Approved by Quality & Patient Safety Committee
21 February 2013

HYPOGLYCAEMIA IN A NEONATE – MONITORING AND MANAGEMENT OF AT RISK NEONATES

This LOP is developed to guide clinical practice at the Newborn Care Centre, Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this LOP.

This LOP has been developed in partnership with obstetric physician, and Endocrine and Metabolic Teams Sydney Children's Hospital

1. AIM

- Early identification of at risk neonates, timely investigations and interventions for hypoglycaemia among neonates

2. PATIENT

- Neonates

3. STAFF

- Registered Midwives
- Student Midwives
- Registered Nurses
- Medical Staff

4. EQUIPMENT

- Glucometer
- Blood gas and electrolyte analyser with incorporated electrochemical glucose biosensors

5. CLINICAL PRACTICE

- Identify the at-risk neonates: Neonates of diabetic mothers, late preterm (34^0-36^6 weeks), small for gestational age (SGA- birth weight less than 10^{th} percentile), large for gestational age (LGA – birth weight greater than 97^{th} percentile – or 4500 g at term)
- Determine if diabetes in mother is poorly controlled (as assessed by the obstetric team, physician/endocrinologist or by elevated fructosamine or HbA_1C ≥6.5%, or elevated maternal BGL>8mmol/L at delivery). Refer to maternal diabetes care plan

At delivery:

- Commence skin-to-skin contact between the mother and her baby as soon as possible after birth
- Commence breast feeding within half an hour of birth.
- Check if the neonate fits the admission criteria ti NICU: Poorly controlled diabetes in mother (as defined above) and/or symptomatic hypoglycaemia
- Monitor the neonate for any clinical symptoms of hypoglycaemia (examples: jitteriness, lethargy, floppiness, central cyanosis, apnoea, poor feeding and seizures):
  - **If no symptoms/signs**, perform the first blood glucose level (BGL) (heel prick using the glucometer) **around 2 hours of age** and follow the **clinical pathway (Appendix A)**
  - **If symptomatic,** perform the first BGL (heel prick using the glucometer) **immediately** and if confirmed (BGL<2.6mmol/L), admit to Newborn care centre (NCC) and follow the **clinical pathway (Appendix B)**

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Ongoing monitoring:

- Monitor at-risk neonates for at least the first 24 hours of life **as per clinical pathway (Appendix A)**
- Continue monitoring until the neonate's BGLs remain at safe levels (≥2.6mmol/L) for at least 24 hours after the last episode of hypoglycaemia, **as per clinical pathway (Appendix A)**
- Determine if the neonate has resistant, recurrent or unexplained hypoglycaemia:
  - **Resistant Hypoglycaemia:** hypoglycaemia requiring infusions of large amounts of glucose (>12 mg/kg/min) to maintain normal BGLs
  - **Recurrent hypoglycaemia**: recurrent hypoglycaemia (if persisting beyond the first few days of life)
  - **Unexplained hypoglycaemia:** hypoglycaemia without recognised predisposing factors such as neonates of diabetic mothers, small or large for gestational age
- Consult endocrine team at Sydney Children's Hospital urgently and consider the **clinical pathway (Appendix C)** for the management. However, remember that clinical pathway (Appendix C) is only a suggested pathway and may vary based on the underlying aetiology and the response of the neonate
- Refer to Appendices D and E for a quick guide on the glucose infusion rates and the list of investigations and relevant sampling for resistant or persistent hypoglycaemia

6. DOCUMENTATION

- Integrated Clinical Notes
- Neonatal Medication chart
- Standard Neonatal Observation Chart.
- Maternal Diabetes Care Plan

