CARE OF THE NEWBORN HYPOGLYCAEMIA

Background

Definition

- A “true” blood glucose of less than 2.6 mmol/L – venous sample.
- Neonatal hypoglycaemia is commonly defined as a “true” blood glucose of less than 2.6 mmol/l (confirmed by clinical symptoms, laboratory results).

Aetiology

- Low glycogen stores, early depletion of the glycogen stores, impaired gluconeogenesis, hyperinsulinism or lack of counter insulinaemic hormones are thought to be solely or in combination the underlying cause for hypoglycaemia.

Complications

- True blood glucose < 2.6 mmol/l on > 5 single days/occasions or for > 48 h is associated with neurodevelopmental and physical growth deficits. Neurological follow-up suggested. True blood glucose < 1.1 mmol/l for > 2 h cause cerebral neuronal necrosis in primates.
- Never give a bolus injection of glucose alone, it must be followed by a continuous glucose infusion +/- milk feeds (risk of rebound hypoglycaemia).
- Any sudden interruption of intravenous glucose may result in profound hypoglycaemia secondary to hyperinsulinism. Tissued iv drips must be urgently resited.
- Never give more than a 12.5% glucose infusion into a peripheral vein (extravasation injury).
- Never give more than 20 mg/kg/min in any line, including central line.

General prevention of hypoglycaemia

For all newborn infants:

- Maintain normal body temperature
- Early feeding
- Manage other clinical concerns promptly

Identification of hypoglycaemic infant

- Symptoms: Irritability, jitteriness, lethargy and stupor, tremor, seizures, hypotonia, apnoea, hypothermia and poor feeding, dry nappies, tachypnoea.

If hypoglycaemia is suspected, a blood glucose measurement should be undertaken from a heel-prick sample immediately.

Point-of-care devices/bedside measurement

- The Haemocue® machine is used for routine assessment of blood sugar. The normal range is 2.6 – 4.5mmol/L.
- At RSCH a blood gas machine is available on TMBU for borderline glucose results (needs 35microliter of blood in a capillary tube).
- Glucometer (incl. gas machine) readings are based on whole blood; hence they tend to underestimate glucose concentrations, especially when < 2.6 mmol/l
- Always perform a plasma blood glucose (venous sample), if the glucometer or gas machine reading is < 2.6 mmol/l.

Identification of at-risk newborn infants

- The following infants should be monitored and placed on the hypoglycaemia pathway

	Issue	Additional information	
Size / birth weight issues	• IUGR < 9th centile	(see growth chart)	
	• Macrosomia > 91st percentile	plus abnormal 28 week modified GTT in mother OR 28 week GTT in mother not available	
Gestation / prematurity issues	• < 37 weeks gestation		
Maternal reasons	• Infant of a diabetic mother	Gestational Diet controlled Anti-diabetic drugs Insulin	
	• Maternal beta-blocker use	during pregnancy only / not if meds commenced in labour	} }All }included }
	• Other maternal drugs	oral hypoglycaemic agents, i.v. glucose infusion	
Newborn reasons	• Hypothermia		
	• Cord pH < 7.1		
	• Hypoxic-ischaemic encephalopathy	Apgar < 5 at 10 min / pH < 7.0	
	• Cardio-respiratory problems	e.g.	transient tachypnoea
			respiratory distress syndrome
			congenital heart diseases
	• Plethoric infant/hyperviscosity	e.g.	polycythaemia
	• Infections	e.g.	neonatal septicaemia
	• Endocrine disorders	e.g.	hypothyroidism
			persistent hyperinsulinemic hypoglycaemia of infancy incl. Beckwith-Wiedemann syndrome
	• Inborn errors of metabolism	e.g.	carbohydrates (e.g. glycogen storage diseases / diseases of gluconeogenesis)
			fatty acids (e.g. MCADD)
			amino acids (e.g. organoacidopathies)
Other	• Other	e.g.	severe Rhesus disease

