UHL Neonatal Guideline for the planning and management of newborn infants born to a family affected with Medium chain acyl-CoA dehydrogenase deficiency (MCADD).

University Hospitals of Leicester NHS
NHS Trust

Trust ref C4/2014

Contents

1. Introduction and Who Guideline applies to

This guidance is intended for those health professionals in Leicester who may be involved with families where there is a known history of MCADD. It has been developed in conjunction with

the Metabolic Service at Sheffield Children's NHS Foundation Trust who work jointly with the Children's Metabolic Team in Leicester in the management of families affected with MCADD.

The aim of this guidance is to ensure adequate information about the risk of MCADD in a subsequent pregnancy at risk of MCADD, and that guidance for the management of the newborn baby is in place before the baby is born. This includes the referral of families with a significant risk of MCADD to the Genetics Services for assessment of the inheritance risk to the unborn baby (the process of referral is described in Appendix 3).

This guidance also relates to the actions required by the Paediatric Metabolic Team in Leicester when informed that the mother of an MCADD affected child is pregnant. Knowledge of the pregnancy may be passed to the Metabolic Team by the family themselves, the GP, the Midwifery Services or the Obstetric Team, or by a Paediatric Team providing care to the affected child. Also included is the information that should be given to the parents and the GP at the time of diagnosis of the affected child.

Key Points

- MCADD is an inherited metabolic disease affecting around 1 in 10,000 infants
- Episodes of decompensation are provoked by prolonged fasting or intercurrent illness with associated poor feeding and vomiting.
- Infants with MCADD are especially liable to episodes of metabolic decompensation in the first few days of life because of poor feeding or inadequate milk supply
- It is recommended that each baby born to a mother who has previously had a child affected with MCADD is managed as if they have the condition until test results for MCADD are available.
- Testing of these babies for MCADD should be undertaken on day 2 of life.
- Formula containing medium chain triglycerides should never be used for infants with, or 'at risk' of MCADD.
- A preterm baby requiring parental nutrition should not be given SMOF lipid a this contains medium chain triglycerides.

2. Guideline Standards and Procedures

2.1 Background:

MCADD is an inherited metabolic disease which affects approximately 1 in 10,000 infants born in England. Without treatment affected children are at risk of life- threatening metabolic decompensation presenting with hypoglycaemia and encephalopathy. Mortality of the condition has been reported as up to 25%, with significant risk of neurodisability amongst those surviving episodes.

Episodes of decompensation are provoked by prolonged fasting or intercurrent illness with associated poor feeding and vomiting. Treatment consists of avoiding fasting and providing high carbohydrate drinks in appropriate quantities at the time of intercurrent illness. With treatment, outcome is excellent with minimal mortality and morbidity.

Newborn infants with MCADD are especially liable to episodes of metabolic decompensation which may present as sudden death. This is because new-born infants may not feed well in the first few days of life, and those who are breast fed may not have sufficient breast milk available to them before the mother's milk supply 'comes in.'

All newborn infants born in England are screened for MCADD as part of the Newborn Bloodspot Screening Programme. Blood samples are taken on day five of life. Results for MCADD screening are available by day 14 and babies are seen by a Paediatrician experienced in MCADD within 48 hours. Treatment is started immediately at the first visit whilst awaiting confirmatory test results.

Infants with MCADD are therefore not detected until up to 14 days of age and are at risk of metabolic decompensation during this period, until the screening result is available and the baby is referred.

Parents who have a child affected with MCADD will have a 1 in 4 chance that each subsequent pregnancy will be affected. If the mother of an affected child has a child with a new partner, the risk of the pregnancy being affected with MCADD is approximately 1in 200. The risk of being affected with MCADD is therefore much greater than that of the general population (1in 10,000). In order to manage the increased risk, it is recommended that each baby born to a mother who has previously had a child affected with MCADD is managed as if they have the condition until test results for MCADD are available. Testing of 'at risk' babies for MCADD should be undertaken on day 2 of life.

Opportunities to provide information to the maternity unit are at any time during pregnancy when there is interaction with healthcare professionals.