7. EDUCATIONAL NOTES

- Blood glucose concentrations reach a nadir in healthy neonates around 1 to 2 hours after birth; and stabilise by 3 to 4 hours. Healthy neonates compensate for "physiologic" hypoglycaemia by producing and using alternative fuels including ketone bodies, lactate and free fatty acids
- Preterm and small for gestation neonates have limited metabolic capacity for production of these alternative fuels
- Neonates of diabetic mothers (IDM) are hyperinsulinaemic which prevents production of alternative fuels
- A widely used cut-off for neonatal hypoglycaemia is <2.6mmol/L
- Abnormal brain stem and somato-sensory evoked potentials, and abnormalities in MRI and brain ultrasounds may be demonstrated in some neonates with BGLs below this level. Furthermore, preterm neonates with recurrent BGL readings less than this level were found to have adverse neurodevelopmental outcomes at 18 months of age. These differences in developmental outcomes were no longer discernible when the children were assessed at 8 years of age
- Portable glucometer test-strip results demonstrate a reasonable correlation with actual plasma glucose concentrations, but the variation from the actual level may be as much as 0.5 to 1.1mmol/L (or 15-20%). This variation is greatest at low glucose concentrations.

ROYAL HOSPITAL FOR WOMEN

LOCAL OPERATING PROCEDURE

CLINICAL POLICIES, PROCEDURES & GUIDELINES

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HYPOGLYCAEMIA IN A NEONATE – MONITORING AND MANAGEMENT OF AT RISK NEONATES cont'd

8. RELATED POLICIES / PROCEDURES / CLINICAL PRACTICE LOP

- Diabetes in pregnancy service LOP
- Obesity in pregnancy, labour and postpartum guideline

9. REFERENCES

1 Adamkin DH, and COMMITTEE ON FETUS AND NEWBORN. Postnatal glucose homeostasis in late-preterm and term neonates. Pediatrics. 2011;127(3):575-9. Epub 2011 Feb 28.
**Current AAP neonatal hypoglycaemia management guideline

2 Alkalay AL, Sarnat HB, Flores-Sarnat L, Elashoff JD, Farber SJ et al. Population meta-analysis of low plasma glucose thresholds in full-term normal newborns. Am J Perinatol. 2006;23(2):115-9.
** First population meta-analysis of low plasma glucose thresholds in full term normal newborn neonates.

3 Arnoux JB, Verkarre V, Saint-Martin C, Montravers F, Brassier A et al. Congenital hyperinsulinism: current trends in diagnosis and therapy. Orphanet J Rare Dis. 2011;6:63.

4 Aynsley-Green A, Polak JM, Bloom SR, Gough MH, Keeling J et al. Nesidioblastosis of the pancreas: definition of the syndrome and the management of the severe neonatal hyperinsulinaemic hypoglycaemia. Arch Dis Child. 1981;56(7):496-508.

5 Bolisetty S, Panaretto K, Patole S, Koh THHG, Tan YM et al. Maternal and neonatal characteristics of diabetes during pregnancy among non-indigenous and indigenous population of Australia. Presented at Fourth Annual Congress of the Perinatal Society of Australia and New Zealand, Brisbane, March 2000.

6 Bolisetty S, Koh THHG, Tan YM, Panaretto K, Whitehall JS. Evaluation of clinical outcomes of neonates of diabetic mothers in a regional perinatal centre. Presented at Fourth Annual Congress of the Perinatal Society of Australia and New Zealand, Brisbane, March 2000.
**This study indicates that most of neonates of diabetic mothers except pre-existing diabetes type 1 can largely be managed with breast and supplementary feeding.

7 Carter PE, Lloyd DJ, Duffty P. Glucagon for hypoglycaemia in neonates small for gestational age. Arch Dis Child. 1988;63(10):1264-6.

8 Charsha DS, McKinley PS, Whitfield JM. Glucagon infusion for treatment of hypoglycemia: efficacy and safety in sick, preterm neonates. Pediatrics. 2003;111(1):220-1.

9 Cheung NW. The Australian Diabetic Society. Australian Diabetes Society Position Statement: Individualization of HbA1c Targets for Adults with Diabetes Mellitus, 2009.

10 Cornblath M, Hawdon JM, Williams AF, Aynsley-Green A, Ward-Platt MP et al. Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds. Pediatrics. 2000;105(5):1141-5.
**First detailed account making pragmatic recommendations for operational threshold for treatment of hypoglycaemia in different subgroups of newborn neonates.