Intrauterine growth restriction operational thresholds < 9th centile		
Gestation	**Boys**	**Girls**
≥ 37 weeks	< 2350 g	< 2250 g
≥ 38 weeks	< 2600 g	< 2500 g
≥ 39 week	< 2800 g	< 2700 g
≥ 40 weeks	< 2950 g	< 2850 g

Macrosomia operational thresholds > 91st centile		
Gestation	**Boys**	**Girls**
≥ 37 weeks	> 3550 g	> 3400 g
≥ 38 weeks	> 3800 g	> 3600 g
≥ 39 weeks	> 4000 g	> 3800 g
≥ 40 weeks	> 4200 g	> 4000 g

- Healthy term babies (weight appropriate for gestational age) are able to utilise alternative fuels e.g. ketone bodies and lactate, and should not require blood glucose analysis.

Management of the at-risk infant and hypoglycaemic infant

General recommendations

- Asymptomatic baby at risk of hypoglycaemia – **see flowchart and follow postnatal ward pathway (A)**
- Symptomatic or persistently hypoglycaemic asymptomatic baby - **follow algorithm (B)**
- Do not discharge babies into community until they are at least 24 hours, maintaining their blood glucose level and feeding well.

Practical aspects of fluid management

- Oral - see flowchart/pathway A and algorithm B
- I.v. and oral - start at least 60 ml/kg/24h of 10 % glucose iv. (4.2 mg/kg/min) topped up with milk as two-hourly feeds to a total of at least 90 ml/kg/day.
- I.v. only - if feeds not tolerated give 90 ml/kg/24h of 10 % glucose or 45 ml/kg/24h of 20 % glucose in a fluid restricted baby (6.3 mg/kg/min).
- Increase infusion by 10 - 20 ml/kg/24h (0.7 – 1.4 mg/kg/min) as required.
- In order to increase infusion to 8 mg/k/min of glucose this is most easily achieved by changing to 15 % glucose at 80 ml/kg/24h or to 20% glucose at 60 ml/kg/24h in a fluid restricted baby (8.3 mg/kg/min).
- For a glucose intake of 10 - 12 mg/kg/min increase fluids to 100 ml/kg/24h of 15 % glucose or 75 ml/kg/24h of 20 % glucose in a fluid restricted baby (10.4 mg/kg/h).

Glucose dose for different infusion concentrations (mg/kg/min)

Infusion Rate	Dextrose Concentration			
	10 %	15 %	20 %	25 %
40 ml/kg/24h	2.7	4.2	5.6	6.9
60 ml/kg/24h	4.2	6.25	8.3	10.4
90 ml/kg/24h	6.25	9.4	12.5	15.6
100 ml/kg/24h	6.95	10.4	13.9	17.4
120 ml/kg/24h	8.3	12.5	16.7	
150 ml/kg/24h	10.4	15.6		

Other treatment options

- If increases of glucose intake further than 12 - 15 mg/kg/min are necessary commence Glucagon infusion (2 mg/kg in 48 ml 5% Dextrose) at 1 ml/h (42 µg/kg/h). In a symptomatic infant where i.v. access cannot be gained give Glucagon 0.1-0.2 mg/kg i.m.
- If Glucagon fails to control blood glucose further glucose may be given using 20% or 25% solutions.
- Rarely steroids may be needed. They are essential in adrenal and pituitary insufficiency. Give hydrocortisone max. 5 - 10 mg/kg/day po, i.v. or i.m. 12 hourly.
- If hyperinsulinaemia has been diagnosed then Diazoxide may be used. Give Diazoxide 1.5 – 6.5 mg/kg 8 hourly p.o.

