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SUPPORTING REFERENCES	Public Health England (2017) NHS Fetal Anomaly Screening Programme. Chorionic Villus Sampling (CVS) and Amniocentesis information for parents. London: Public Health England. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/610185/FASP88_CVS_and_amnio_leaflet_210417.pdf Royal College of Obstetricians and Gynaecologists (2011) Information for you: chorionic villus sampling and amniocentesis. London: RCOG https://www.rcog.org.uk/globalassets/documents/patients/patient-informationleaflets/pregnancy/pi-chorionic-villus-sampling-and-amniocentesis.pdf Royal College of Obstetricians and Gynaecologists (2010)

	Amniocentesis and Chorionic Villus Sampling. Green top Guideline No. 8. London: RCOG https://www.rcog.org.uk/globalassets/documents/guidelines/gtg_8.pdf International Society for Ultrasound in Obstetrics and Gynaecology - ISUOG Practice guidelines: Invasive procedures for prenatal diagnosis Ultrasound Obstet Gynecol 2016; 48: 256-268

CONSULTATION		
	Committee/Group	Date
Consultation	Fetal Medicine team – consultants/midwives/screening team	
Approval Committee	Women and Newborn QSB	September 2021
Ratification date at WNQSB	9th September 2021	
NEXT REVIEW DATE:	September 2024	
AMENDMENTS:	Section 4 – feticide added. **Dec 2021 - All women on the Maternity Badgernet EPR will have their records completed within the new system. Any templates within guidelines are only required for the existing paper records unless expressly stated in the Badgernet SOP**	

Contents

Fetal Medicine – Invasive Procedures Guideline

1 Introduction

The aim of this document is to describe the main aspects of invasive fetal procedures for prenatal diagnosis.

a. Clinical Indications for invasive testing

Detailed counselling should precede any invasive procedure, covering the expected benefits, risks and technical aspects of the test. This counselling may be carried out by a Fetal Medicine Consultant performing the test, a specified midwife or genetic counsellor.

Indications for invasive testing include:

- Increased chance of fetal aneuploidy on a screening test
- Increased risk for a known genetic or biochemical disease of the fetus
- Increased risk of maternal transmittable infectious disease (primary maternal toxoplasma, CMV or rubella)
- Ultrasound findings of abnormalities consistent with genetic or chromosomal syndromes
- Parents are known carriers of genetic conditions
- Family history of genetic conditions
- Maternal request

b. Types of genetic testing

- **Full karyotype**

- **Rapid testing**
  Rapid testing, such as QF-PCR may be carried out on villi or amniotic fluid to test for specific chromosomes (21, 18, 13, X, Y). These tests provide results in 1-2 days and are commonly employed on a screen-positive result or in a fetus with ultrasound findings or markers of common aneuploidies.

- **Molecular diagnosis of chromosome imbalances**
  Microarray techniques (e.g. array comparative genomic hybridization (aCGH)) are able to detect submicroscopic chromosomal deletions and duplications. Currently, the use of these technologies is recommended in cases of fetal structural anomalies or NT >3.5mm in the first trimester.

- **Diagnosis of monogenic disease**
  Invasive procedures may be used in the prenatal diagnosis of any monogenic disease whose molecular defect is well known or has been characterised.

- **Whole Exome Sequencing (WES)**

This process involves sequencing the whole exome, or the coding parts of the genome. The exome represents only 1-2% of the genetic code but contains approximately 85% of known disease-related variants. It can be useful in certain fetal anomalies, and requires careful counselling by a Fetal Medicine Consultant, and a genetic counsellor.

2 Amniocentesis

a. Aim

Amniocentesis is usually performed when there are concerns regarding fetal karyotyping (e.g., Trisomy 21, 18 or 13) but can also be carried out with intentions of obtaining biochemical, metabolic, or genetic information (e.g., specific genes such as cystic fibrosis). The test can be performed from 15+0 weeks gestation.

b. Risks

The most common side effect of an amniocentesis is discomfort on inserting the needle, most risks are infrequent or rare. Patients should be informed regarding the following when considering an amniocentesis: -

Risks of an Amniocentesis
Discomfort – From needle insertion
Failure to obtain an amniotic sample (6% of cases)
Blood stained sample (0.8% when using ultrasound guidance, 2.4% if blind procedure) **
Miscarriage (0.5%) - Majority within 3 days of amniocentesis but can occur up to 3 weeks post procedure
Fetal injury (Rare)
Maternal bowel injury (Rare – minimised by ultrasound guidance)
Prolonged or temporary amniotic fluid leakage
Infection – including Chorioamnionitis (severe sepsis <1:1000)
Failure of cell culture in lab (0.01%)