These are:

- GP
- Local Paediatric Metabolic team based at Leicester Royal Infirmary
- Metabolic Team at Sheffield Children's NHS Foundation Trust
- Midwifery Team
- Obstetric Team

Information given to the parents at the time of diagnosis of an MCADD affected child.

The risk of a subsequent child being affected with MCADD should be explained to the parents. Early testing of subsequent children should be explained together with the need for treatment until results are available. It should be explained that if a further pregnancy is embarked upon, the parents should inform the Metabolic Team as soon as possible.

Written information will be given to the parents at the time their child is diagnosed with MCADD a copy will also be sent to the GP. A standard letter is found in Appendix 1.

2.2 Family history of MCADD be discussed at the booking appointment with the Midwife.

- All hand-held notes should be sent into the Consultant Unit where the woman has chosen to give birth for review and risk assessment by the Antenatal Core Midwives.
- All women with a family history of MCADD but not a first degree relative should be

contacted by the Core Midwife and a referral made to the Genetics Department in order to ascertain the risk of inheritance.
- The Newborn Screening Coordinator should be informed of all women with a family history of MCADD in a first degree relative by the Antenatal core Midwife. They should then refer the woman to the Consultant Metabolic Paediatrician by email or telephone (Appendix 3)

2.3 Pregnant women who have a child affected with MCADD should be referred to the Paediatric Specialist Metabolic Team.

- The New-born Screening Coordinator should be informed of all women with a previous child affected with MCADD by the Antenatal Core Midwives.
- The New-born Screening Coordinator should refer these women to the Consultant Metabolic Paediatrician by email or telephone.

2.4 Actions to be taken by the Paediatric Metabolic Team when informed of a pregnancy at risk of MCADD.

- The Paediatric Metabolic Consultant should write to the caring Obstetrician and the Lead Paediatrician for Neonates at the Maternity Unit where the baby is expected to be born (see Appendix 2).
- The Metabolic Team at Sheffield should be informed by the Paediatric Metabolic Consultant.
- The maternity unit should be informed that the baby is at high risk of being affected with MCADD and that they should be treated as if affected until the results of definitive testing as available.
- Babies known to be at high risk of MCADD should be delivered in a Consultant led Obstetric Unit - either the Leicester Royal Infirmary or the Leicester General Hospital
- Guidance on feeding should be provided and the actions to be taken in the event of failure to tolerate feeds (Section 3.2)

The baby should not be discharged until it is certain that adequate feeding is established.

2.5 Children suspected of having MCADD as a result of new-born screening or clinical presentation should be seen by the Paediatric Metabolic Team in the Children's Hospital at the Leicester Royal Infirmary

- During the initial referral, the inheritance pattern of MCADD will be explained to parents. They will be informed that any further pregnancy will have a 1in 4 chance of being affected with MCADD and that if the parents have another child, arrangements will be made to offer an early rapid test for MCADD on day 2. This is in addition to the standard new-born screening on day 5. The baby will be treated as if affected with MCADD until the result of the test is known.
- Those diagnosed with MCADD will be offered ongoing treatment and review by the Paediatric Metabolic Team.
- Following referral to the Paediatric Metabolic Team families will be given written information about MCADD and treatment is initiated.
- Once the diagnosis is confirmed, outpatient review is arranged at 3, 6, 9 and 12 months

of age and then every 6 months until age 16 when referral is made on to an adult metabolic service.
- At subsequent clinic visits, there is an opportunity to determine if any further pregnancies are planned or have been embarked upon, which would allow communication of the plan for early testing at the family's maternity unit and the need for treatment of the baby until results are available. If a further pregnancy is embarked upon, the parents should inform the Paediatric Metabolic Team as soon as possible.
- Written information should be given to the parents and their GP (Appendix 1).

2.6 Information provision

Provide the parents with information;

- At the time of the diagnosis of the proband.
- At routine follow up clinic visits.
- During antenatal care.