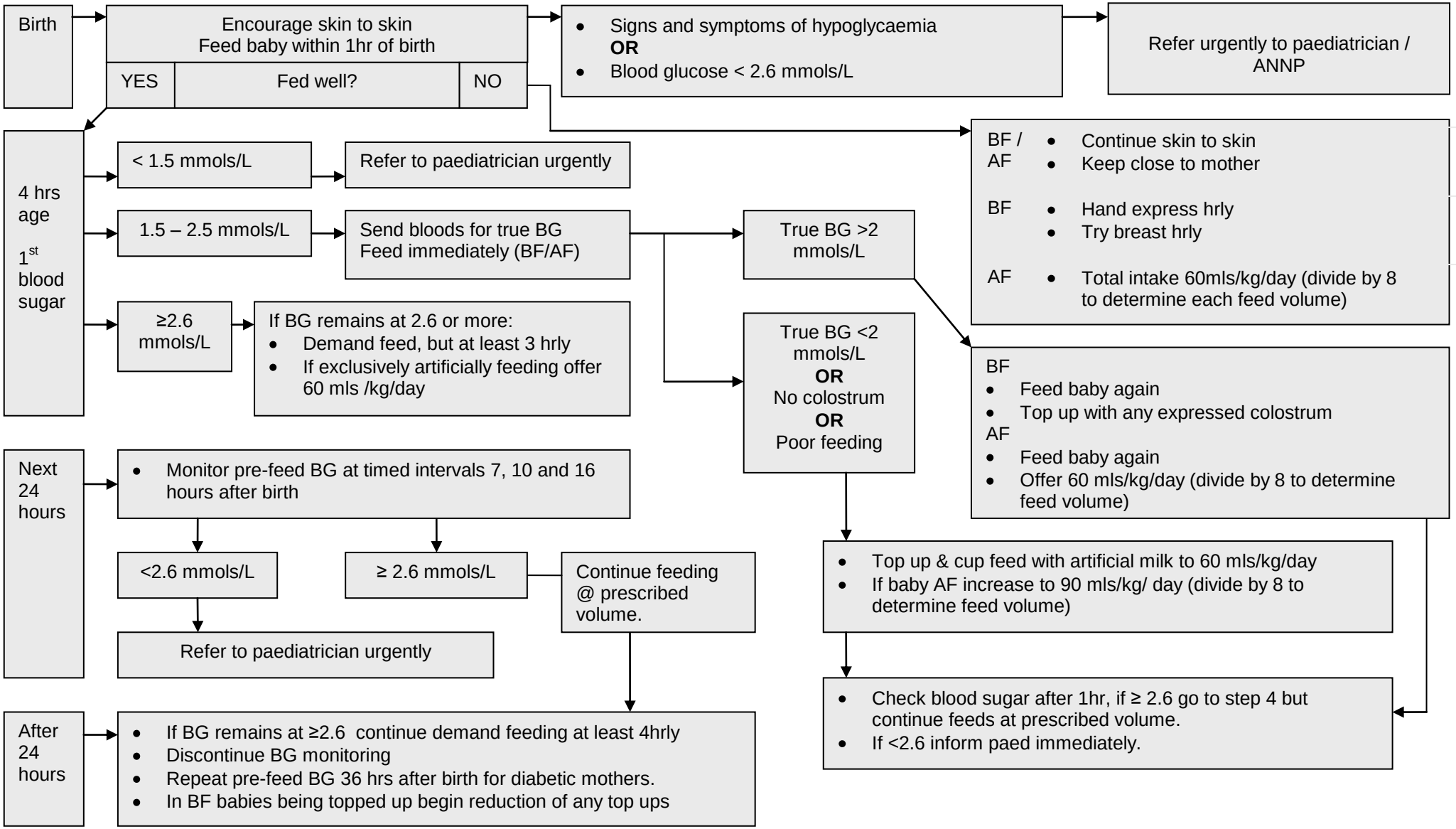
Weaning from high glucose concentrations and Glucagon