** if the sample is blood stained the Rapid Test (QF-PCR) may not be able to be performed (See 9. Results of amniocentesis)

c. Clinical Recommendations

Formal written consent should be taken prior to procedure – the procedure process should be explained and risk (see section 4) should be outlined to the patient. Written patient information leaflet should also be provided.
Other information to be explained:-

- What results are possible from the amniocentesis
- Reporting time

- How and who will contact them with the results
- How to seek emergency medical help following the procedure

d. Procedure for Singleton Pregnancy

The procedure is performed in the Fetal Medicine Unit (FMU) by, or under direct supervision of, a Fetal Medicine Consultant.

Pre-procedure

Prior to the procedure the patient should have received the NHS Fetal Anomaly Screening Programme.

Written consent should be obtained and the patient identify should be checked prior to commencing the procedure.

The patients Rhesus status and HIV status should be checked

Viability should be confirmed on ultrasound scan, as well as fetal and placental position.

A LOCCSIP form should be commenced prior to starting procedure, and completed on finishing procedure.

Procedure

The patient's abdomen is cleaned with chlorhexidine solution and an aseptic technique is used throughout the procedure. An ultrasound probe cover should be used, to maintain sterility.

Whilst using constant ultrasound visualisation a 20-22 Gauge needle is inserted through the patient's abdomen into the liquor. Constant ultrasound should be used to ensure that the needle is not inserted into placenta*, maternal bowel, umbilical cord or the fetus.
**Transplacental amniocentesis should be avoided unless it provides the only access to adequate pool of liquor.*

Approximately 20mls of amniotic fluid is taken as a sample.

Samples should be labelled in the presence of the patient to make sure patient identifying information is correct, in addition this should be checked by two members of staff to prevent laboratory rejection of samples. Samples are then boxed and placed in a refrigerator, whilst awaiting transport.

Post-procedure

Samples are then transported to the cytogenetics laboratory to be processed.

A Viewpoint ultrasound report detailing the procedure will be printed a copy filed in the patient's records.

Anti-D prophylaxis should be given to women who have a negative rhesus status and the fetus is

known to be rhesus positive/unknown.

After care advice should be provided to the patient: -

- How long results take (3-4 days for the rapid test, 10-14 for cell culture and micro-array analysis)
- To contact Early pregnancy unit (< 20 weeks) or Maternity Triage (>20 weeks) if any vaginal bleeding, signs of ruptured membranes, fevers, rigors or pain.
- The screening team/FMU contact details will be provided to the patient.

Follow-up arrangements will be made depending on the clinical findings and test results.

e. Procedure for multiple Pregnancy

We do not currently offer amniocentesis for multiple pregnancies at East Lancashire Hospital Trust. Patients with multiple pregnancies who require invasive testing should be referred to a tertiary centre offering this service.

f. Risks of Transmission of Infection

Invasive pre-natal testing should not be carried out without reviewing the blood borne virus status of the patient.

In patients that have declined blood borne virus screening the risk of vertical transmission to the fetus should be discussed and documented.

In patients with HIV where the viral load is undetectable amniocentesis can be performed. However if the viral load is detectable the procedure should be delayed.

There is limited data available for transmission of Hepatitis B and C to fetus via pre-natal testing and this should be explained to patients.

g. Results of Amniocentesis

The amniotic fluid is processed in two ways: -

a) Rapid Test – QF-PCR.
Rapid test identifies approximately 80% of chromosomal abnormalities and usually takes around 1-3 working days. The rapid test fails to achieve a result in 2.2% of cases, mainly because of a blood-stained sample.

b) Microarray
This test is performed in the presence of confirmed structural abnormality only and usually takes around 10 working days to obtain a result. Appropriate details will need to be entered onto the request form for this test to be performed by the cytogenetics laboratory.

The results of amniocentesis are placed on NHS portal system. This is reviewed daily by the screening team, who will contact the patient with the results and arrange follow up as required.