Provide information to the maternity unit at any time during pregnancy when there is interaction with health care professionals;

- By the GP
- By the local Paediatric Metabolic Team based at the Leicester Royal Infirmary
- By the Metabolic Team at Sheffield Children's HNS Foundation Trust
- By the Midwifery Team
- By the Obstetric team

3. Recommendations for the management of a newborn baby at risk of MCADD.

MANAGEMENT OF NEWBORN BABIES WITH A FAMILY HISTORY OF MEDIUM CHAIN ACYL-CoA DEHYDROGENASE DEFICIENCY

Medium-chain acyl-CoA dehydrogenase deficiency (MCADD) is an inherited disorder of fat breakdown and one of the most common inherited disorders of metabolism.
With a regular dietary intake, individuals can live a normal healthy life, but prolonged fasting or illnesses with vomiting can lead to encephalopathy, coma or sudden death. The disease affects about 1 in 10,000 babies born in the UK. If both parents are MCADD carriers as in this family's case, there is a 1 in 4 chance of their child being born with MCADD.

In the first 2-3 days of life, when regular feeding is not fully established, newborn babies are heavily dependent on fat metabolism for their energy needs and those with MCADD are especially vulnerable to early neonatal death.

All babies with a family history of MCADD should be treated as having MCADD until it is established whether they are affected or not.

3.1 Early testing

A baby with a family history of MCADD should have rapid testing 24 to 48 hours after birth. Samples should be sent as follows:

- Plasma (1ml lithium heparin sample) for C8 and acylcarnitines
- Urine (plain tube) for organic acids
- Four blood spots on a blood spot card marked 'Family history of MCADD'.

Samples should be sent to the UHL Biochemistry department who will process them and forward them to Sheffield for analysing.

The request form should be completed and in addition state:
'Family history of MCADD'. Please report results to ***name*** (insert name of Paediatric Consultant responsible for metabolic disorders in Leicester - currently Dr Jo Forster) as well as name of consultant neonatologist the child is born under).

The metabolic section of the Clinical Chemistry laboratory at Sheffield Children's Hospital should also be informed (0114 271 7445) to expect the sample.

3.2 Dietary management

Prior to confirmed diagnosis it is essential to ensure that the baby maintains a good milk intake. Fasting can result in the accumulation of toxic fatty acids.
Hypoglycaemia also occurs, but only at a relatively late stage so it is not safe to base the management on monitoring of blood glucose. Normal blood sugars are not to be relied on as an indication of well-being, thus blood sugar testing is not routinely recommended. Attention should be paid to the adequacy of feeding, as this will prevent decompensation.

The aim of treatment is to provide an alternative energy substrate and inhibit mobilisation of fatty acids by providing an ample glucose supply, enterally or intravenously.

Bottle fed baby:

A new-born term baby should be fed at least every 3 hours using a normal infant formula. A preterm infant may need to be fed at least every 2 hours (likely to require admission to the neonatal unit). Formula containing medium chain triglycerides should never be used. Feed volumes should be gradually increased during the first week from 60ml/kg on day 1, to 150ml/kg by day 6-7 but ideally as quickly as possible. A guide to feed volumes is given in Table 1 with more detailed calculations in Appendix 4A.

Table 1: Suggested feed volumes for bottle fed babies.

(Please note that the baby may feed greater than the suggested volumes so that feeds are built up more quickly).

Day 1 Approx. 60ml/kg
Day 2 Approx. 70ml/kg
Day 3 Approx. 90ml/kg
Day 4 Approx. 110ml/kg
Day 5 Approx. 130ml/kg
Day 6 Approx. 150ml/kg

*If the target volumes are not taken or not tolerated e.g. vomiting:

1) Try giving smaller, more frequent feeds e.g. 2 hourly instead of 3 hourly

2) Try reducing the volumes slightly observing carefully
3) If target volumes are still not met then a nasogastric tube should be passed and the bottle feeds topped up to the target volumes.
4) If infant formula is not tolerated orally or via nasogastric tube, then use 10% glucose polymer solution – see Table 3.