11 Diderholm B. Perinatal energy metabolism with reference to IUGR & SGA: studies in pregnant women & newborn neonates. Indian J Med Res. 2009;130(5):612-7.

12 Kalhan SC, Savin SM, Adam PAJ. Measurement of glucose turnover in the human newborn with glucose-1-13C. J Clin Endocrinol Metab 1976;43:704e7.

13 Harris DL, Weston PJ, Battin MR, Harding JE. Randomised Trial of Dextrose Gel for Treating Neonatal Hypoglycaemia: The Sugar Babies Study. Pediatric Research. 2011; 70, 652–652; doi:10.1038/pr.2011.877

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14 Hawdon JM, Ward Platt MP, Aynsley-Green A. Patterns of metabolic adaptation for preterm and term neonates in the first neonatal week. Arch Dis Child. 1992;67(4 Spec No):357-65
**A cross sectional study was performed of 156 term neonates and 62 preterm neonates to establish the normal ranges and interrelationships of blood glucose and intermediary metabolites in the first postnatal week, and to compare these with those of 52 older children
15 Hussain K. Investigations for neonatal hypoglycaemia. Clin Biochem. 2011;44(7):465-6.
16 Koh TH, Aynsley-Green A, Tarbit M, Eyre JA. Neural dysfunction during hypoglycaemia. Arch Dis Child. 1988;63(11):1353-8
*Study assessing sensory evoked potentials in relation to glucose level to establish glucose level causing neural dysfunction
17 Lilien LD, Pildes RS, Srinivasan G, Voora S, Yeh TF. Treatment of neonatal hypoglycemia with minibolus and intraveous glucose infusion. J Pediatr. 1980;97(2):295-8
*A study describing effect of glucose minibolus prior to continuous intravenous glucose infusion
18 Lucas A, Morley R, Cole TJ. Adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia. BMJ. 1988;297(6659):1304-8.
**First description defining a glucose level in relation to adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia in newborn neonates
19 Marles SL, Casiro OG. Persistent neonatal hypoglycemia: Diagnosis and management. Paediatr Child Health. 1998;3(1):16-9.
20 NSW Health Western Sydney Local Health District. Hypoglycaemia Management-Newborn Neonate. Westmead Hospital, Centre for Newborn Care Guidelines. [Internet] 2010. [Revised: August 2011]. [Accessed May 12, 2012].
21 Queensland Health. Neonatal hypoglycaemia and blood glucose level monitoring. Queensland Maternity and Neonatal Clinical Guideline. [Internet] 2010 Feb. Available from: http://www.health.qld.gov.au/qcg [Accessed May 12, 2012]
** Comprehensive neonatal hypoglycaemia management protocol with available evidence
22 Srinivasan G, Pildes RS, Cattamanchi G, Voora S, Lillen LD. Plasma glucose values in normal neonates: a new look. J Pediatr 1986;109:114e7
** First prospective study attempting to establish normal blood sugar level in healthy full term newborn neonates
23 Taylor R, Lee C, Kyne-Grzebalski D, Marshall SM, Davison JM. Clinical outcomes of pregnancy in women with type 1 diabetes(1). Obstet Gynecol. 2002;99(4):537-41

