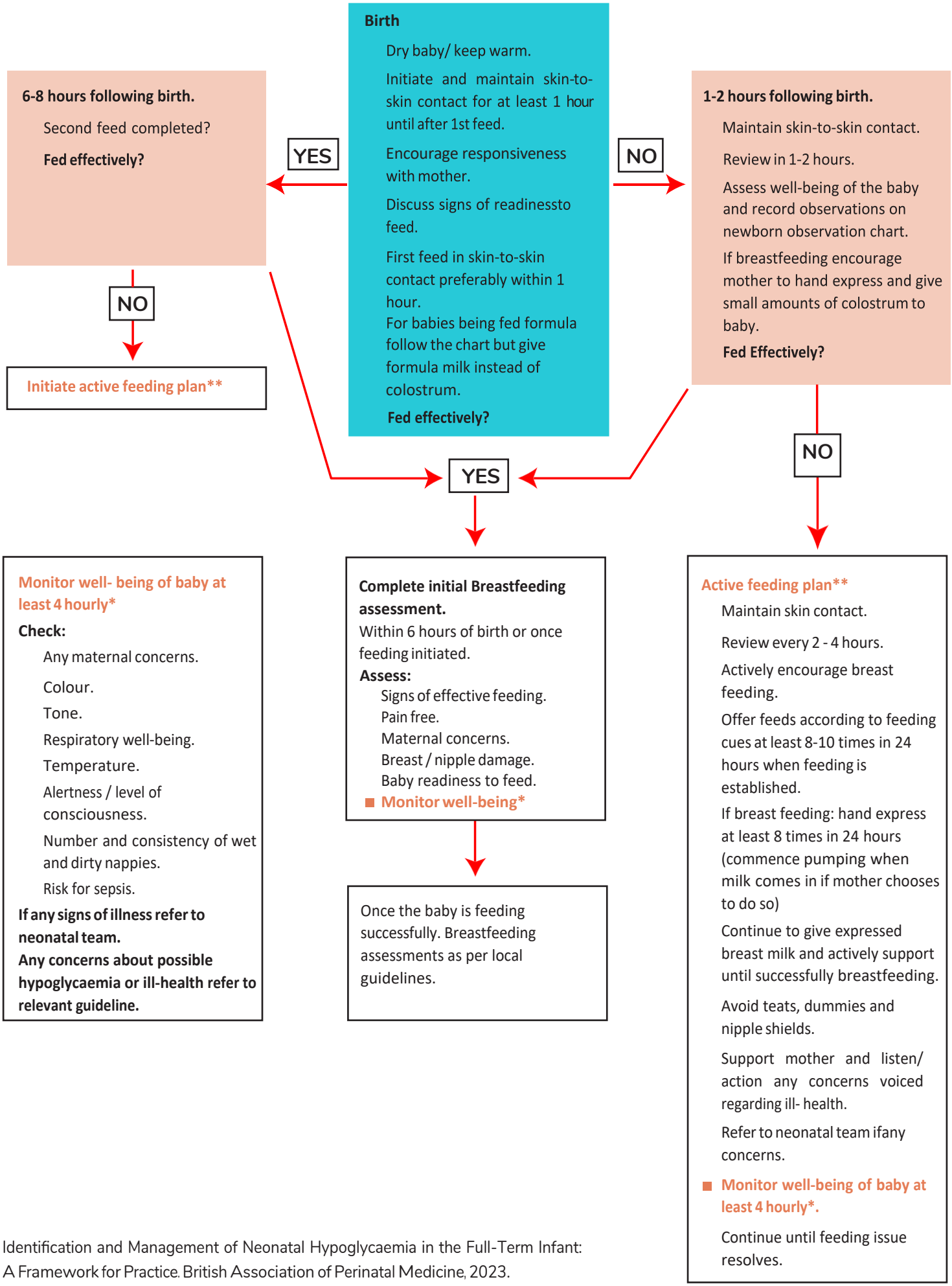
Flowchart D. Management of reluctant feeding in healthy term infants ≥ 37 weeks



Identification and Management of Neonatal Hypoglycaemia in the Full-Term Infant: A Framework for Practice. British Association of Perinatal Medicine, 2023.

BAPM

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We are a professional association of neonatologists, paediatricians, obstetricians, nurses, midwives, trainees, network managers and other health professionals dedicated to shaping the delivery and improving the standard of perinatal care in the UK.

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