3 Chorionic Villous Sampling (CVS)

a. Aim

CVS is performed most often when there are concerns regarding fetal chromosomal abnormalities. It can also be carried out with intentions of obtaining biochemical, metabolic, or genetic information (e.g., Specific genes such as cystic fibrosis). The test can be carried out between 11+0-14 weeks.

b. Clinical Indications

- Increased chance of chromosomal conditions – current recommendation is if 1:150 chance.
- Chromosomal/genetic problems in previous pregnancy
- Ultrasound screening identified abnormalities consistent with genetic or chromosomal syndromes
- Parents are known carriers of genetic conditions
- Family history of genetic conditions

c. Risks

Risks of a Chorionic Villous Sampling procedure
Discomfort – From needle insertion
Miscarriage (1%)
Placental cell mosaicism (1% of procedures) – genetic counselling and amniocentesis would be required
Vaginal bleeding (1 in 10 cases)
Amniotic fluid leakage (rare <0.5% of cases)
Fetal injury (Rare)
Maternal bowel injury (Rare – minimised by ultrasound guidance)
Chorioamnionitis/uterine infection (rare 1-2/3000)
Failure to obtain a sufficient sample (5%)
Failure of cell culture in lab (0.5%)

d. Clinical Recommendations

Formal written consent should be taken prior to procedure – the procedure process should be explained and risk (see section 4) should be outlined to the patient. Written patient information leaflet should also be provided.

Other information to be explained:-

- What results are possible from the CVS
- Reporting times
- How and who will contact them with the results

- How to seek emergency medical help following the procedure

e. Procedure

The procedure is performed in FMU by, or under direct supervision of, a Fetal Medicine Consultant.

Pre-procedure
The cytogenetics laboratory should be informed of any CVS procedure at least 24 hours beforehand so that they are ready to accept and analyse the sample. The samples cannot be stored overnight in the refrigerator and should be transported as soon as possible to the laboratory after sampling. Prior to the procedure the patient should have received the NHS Fetal Anomaly Screening Programme. Written consent should be obtained and the patient identify should be checked prior to commencing the procedure. The patients Rhesus status and HIV status should be checked Viability should be confirmed on ultrasound scan, as well as fetal and placental position. A LOCCSIP form should be commenced prior to starting procedure, and completed on finishing procedure.
Procedure
The patient's abdomen is cleaned with chlorhexidine solution and an aseptic technique is used throughout the procedure. An ultrasound probe cover should be used, to maintain sterility. The site of needle insertion should be anaesthetised with local anaesthetic prior to starting the test. Whilst using constant ultrasound visualisation a 19-20 Gauge needle is inserted through the patient's abdomen into the placenta. Constant ultrasound should be used throughout. Once the needle has reached the target within the placenta, between one and ten back-and-forth movements are performed while the vacuum is maintained and samples are aspirated either manually or by an assistant. The amount of villi obtained should be checked visually. A minimum amount of 5mg villi in each sample is required to achieve a valid result. Samples should be labelled in the presence of the patient to make sure patient identifying information is correct. In addition, this should be checked by two members of staff to prevent laboratory rejection of samples. Samples are then boxed and placed in a refrigerator, whilst awaiting transport.

Post-procedure
Samples are transported to the cytogenetics laboratory to be processed as soon as possible. A Viewpoint ultrasound report detailing the procedure will be printed and a copy filed in the patient's records. Anti-D prophylaxis should be given to women who have a negative rhesus status and the fetus is known to be rhesus positive/unknown. After care advice should be provided to the patient: - - How long the results will take. - To contact the early pregnancy unit (< 20 weeks) or Maternity Triage (>20 weeks) if any vaginal bleeding, signs of ruptured membranes, fevers, rigors or pain. - The screening team/FMU contact details will be provided to the patient. Follow-up arrangements will be made depending on the clinical findings and test results.

f. Procedure for multiple Pregnancy

We do not currently offer CVS for multiple pregnancies at East Lancashire Hospital Trust. Patients with multiple pregnancies who require invasive testing should be referred to a tertiary centre offering this service.

g. Risks of Transmission of Infection

Invasive pre-natal testing should not be carried out without reviewing the blood borne virus status of the patient.

In patients that have declined blood borne virus screening the risk of vertical transmission to the fetus should be discussed and documented.

In patients with HIV where the viral load is undetectable CVS can be performed. However if the viral load is detectable the procedure should be delayed.

There is limited data available for transmission of Hepatitis B and C to fetus via pre-natal testing and this should be explained to patients.

4. Feticide

a. Aim

When undertaking a termination of pregnancy, the intention is that the fetus should not survive, and that the process of ending the pregnancy should achieve this. Death may occur before delivery, as a consequence of a compromised fetus being unable to tolerate induced labour. Death may also occur after birth, either because of the severity of the abnormality for which termination was performed or because of extreme prematurity (or both).