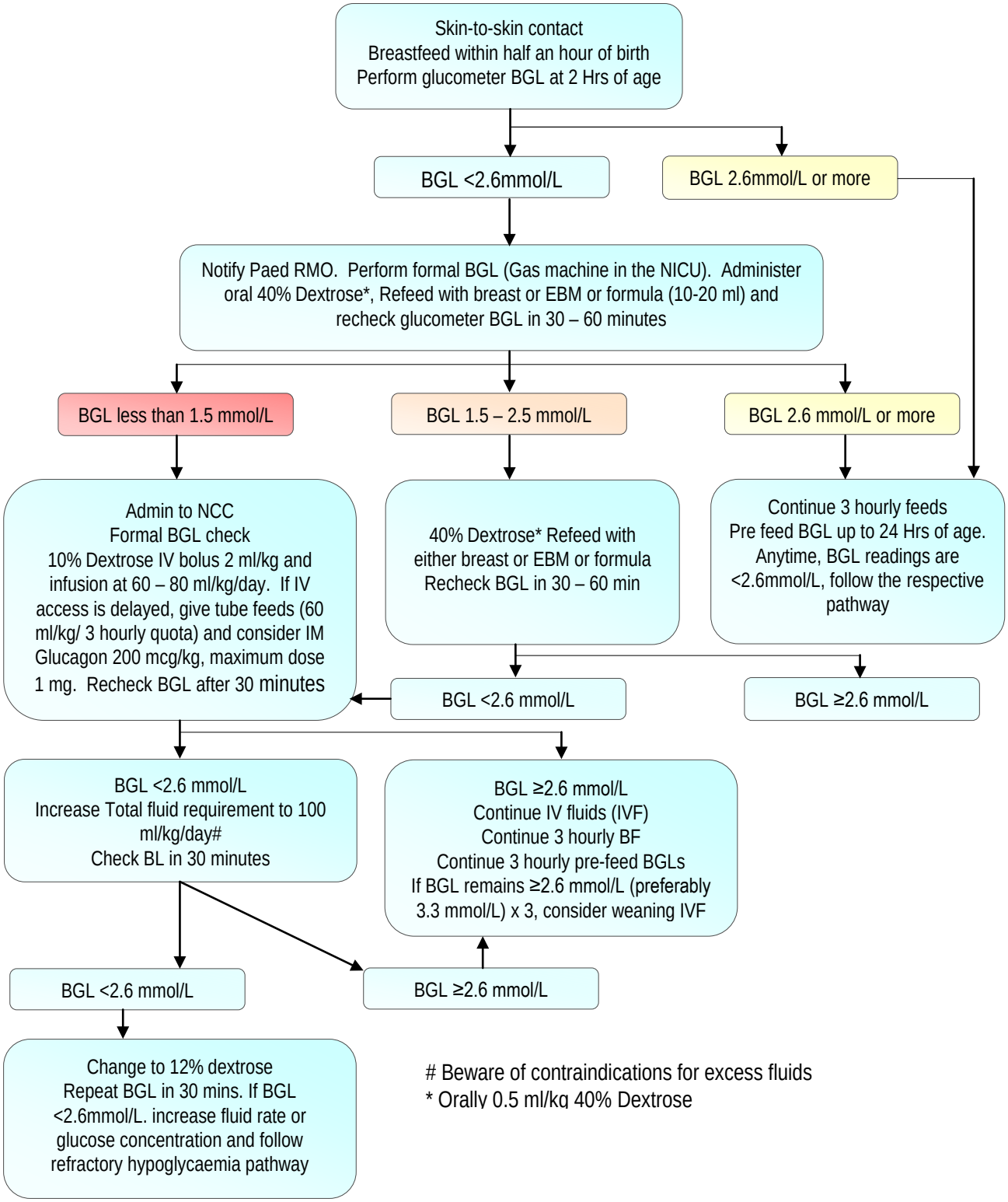
REVISION & APPROVAL HISTORY

Minor amendment July 2013
Endorsed Therapeutic & Drug Utilisation Committee 19/2/13 and Maternity Services LOPs Feb 2013
Replacing '*Postnatal Ward Management of Term Infants at risk of Hypoglycaemia'*
Endorsed Neonatal Clinical Committee 8/2/05, Approved Quality Council 21/2/05

…../Appendix A - E

APPENDIX 'A'

Asymptomatic neonates at risk of Hypoglycaemia
(Maternal diabetes, late preterm 34 – 36+6/40, Term SGA and LGA infants)



Beware of contraindications for excess fluids
* Orally 0.5 ml/kg 40% Dextrose

APPENDIX ‘B’