If the baby fails to tolerate 10% glucose polymer by nasogastric tube, intravenous therapy should be commenced.
Once the medical team is happy that the baby is feeding normally the baby can go home. The parents should have clear instructions to return to hospital if feeding is poor.

Breast fed baby:

Breast fed babies in particular are more at risk in the first 72 hours when the supply of breast milk is poor, and feeding is not established. Top-up bottle feeds or cup feeds of infant formula are advised for the first 3 complete days (72 hours). Some mothers may wish to try to and express milk for top-up feeds.

The baby should be allowed to breast feed for at least 10 minutes and observed to check that he/she has latched on well and has a slow rhythmical suck and swallow (i.e. good technique). The baby should then be offered a top up bottle feed using expressed breast milk or infant formula (or 10% glucose polymer solution if parents prefer) (Table 2, more detailed calculations in Appendix 4B).

Table 2: Suggested feed volumes for breast fed babies
– guide to target top-up volumes for first 72 hours.

Day 1 Approx. top up: 25ml/kg
Day 2 Approx. top up: 40ml/kg
Day 3 Approx. top up: 60ml/kg

If there is any doubt about the adequacy of the breast feed and the top up bottle is refused, then a nasogastric feed tube should be passed & the feed volumes given as for a bottle-fed baby above.
If infant formula or breast milk is not tolerated orally or via nasogastric tube, even after trying 2 hourly feeds, then use 10% glucose polymer solution:

If the baby fails to tolerate 10% glucose polymer by nasogastric tube, intravenous therapy should be commenced (see below).

Table 3: Glucose polymer products to make 10% solution

Polycal® (Nutricia)	10g - 2 level x 5g scoops (provided) made up to 100ml with cool boiled water or sterile water
S.O.S® (Vitaflo)	Make up contents of S.O.S 10 sachet to 200ml with cool boiled water or sterile water

3.3 Intravenous therapy

If enteral feeds are not tolerated, start an intravenous infusion of 10% glucose (or 10% glucose with additives as per unit policy) at 100 ml/kg/day. 1. If there is no oral intake, the volume should be increased over 3 days to 150 ml/kg/d.

If the baby seems drowsy or unwell in any other way, transfer to the neonatal unit urgently and give an intravenous bolus of 2 ml/kg 10% glucose followed by an infusion of glucose 10% (or 10% glucose with additives) at 100 ml/kg/day. If there is no oral intake, the volume should be increased over 3 days to 150 ml/kg/d. Monitor blood glucose and plasma electrolytes but base treatment on the clinical state (since hypoglycaemia occurs at a late stage, see above).

SMOF lipid should not be given if parental nutrition is required (MCT content is contraindicated).

3.4 Discharge planning

A judgement should be made on the child's feeding ability before considering discharge, with the parents having clear instructions to return to hospital if feeding is poor. The paediatrician responsible for the metabolic service in Leicester should be involved in any management plans and certainly in any discharge plans. The feeding regime should be kept in place until the results of definitive MCADD testing are available. At this time parents should be contacted (either by the local team or the metabolic team based at Sheffield Children's Hospital) to inform them of the result and advise on subsequent management.

Prior to discharge parents should be made aware of local arrangements for dealing with medical emergencies. Patients in Leicester should be brought to the Children's Emergency Department at Leicester Royal Infirmary should the baby become unwell or is not feeding. The parents will be contacted with the test results and be given appropriate follow-up appointments where appropriate.

If MCADD is confirmed by the Clinical Chemistry Laboratory at Sheffield Children's Hospital the baby and its parents will be seen by the Paediatric Metabolic Team at Leicester Royal Infirmary. They will arrange emergency regimens for home.

4. Education and Training

None

5. Audit Criteria

1. A significant family history of MCADD is identified in all cases. Every family who have the history of MCCAD the future pregnancy should be monitored and clear should be made before delivery. (100%).
2. Early testing is carried out as indicated above on day 2 (100%).