- Once glucose concentrations have stabilised for 24 h start weaning.
- Wean glucose 10 – 20 ml/kg/d (0.7 – 1.4 mg/kg/min) every 12 hours.
- If glucose concentrations higher than 15 % were used, reduce to 15% for 12 hours, then reduce to 12.5 % for 12 hours, and then 10%.
- A blood glucose level of 2.6 – 4.5 mmol/l is acceptable. Check the blood glucose 2 and 6 hours after weaning and at 12 hours prior to next wean.
- Increase fluid volumes daily as per the fluid requirement protocol.
- Once on 10%, oral feeds may be increased overlapping with the i.v. fluids by increasing oral feeds every 4 hours.
- Once established on full oral feeds Glucagon should be reduced very slowly (reduce by 0.1 ml every 4 hours).

Useful information on glucose infusions

- 500 ml bags of 10% and 20% glucose and 50 ml ampoules of 50% glucose are stocked on the Unit:
    - To make a 12.5% glucose solution add 25 ml of 50% glucose to 375 ml of 10% glucose
    - To make a 15% glucose solution add 50 ml of 50% glucose to 350 ml of 10% glucose
    - To make a 25% glucose solution add 50 ml of 50% glucose to 250 ml of 20% glucose

Flow chart for the management of asymptomatic babies at risk of hypoglycaemia on postnatal wards (A)



Postnatal Ward Pathway (A)
Monitoring Asymptomatic Babies at Risk of Hypoglycaemia

Name:				**DOB:**		
Hospital no:				**Time of birth:**		
Reason for Monitoring:						
Step 1: Promote breastfeeding and prevent hypoglycaemia						
• Encourage skin to skin. • Feed baby within 1 hour of delivery i.e. put to breast or give as much colostrum as is available. • Try hourly if not feeding well, hand express and offer colostrum. • If artificially feeding, offer artificial milk at 60 ml/kg in 24 h (3 hrly feeds or 8 feeds per day) by cup or bottle.						
Time at breast/ amount taken:			Time:		Signature:	
Step 2. First blood sugar check						
• Take blood sugar shortly before next feed (no earlier than 3 h and no later than 4 h after birth). • Check body temperature.						
Result:			Time:		Signature:	
If	BM	≥ 2.6	mmols/L	go to step 4		
		>1.5 – 2.5	mmols/L	go to step 3		
		< 1.5	mmols/L	inform paediatrician to assess for admission to SCBU		
Step 3. Blood sugar > 1.5 - 2.5 mmol						
3a • Verify result from step 2 with lab. blood sugar (do not wait for result before feeding).						
Result:			Time:		Signature:	
3b • If blood sugar **> 2.0** at **first blood sugar check**, feed baby by breast and top-up with any volume of EBM/colostrum. • If blood sugar **≤ 2.0** or no EBM/colostrum available or poor breastfeeding or recurrent abnormal blood sugars, top-up with formula milk to 60 ml/kg/day divided in 3 hrly feeds (8 feeds) by cup (1st choice) or bottle (if baby reluctant to cup feed). • If exclusively artificially feeding, increase artificial milk to 90 ml/kg in 24 h (3 hrly feeds or 8 feeds per day) by cup, bottle or NG tube.						
Time at breast/ amount taken:			Time:		Signature:	
3c • Check blood sugar after 1 h.						
Result:			Time:		Signature:	
If	BM	≥ 2.6	mmols/L	go to step 4 - but continue feeds at prescribed volume		
		< 2.6	mmols/L	inform paediatrician to assess for admission to SCBU		
Paediatric Review (follow algorithm B): Signature:						

Step 4. Blood sugar 2.6 mmol/l and above

4a.