The RCOG currently recommends feticide for terminations over 21+6 weeks. The only exception to this rule is when the fetal abnormality itself is so severe as to make early neonatal death inevitable irrespective of the gestation at delivery. At ELHT, we currently offer feticide over 18+0 weeks, following careful and detailed consultation from a Fetal Medicine Consultant.

b. Clinical Indications

- Prior to Termination for Medical Reasons after 18+0 weeks, for conditions under section E the Abortion Act 1967.

c. Risks

Risks of a Feticide Procedure
Discomfort – From needle insertion
Vaginal bleeding (1 in 10 cases)
Amniotic fluid leakage (rare <0.5% of cases)
Maternal bowel injury (Rare – minimised by ultrasound guidance)
Chorioamnionitis/uterine infection (rare 1-2/3000)
Failure to complete procedure at first attempt (minimised by ultrasound guidance and post-procedure scan)

d. Clinical Recommendations

Formal written consent should be taken prior to procedure – the procedure process should be explained, and risks (see section c) should be outlined to the patient. Written patient information leaflet on ending a pregnancy should also be provided.

Other information to be explained: -

- What will happen next – administration of mifepristone, admission immediately or after 24-48 hours to continue process of ending the pregnancy.
- The medical process of ending the pregnancy, including a consent form.
- Investigations to be offered following birth, where appropriate.
- How to seek emergency medical help following the procedure.

e. Procedure

The procedure is performed in FMU by a Fetal Medicine Consultant.

Pre-procedure

Prior to the procedure the patient should have been seen by a Fetal Medicine Consultant to discuss the fetal abnormalities, and the options available to the patient.

Central Birth Suite should be made aware of the patient and the anticipated admission date/time (immediate or delayed). Bed status, particularly the availability of the Bereavement Suites should be checked.

Written consent should be obtained and the patient identity should be checked prior to commencing the procedure. Certificate A should also be completed with two clinician signatures.

The patients Rhesus status should be checked.

The patient should be offered a prescribed sedative, to be administered at least 30 minutes prior to the procedure.

Viability should be confirmed on ultrasound scan, as well as fetal and placental position.

A LocSSIPs form should be commenced prior to starting procedure and completed on finishing procedure.

Procedure

The patient's abdomen is cleaned with chlorhexidine solution and an aseptic technique is used throughout the procedure. An ultrasound probe cover should be used, to maintain sterility.

The site of needle insertion should be anaesthetised with local anaesthetic prior to starting the test.

Whilst using constant ultrasound visualisation a 20-22 Gauge needle is inserted through the patient's abdomen into the fetal chest and cardiac ventricle. Constant ultrasound should be used throughout.

Once the needle has reached the target within the cardiac ventricle, the position should be checked by aspiration of 1ml of fetal blood.

Following confirmation of needle position within the fetal cardiac ventricle, 2-3ml of 15% potassium chloride is administered via the needle by an assistant. A second dose can be repeated if asystole is not achieved within 30- 60 seconds.

Fetal cardiac asystole should be observed for at least two minutes before finishing the procedure.

A second ultrasound scan should be performed 30 minutes later to finally confirm death of the fetus.

Post-procedure

A Viewpoint ultrasound report detailing the procedure will be printed and a copy filed in the patient's records.

Anti-D prophylaxis should be given to women who have a negative rhesus status and the fetus is

known to be rhesus positive/unknown.

200mg oral mifepristone should be offered and administered.

The patient should be offered immediate admission if they wish. They may wish to delay admission for 24-48 hours, in which case the following after care advice should be provided: -

- Information on the process of ending the pregnancy.
- To contact Central Birth Suite in the event of any vaginal bleeding, signs of ruptured membranes, fevers, rigors, pain or if the patient wishes earlier admission than originally planned.

Follow up will be arranged with a Fetal Medicine Consultant (or the patient's named consultant if this is preferred) with any relevant investigation results.

f. Procedure for multiple Pregnancy

We do not currently offer feticide/selective reduction for multiple pregnancies at East Lancashire Hospital Trust. Patients with multiple pregnancies who require feticide/selective reduction should be referred to a tertiary centre offering this service.

g. Risks of Transmission of Infection

In view of the aim to end the pregnancy, the risk of transmission of blood-borne viruses, such as HIV and hepatitis B and C are not a contraindication to feticide.

1. Audit

Annual audit of invasive procedures will be conducted as per the RCOG recommendations and presented at the appropriate forums.