6. Supporting References

- National Patient Safety Agency Rapid Response Report NPSA 2011 RRR002 'Keeping

newborn babies with a family history of MCADD safe in the first hours and days of life'

- **http://www.bimdg.org.uk/site/guidelines.asp**
- MCAD Deficiency: Management of newborn babies with a family history.
- https://www.bimdg.org.uk/store/guidelines/MCADD_Dietary_BIMDG_babies_2015v0_7_742847_13052015.pdf
- MCAD Deficiency Guidelines https://www.bimdg.org.uk/store/enbs//MCADD_clinical_management_guidelines_2017_294592_14092017.pdf

7. Key Words

Feeding, Genetics, Medium chain triglycerides, Metabolic, Metabolic Decompensation, Newborn Bloodspot Screening, Pregnancy

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

EDI Statement

We are fully committed to being an inclusive employer and oppose all forms of unlawful or unfair discrimination, bullying, harassment and victimisation.

It is our legal and moral duty to provide equity in employment and service delivery to all and to prevent and act upon any forms of discrimination to all people of protected characteristic: Age, Disability (physical, mental and long-term health conditions), Sex, Gender reassignment, Marriage and Civil Partnership, Sexual orientation, Pregnancy and Maternity, Race (including nationality, ethnicity and colour), Religion or Belief, and beyond.

We are also committed to the principles in respect of social deprivation and health inequalities.

Our aim is to create an environment where all staff are able to contribute, develop and progress based on their ability, competence and performance. We recognise that some staff may require specific initiatives and/or assistance to progress and develop within the organisation.

We are also committed to delivering services that ensure our patients are cared for, comfortable and as far as possible meet their individual needs.

Contact and review details			
Guideline Lead (Name and Title) Moira French - Senior Specialist Paediatric Dietitian Dr J Forster – Paediatric Consultant		**Executive Lead** Chief medical officer	
Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
April 2012	**1**	Original guideline (Maternity and AEC)	
Nov 2018 – Jan 2019	**2**	Reviewed by new author (MF) Neonatal Guidelines Meeting Neonatal Governance Meeting	– minor amendments suggested - **Approved**
Nov 2021- Dec 2021	**3**	Reviewed by author MF Neonatal Guideline and Governance Meeting	• Day 1 feeding volumes for bottle fed babies increased from 50ml/kg to 60ml/kg and ranges of weight specific day 1 volumes per feed increased in line with this • Maxjul & Vitajoule removed as glucose polymer products options • Added 'cooled boiled water' as an option to when making up glucose polymer solutions • References updated • Format updated - Approved
January 2025	**4**	Reviewed by author JF Neonatal Guideline and Governance Meeting	• No changes

Appendix 1: Standard letter to the parents and GP of a child affected with MCADD at the time of diagnosis.

Your new baby, ***name*** has the condition Medium chain acyl-CoA dehydrogenase deficiency (MCADD). The Metabolic Team have explained how this is an inherited condition and how the condition is treated. The team have explained that with these simple treatment measures your baby will grow up entirely normally and be able to do all the things other children can do.

Any further babies you have will have a one in four chance of having MCADD. It is important that if you have any further babies, we ensure that the baby feeds well and takes an adequate amount of milk in the days after birth to prevent them becoming ill should they have MCADD. A special blood and urine test can be performed on the second day of life to find out if the new baby has MCADD. The results of these tests will be available sooner than the results of the routine new-born screening test.
These tests are in addition to the usual bloodspot screening test carried out on day five.

To make sure that all the necessary measures can be put in place for any further babies you have, it is important that the hospital where you are to have the baby knows that there is a high chance of the baby having MCADD. If you let any member of the Paediatric Metabolic Team in Leicester know that you are pregnant, we will arrange to pass the information about MCADD in new babies onto the hospital where you are planning to have the baby. It will be very helpful if you can tell us the name of the obstetrician who is caring for you during the pregnancy, and also what your expected date of delivery is. You should also make sure that your midwife is aware that you have had a child with MCADD and that your next baby has an increased chance of having MCADD.

Your GP may also wish to inform me of any further pregnancies and your arrangements for the birth.