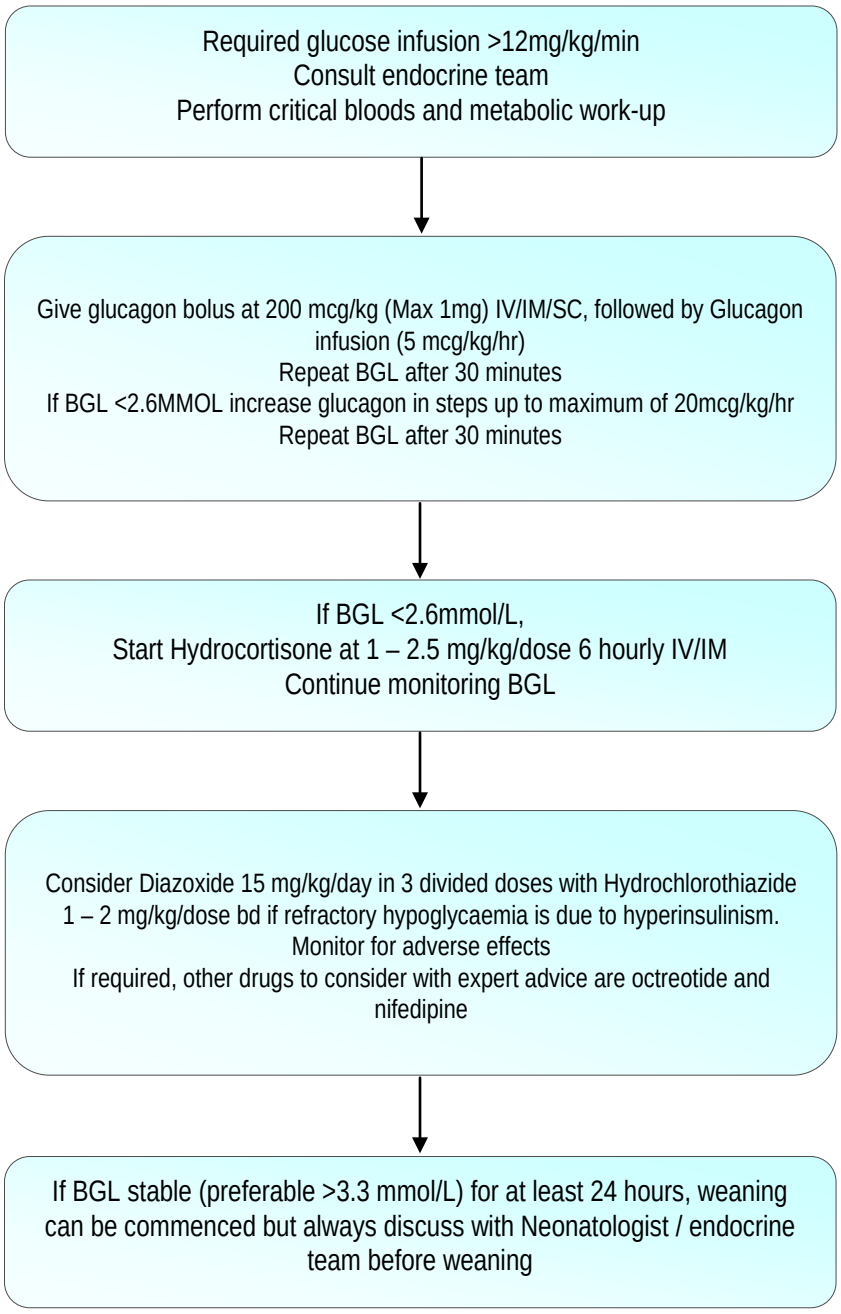
Symptomatic Hypoglycaemia*

Urgently check formal BGL
Administer 40% dextrose if oral solution allowed
Insert cannula, give 10% Dextrose IV bolus at 2ml/kg and commence IV
Dextrose infusion at age appropriate fluid rate
Repeat BGL after 30 minutes

