Cytogenetic and Molecular Genetic Samples - Antenatal and Postnatal - Full Clinical Guideline

Reference No.: AN/01:17/F5

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1. Introduction

When an abnormality is suspected in a fetus or a baby, parents are normally offered the option of cytogenetic or molecular genetic testing on samples which can be obtained from the fetus/baby or placenta. Staff should be experienced in non-directive counselling with access to specialist advice to enable the parents to feel confident in making a decision about genetic testing.

2. Purpose and Outcome

This guideline provides information of when to consider Cytogenetic &/or Molecular Genetic testing. How to obtain the correct samples, appropriate documentation on the request form and safe transport to the correct laboratory (NHS 2008) (NMC 2004).

3. Abbreviations

CVS	-	Chorionic Villus Sampling
EDTA	-	Ethylene Diamine Tetra Acetic Acid
EU	-	European Union Regulations
FISH	-	Fluorescent In-situ Hybridisation
FMMC	-	Fetal and Maternal Medicine Centre
MHHR	-	Maternity Hand Held Records
POC	-	Products of Conception
QF PCR	-	Quantative Fluorescent Polymerase Chain Reaction
RCOG	-	Royal College of Obstetrics and Gynaecology

Invasive Procedures

Invasive procedures include Amniocentesis and Chorionic Villus Sampling (CVS).
Amniocentesis is usually performed from 15+ weeks of pregnancy CVS can usually be performed from 11+ weeks of pregnancy. These procedures are performed by Fetal Medicine Consultants, please see Amniocentesis and chorionic villus sampling guideline AN03.
Amniocentesis has about a 1:100 risk of miscarriage. CVS has about 1-2% risk of miscarriage.
Where there is an indication to consider invasive testing, parents should be given appropriate information, opportunity to ask questions, time for reflection and support during the decision making process.
Written consent is required prior to amniocentesis or CVS.

Record Keeping
Invasive procedures are documented by the Fetal Medicine Consultant in the obstetric notes and a copy of the report is filed in the Maternity Hand Held Records (MHHR).
The fetal medicine midwife will complete the invasive procedures and antenatal screen forms within the Lorenzo maternity system and fetal medicine audit.

5. Pre Natal Samples

Amniocentesis
All amniocentesis samples will be sent with a maternal blood sample to exclude maternal contamination (4mls in EDTA). This is particularly important for QF PCR.
Gender is not currently tested on QF PCR. If gender testing is required (e.g. possible Turner presentation or a history of sex-linked disorder) as part of the preliminary report, the laboratory needs to be contacted as an alternative test would be required. If microarray is clinically indicated this will be requested by the fetal medicine consultant. Maternal and paternal blood samples in EDTA tubes are required at the time of the amniocentesis if microarray testing is requested. QF-PCR results are usually reported 2-3 working days following receipt of the sample, 95% of culture results are reported within two weeks of receipt.
Late gestation amniocentesis (third trimester) may report a failed result or a culture result later than two weeks due to sub optimal quality fetal cells.

CVS
CVS for karyotype will not require a maternal blood sample however; CVS for molecular genetic analysis sometimes require a maternal and paternal blood sample. Clinical genetics will advise if this is required.
Direct results should be available the next working day after the sample receipt unless the sample has failed or further testing is required. Failed direct results will be analysed by FISH for Trisomy 21 if an increased risk for Downs Syndrome. FISH for Trisomy 13, 18, 21 and sex chromosomes is available if CVS is requested for a fetal abnormality, for example increased NT. If microarray is clinically indicated this will be requested by the fetal medicine consultant. Maternal and paternal blood samples in EDTA tubes are required at the time of the CVS if microarray testing is requested. 95% of culture results are reported within two weeks of receipt.

6. Post Natal Samples

Karyotype testing often fails to produce a result because cells do not grow successfully in culture. Therefore microarray testing will be performed on all samples.
Requests for cytogenetic testing should be restricted to:-

- Any case with previous recurrent pregnancy loss (3 or more- including this pregnancy)
- Fetal dysmorphism (detected by scan or at birth)
- History of chromosomal abnormality
- History of antenatal karyotyping in the current pregnancy

Any information relating to the above should be clearly detailed on the referral form. Cytogenetics WILL NOT process the samples unless at least one of the above criteria is met.
Any requests outside these criteria will be considered following consultation with a scientist in the laboratory.

Types of Sample for Cytogenetics:-

Early gestation
A sample of the material from the products of conception (preferably not the entire P.O.C.) containing fetal tissue and/or placental structures.

Verbal consent for genetic testing to be taken prior to the samples, and documented on the bereavement checklist and in the obstetric/gynaecology notes.

Late gestation
Placental tissue sample i.e. from the fetal surface at the base of the cord, approximately 1cm cubed PRIOR to putting placenta into formalin.
(Both placental and skin samples have a high success rate for microarray testing)**Fetal skin** Full thickness and not macerated, 1-2mm cubed PRIOR to formalin.