Yours sincerely,

Consultant Paediatrician with an Interest in Metabolic Disease

Copy to GP

Appendix 2: Letter to obstetric and neonatal staff of the University Hospitals of Leicester/ Maternity Service where baby at risk of MCADD is to be delivered.

This letter may also be used to alert obstetric and neonatal teams at out of area hospitals where a baby at risk of MCADD is to be delivered.

Name has a child affected with the inherited metabolic disease Medium chain acyl- CoA dehydrogenase deficiency (MCADD). She is again pregnant with delivery expected on ***date***. If affected with MCADD the baby is at high risk of metabolic decompensation in the newborn period, usually secondary to inadequate intake of milk. The baby should be treated as if affected with MCADD until definitive test results are available.

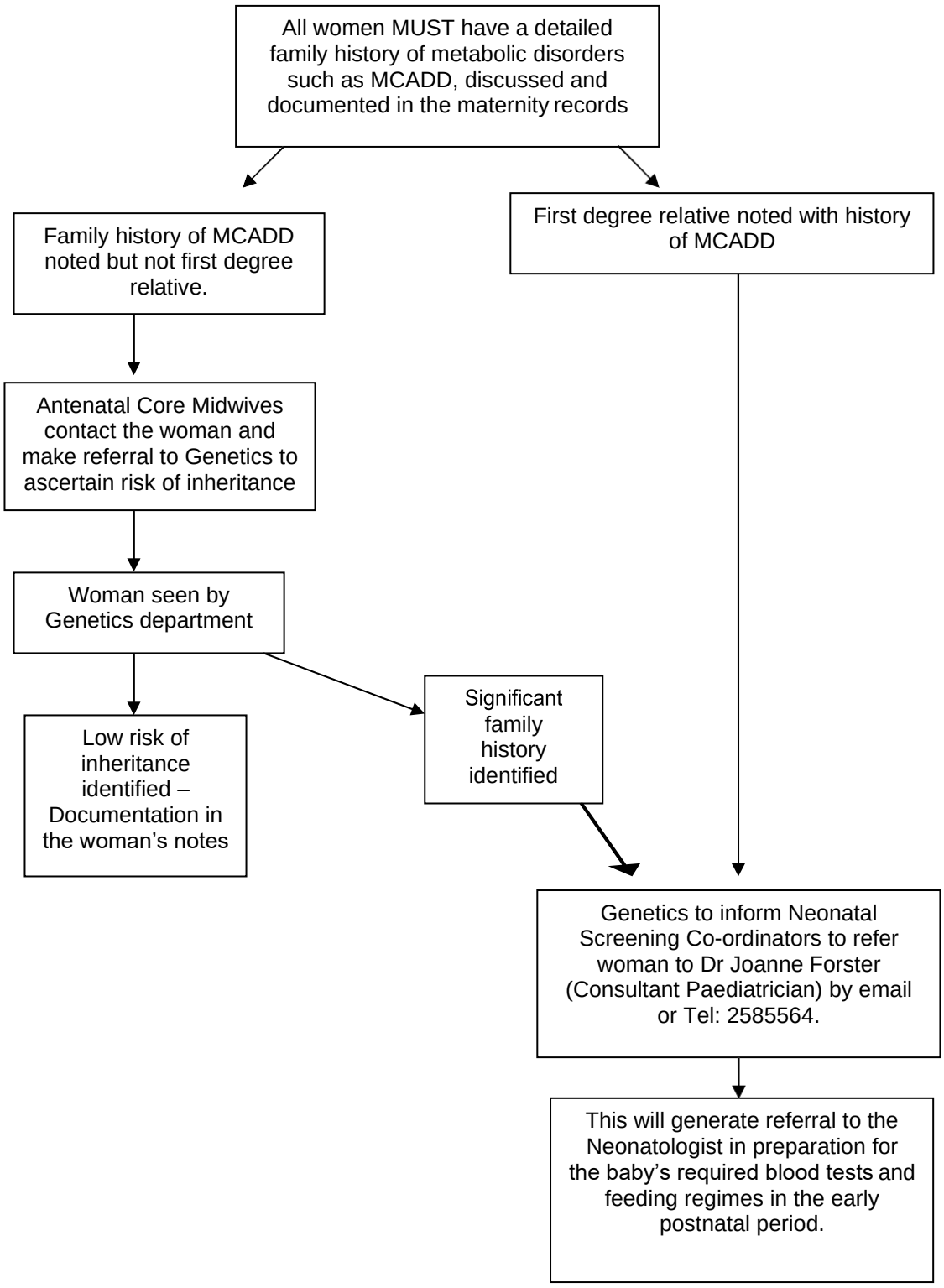
Early testing of the baby should be carried out on day two of life with the result being available more rapidly than from routine new-born screening testing.