- Aim for demand feeds or at least 3 hourly feeds by breast, if blood sugar checks at regular intervals remain ≥ 2.6 mmol/l.
- If artificially feeding, offer artificial milk at 60 ml/kg in 24 h (3 hrly feeds or 8 feeds per day) by cup or bottle.
- During the next 24 hours monitor pre-feed blood sugars at intervals timed from the first feed after birth (latest 4 h after birth).
- After 24 hours of monitoring, if blood sugar remains ≥ 2.6 mmol/l and above continue demand or at least 3 hourly and discontinue blood sugar monitoring.
- Repeat pre-feed blood sugar after a further 12 hours in infants of diabetic mothers.
- If babies have moved to step 4 from step 3 begin reduction of any topping up after breastfeeds.

Blood sugar check:

	Result	Time	Signature
4 hrs			
7 hrs			
13 hrs			
25 hrs			
37 hrs			

4b.

- All babies moving onto demand breastfeeding should not remain without feeds for > 4 hours.
- When moving onto regular formula feeds 4 hourly give first 4 hourly feed volume at 3 hours, and check blood sugar prior to next 4 hourly feed.

Blood sugar check:

Result		Time		Signature	

- **If 2.6 mmol/l and above, continue demand feeding (no longer than 4 hours without feeds)**

4c.

- If blood sugar < 2.6 mmol/l at any of the above points, return to stage at which baby's blood sugar was stable and discuss with Paediatrician.

OR

- If baby stops feeding, does not tolerate feeds or becomes unwell, inform Paediatrician.

Paediatric Review (follow algorithm B):

Signature:

Observation and Feeding Chart

Date & Time	Type of Feed	Amount taken	Temp.	Comments (e.g. vomiting, nappy changes)

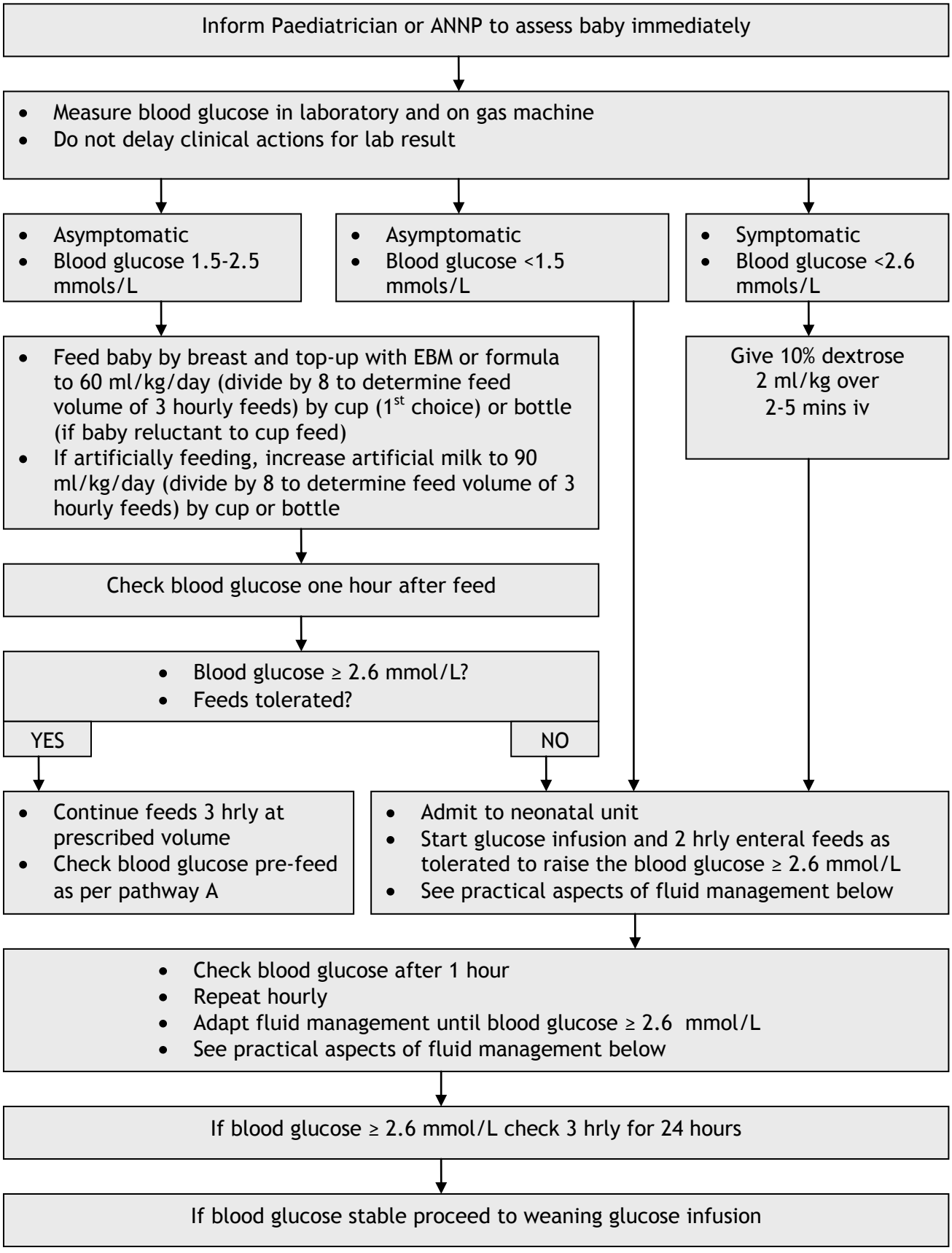
Variances from Pathway:

Date	Step on Pathway (e.g. 3a)	Reason for Variance	Action taken

Signature and date for midwife caring for mum and baby:

Day shift	Night shift

Management of the symptomatic or persistently hypoglycaemic asymptomatic baby (B)



Investigations for hypoglycaemia

- Glucose requirements > 10 mg/kg/min (mostly 12-15 mg/kg/min) are suggestive of an underlying disorder.
- In the case of profound hypoglycaemia (< 1.1mmol/l) or prolonged/repetitive hypoglycaemia despite adequate substrate administration take the following basic diagnostic specimens during a hypoglycaemic episode (during normoglycaemia many disorders can be missed):
  - Blood: FBC, plasma glucose, Na, K, Ca, Mg, creatinine, CRP, LFT, TFT, blood gas, lactate, free-fatty acids, amino-acids, insulin/C-Peptide, GH, Cortisol, ammonia, ketone bodies, acylcarnitines
  - Urine: Ketones, organic acids
  - CSF: Cell count, Protein and Glucose in symptomatic hypoglycaemias, cave GLUT 1 defect can present as normal plasma glucose, but have decreased CSF glucose (CSF/plasma ratio < 0.35)

First interpretation of results

System of disorder	Blood gas	Lactate	Free fatty acids	Urine ketones
Endocrine	Normal	Normal	Normal - decreased	Not increased
Carbohydrate metabolism	Metabolic acidosis	Increased	Normal – (increased)	Normal – (increased)
Amino acid metabolism	Variable	Variable	Increased	Increased
Fatty acid metabolism	Variable	Increased	Increased	Not increased

- Discuss results and further investigations with consultant and/or specialist in Paediatric Endocrinology and/or Inborn Errors of Metabolism.

How to send the samples

Tests	Tube	Blood Volume (ml)	Comments
Glucose and lactate	Grey top, fluoride oxalate	0.6	Please send samples to the lab, on ice, to arrive within 30 minutes of sampling. Ring ext 4782 to say the samples are on their way.
Cortisol and growth hormone	Green top microtainer, no additive	0.6	
Ammonia and ketone bodies	Purple/grey top microtainer, heparin preservative	0.6	
Amino acids and insulin/C-peptide	Green top microtainer, heparin preservative	0.6	
Free fatty acids	Green top microtainer, heparin preservative	0.6	
Acylcarnitines	Guthrie card	Blood spots	Sent to Guys by UNIT staff
Organic acids	Sterile container	2 ml of urine	Sent to Guys by biochemistry lab