Placental, skin and POC samples should be sent in sterile saline in a sterile universal bottle.

If possible a cord blood sample should be taken (1-2mls in heparinised bottle) to accompany the placental or skin sample.

7. Transport Ante Natal Cytogenetic and Molecular Genetic Samples

Amniocentesis samples will be taken to the post room at RDH for special delivery post Monday-Thursday before 1630hrs to guarantee arrival by 1300hrs in the laboratory the following day. **On Fridays samples must be sent via taxi by 1400 hours.**

CVS samples will always be sent by taxi Monday-Friday and **must arrive in the laboratory by 14.30 hours**. This will enable processing of a direct result within 24hours.

FMMC will telephone the laboratory when samples are dispatched by taxi. It is not necessary to phone about samples sent via special delivery post.

8. Transport of Post Natal Cytogenetic Samples including POC

Postnatal samples will be taken to the post room at RDH for special delivery post Monday-Thursday before 1630hrs to guarantee arrival by 1300hrs in the laboratory the following day**. On Fridays samples will be sent via taxi up to 14.00 hours, if this is not possible the sample needs to be stored in the fridge and sent via special delivery post after the weekend.**

9. Preparation of Samples for Transport to Laboratory

CVS samples and antenatal placental biopsies are sent in specialist transport medium which is supplied by the laboratory.
Amniotic fluid is sent in a sterile universal container.
POC, postnatal placental tissue and fetal skin are sent in sterile saline in a sterile universal container.

Before sending the samples ensure that the following are completed:

- Fully completed request form with all appropriate clinical information.
- Sample must be secured within the bag attached to the request form.
- If blood sample required this must accompany the sample.
- If paternal blood is accompanying the sample please cross reference it to his partner
- Sample and request form to be secured into the cardboard transport box.

- Ensure pre-printed address label for the cytogenetics department is attached to the top of the box.
- Place the cardboard box into the Royal Mail transport plastic bag (UN3373) as per EU regulations (NHS 2008 Appendix 3).
- Ensure the UN3373 bag has destination label for the cytogenetics department attached.

POSTAL ADDRESS for all samples:

Cytogenetics Department
Gate Three
Nottingham City Hospital Campus
Nottingham University Hospitals (NUH)
Hucknall Road
Nottingham
NG5 1PB
Telephone Numbers:-
Cytogenetics Department: 0115 9627617 (direct line)
Cytogenetics Dept. FAX: 0115 8402611
Molecular Genetics Department: 0115 9627743

10. Results

Antenatal results will be given to the woman as discussed at the invasive procedure consultation. The woman may choose to have a telephone conversation and/or a face to face appointment, with the fetal medicine midwife for the results.

Postnatal results are the responsibility of the Consultant Obstetrician/Gynaecologist who will make arrangements to share this information with the woman.

11. Monitoring Compliance and Effectiveness

Monitoring requirement	Data as set by Antenatal Screening Audit for the National Screening Committee
Monitoring method	Ongoing audit spreadsheet
Report prepared by	Specialist Midwife in Fetal medicine Antenatal and Newborn Screening Specialist Midwife
Monitoring report sent to:	Maternity Development Committee Maternity Governance Committee National Screening Committee
Frequency of report	Annually

12. References

National Health Service (NHS 2008) Amniocentesis and Chorionic Villus Sampling. Policy, Standards and Protocols. Fetal Anomaly Screening Programme. Antenatal Screening Wales

National Health Service (NHS 2008) Amniocentesis and Chorionic Villus Sampling. Policy, Standards and Protocols. Fetal Anomaly Screening Programme. Antenatal Screening Wales. Appendix 3 p22

Nursing and Midwifery Council (NMC 2013) Midwives Rules and Standards

Royal College of Obstetricians and Gynaecologists (RCOG 2010) Amniocentesis and Chorionic Villus Sampling. Greentop Guideline June No 8

Documentation Control

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Version / Amendment	Version	Date	Author	Reason
	1	Mar 2004	Carole Adcock – Clinical Specialist Midwife, Jeanette Steward – Audit Co-ordinator	New
	2	Aug 2012	Carol Adcock - Specialist Midwife Fetal Medicine. Sue Rucklidge -Bereavement Midwife.	Update
	3	Oct 2016	Carol Adcock - Specialist Midwife – Fetal Medicine. Sue Rucklidge - Bereavement Midwife.	Update
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To be read in conjunction with: IOL following IUFD-fetal loss. Antenatal Screening For Down's Syndrome Guideline 2010.				
Development / review of Guideline:			Carol Adcock -Specialist Midwife – Fetal Medicine. Sue Rucklidge - Bereavement Midwife.	
Consultation with:			Midwifery, Obstetric & Gynaecology Staff	
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