Suggested guidance for the management of the new baby is attached. Details of early testing are included. It is recommended that a paediatric alert is attached to the maternal notes and that a copy of our recommended guidance (Appendix 3) is available in the notes at the time of the delivery.

Yours sincerely,

Consultant Paediatrician with an Interest in Metabolic Disease

Appendix 3 Process for the referral of pregnant women with a family history of MCADD.



Appendix 4A Suggested target feed volumes for BOTTLE FED babies.
(Please note that the baby may feed greater than the suggested volumes so that feeds are built up more quickly).

Day 1 Approx. 60ml/kg
Day 2 Approx. 70ml/kg
Day 3 Approx. 90ml/kg
Day 4 Approx. 110ml/kg
Day 5 Approx. 130ml/kg
Day 6 Approx. 150ml/kg

Day 1 Approx. 60ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	15-19ml
2.5-3.0kg	19-23ml
3.0-3.5kg	23-26ml
3.5-4.0kg	26-30ml
4.0-4.5kg	30-34ml
4.5-5.0kg	34-38ml

Day 2 Approx. 70ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	18-22ml
2.5-3.0kg	22-26ml
3.0-3.5kg	26-31ml
3.5-4.0kg	31-35ml
4.0-4.5kg	35-39ml
4.5-5.0kg	39-44ml

Day 3 Approx. 90ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	23-28ml
2.5-3.0kg	28-34ml
3.0-3.5kg	34-39ml
3.5-4.0kg	39-45ml
4.0-4.5kg	45-50ml
4.5-5.0kg	50-56ml

Day 4 Approx. 110ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	28-34ml
2.5-3.0kg	34-41ml
3.0-3.5kg	41-48ml
3.5-4.0kg	48-55ml
4.0-4.5kg	55-62ml
4.5-5.0kg	62-69ml

Day 5 Approx. 130ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	33-41ml
2.5-3.0kg	41-49ml
3.0-3.5kg	49-57ml
3.5-4.0kg	57-65ml
4.0-4.5kg	65-73ml
4.5-5.0kg	73-81ml

Day 6 Approx. 150ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	38-47ml
2.5-3.0kg	47-56ml
3.0-3.5kg	56-66ml
3.5-4.0kg	66-75ml
4.0-4.5kg	75-84ml
4.5-5.0kg	84-94ml

Appendix 4B (extension of Table 2) Suggested feed volumes for BREAST FED babies – guide to target top-up volumes for first 72 hours.

Day 1 approx top up: 25ml/kg
Day 2 approx top up: 40ml/kg
Day 3 approx top up: 60ml/kg

Day 1 Approx. top up: 25ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	8ml
2.5-3.0kg	8-10ml
3.0-3.5kg	10-11ml
3.5-4.0kg	11-13ml
4.0-4.5kg	13-14ml
4.5-5.0kg	14-16ml

Day 2 Approx. top up: 40ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	12-13ml
2.5-3.0kg	13-15ml
3.0-3.5kg	15-18ml
3.5-4.0kg	18-20ml
4.0-4.5kg	20-23ml
4.5-5.0kg	23-25ml

Day 3 Approx. top up: 60ml/kg	
Weight	3 hourly (8 feeds)
2.0-2.5kg	15-18ml
2.5-3.0kg	18-23ml
3.0-3.5kg	23-26ml
3.5-4.0kg	26-30ml
4.0-4.5kg	30-34ml
4.5-5.0kg	34-38ml