* Symptomatic hypoglycaemia : Defined as symptoms including irritability, tremors, exaggerated Moro reflex, high-pitch cry, seizures, lethargy, floppiness cyanosis, apnea and poor feeding with a corresponding BGL of <2.6mmol/L

APPENDIX 'C'

Refractory Hypoglycaemia*



* Refractory Hypoglycaemia is defined as Hypoglycaemia requiring infusions of a large amount of glucose (>12 mg/kg/min) to maintain normoglycaemia

APPENDIX 'D'

Values of different dextrose concentrations and infusion rates for glucose infusion

Table 1 : Preparation of higher dextrose concentration fluid for 100ml burette

ADD THE VOLUME OF 50% DEXTROSE TO THE VOLUME OF 10% DEXTROSE TO MAKE UP A TOTAL OF 100 ML		
DESIRED DEXTROSE CONC.	VOLUME OF 10% DEXTROSE	VOLUME OF 50% DEXTROSE
12%	95 ml	5 ml
14%	90 ml	10 ml
16%	85 ml	15 ml
18%	80 ml	20 ml
20%	75 ml	25 ml

Table 2 : Glucose infusion rate in mg/kg/min by dextrose infusion rate in ml/kg/day with different dextrose strengths

GLUCOSE INFUSION	DEXTROSE STRENGTH WITH INFUSION RATE IN ML/KG/DAY			
mg/kg/min	10%	12.5%	15%	20%
5	72	58	48	36
6	86	69	58	43
7	101	81	67	50
8	115	92	77	58
9	130	104	86	65
10	144	115	96	72
11	158	127	106	79
12	173	138	115	86
13	187	150	125	94
14	202	161	134	101
15	216	173	144	108
16	230	184	154	115
17	245	196	163	122
18	259	207	173	130
19	274	219	182	137
20	292	230	192	146

Formula for calculating glucose infusion rate in mg/kg/min

$$\text{Glucose infusion rate (mg/kg/min)} = \frac{\text{Dextrose concentration} \times \text{Vol. infused in ml/kg/day}}{144}$$

APPENDIX 'E'

List of investigations and relevant sampling for resistant or persistent hypoglycaemia

NO	TEST	AMOUNT	CONTAINER	SAMPLE
A.	**INVESTIGATIONS THAT ARE MORE RELIABLE WHEN THE FORMAL BLOOD GLUCOSE <**			
1	Insulin, Cortisol, and Growth Hormone	1300 uL	Gold	Serum
2	Plasma Ketones #	200 uL	Grey	Plasma
3	Blood Lactate #	300 uL	Grey	Plasma
4	Urine for a metabolic screen to include ketones, amino acids, organic acids and acylcarnitine	10 ml	Sterile Yellow Urine Jar	Urine
5	Urine Ketones		Clinistix	
6	Urine for reducing substances*	5 ml	Yellow Urine Jar	Urine
B.	**CONSIDER FURTHER INVESTIGATIONS**			
1	Capillary gas		Capillary tube	Blood
2	Carnitine#	250 uL	Dark Green	Plasma
3	Aspirate aminotransferase (AST)	100 uL	Gold	Serum
4	Alanine aminotransferase (ALT)	100 uL	Gold	Serum
5	Uric acid	200 uL	Gold	Serum
6	Lactic acid#	300 uL	Grey	Plasma
7	Plasma amino acids #	250 uL	Dark Green	Plasma
8	Creatine kinase (CK)	100 uL	Gold	Serum
9	Ammonia#	500 uL	Purple	Plasma
10	Acylcarnitine profile#	250 uL	Dark Green	Blood
11	DNA for MCAD mutation	3 ml	Purple	Blood
	The last two investigations can be done from the neonatal screening blood spots.			
C.	**OTHERS**			
1	Ophthalmic examination			
2	Cranial ultrasound scan and/or MRI (specifically requesting pituitary views)			

Specimens that need to go on ICE
* Specimen needs to send to laboratory within 30 minutes