Brighton and Sussex University Hospitals NHS Trust

Management of Recurrent Miscarriages

Protocol: GP019

Updated: September 2017

Guideline Reviewer:	Tasneem Singhal & Aye Aye
Version:	2.0
Approval Committee:	Women's Services Safety & Quality Committee
Date agreed:	October 2017
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Key Principles

A protocol is a set of measurable, objective standards to determine a course of action. Professional judgement may be used in the application of a protocol.

Scope

This guideline applies to: All women attending for Recurrent Miscarriages

Responsibilities

Nursing staff & Gynaecologists:

- To access, read, understand and follow this guidance
- To use their professional judgement in application of this protocol

Management:

- To ensure the protocol is reviewed as required in line with Trust and National recommendations
- To ensure the protocol is accessible to all relevant staff
- To ensure the protocol is available to service users on request

1 Patient Selection (Criteria for investigation)

1.1 3 or more consecutive first trimester miscarriages

1.2 one or more second trimester miscarriages

1.3 2 consecutive first trimester miscarriages in a woman above age 38y years

1.4 A woman who has suffered miscarriages and has other markers indicative of Antiphospholipid syndrome in previous pregnancy e.g. severe PET, recurrent APH.

2 Investigations

2.1 Arrangement for blood tests for Antiphospholipid antibodies should be made before discharge from EPU clinic. This will be organised by EPU clinic nurse/doctor.

2.2 The test is to be performed 6 weeks after the miscarriage

2.3 Patient's details should be given the EPU Sister at each site

2.4 Advise the patient that they will be contacted about result of the test but this may take up to 3 months

2.5 Follow up for all patients will then be arranged in the Recurrent Miscarriage Clinic

3 Test for Antiphospholipid Syndrome (APLS)

3.1 Screening should be performed at least 6 weeks after a pregnancy /loss to avoid false positive results

3.2 It includes test for lupus anticoagulant and anticardiolipin antibodies (IgG and IgM)

3.3 If the first test is negative – take it as negative

3.4 Woman with APLA should have a positive test on 2 occasions 12 weeks apart. (2- blue top tubes and 1-gold top tube)

3.5 If 1st test is Positive and subsequent test is negative, it should be taken as negative

4 Cytogenetics for product of Conception

4.1 The karyotype obtained from the miscarriage tissue or products of conception (POC) may be useful for providing prognosis for subsequent pregnancy outcomes.

4.2 The aim of this test is to look for evidence of unbalanced translocations in the Fetus/POC. If positive, this will prompt screening for both parents for balanced translocations.

4.3 Fetal Karyotyping should be offered to women at the third consecutive miscarriage.

4.4 Tissue obtained from all types of management of miscarriage, (SMM, medical or conservative) should be sent for karyotyping if women fulfil the criteria of recurrent miscarriages.

4.5 The woman should be given the appropriate container and advised to collect any pregnancy tissue should they miscarry at home and try to bring this to hospital within 24 hours.

4.6 Should this happen over a week-end, the specimen in to be sent to be stored in the refrigerator in pathology lab VERY CLEARY LABLED – NOT FOR ANALYSIS. TO BE COLLECTED BY HK WARD ON MONDAY MORNING. Inform EPU NURSE BY EMAIL AND WRITE ON HANDOVER SHEET to arrange courier to collect on Monday morning.

4.7 At their EPU clinic appointment, we would provide them with forms for bloods in 6 weeks and continue the usual referral process.

4.8 Tissue will then be sent to Guys for analysis.

4.9 For women undergoing SMM, portion of POC needs to be separated after the procedure and placed in the appropriate container for cytogenetics (pot will be available in theatre). The remainder needs to go for histology for routine analysis to confirm pregnancy and exclude molar change.

4.10 If tissue cannot be sent or cannot be analysed, then attempt to send tissue in subsequent pregnancy.

4.11 For all specimens, an appropriate referral form for karyotyping needs to be filled in completely by the doctor or EPU nurse (Attached in the appendix).

4.12 Couples found to have a balanced translocation would be offered a referral to Guys genetic unit for further discussion

5 To send Tissue for Karyotyping

- Place the pregnancy tissue into a dry sterile pot (i.e no formalin)
- Place that pot into a second container that has a piece of absorbent material in (order number 78.897)
- These combined containers are then placed inside the box with the code and hazardous materials written on it (order no. 95.901)
- With the usual chromosome form completed correctly with the date and the gestational age of when the miscarriage occurred.
- Contact the medical couriers 818285 with the cost code 0017414.
- There are stickers with the address for Guys hospital on them. In the recurrent miscarriage drawer in EPU.
- The specimen needs to be sent off with one of the usual chromosome analysis form completed with the mother's information and gestational age and date of miscarriage.
- If a patient wants to send off her own products she can follow the above information but we can give her a jiffy bag to put the pots in.
- These need to be sent off through the post office and sent by guaranteed next day delivery.

6 Thrombophilia Screen

6.1 Indication

- Full Thrombophilia screen is indicated in woman with second trimester miscarriage only.
- It should include F.V Leiden, protein C, protein S, Antithrombin III, and prothrombin gene mutations (1 purple top bottle and 2 blue top bottles, all required test written on the form).

6.2 Treatment

- Treatment should be discussed and initiated with consultant discussion (hence the following is for reference only)

6.3 Antiphospholipid Syndrome

- Women with a positive anticardiolipin or lupus anticoagulant screen on two occasions should be advised to use Aspirin (75mg daily) and LMWH (Tinzaparin 4500units per day).
- LMWH and Aspirin can be started with a positive PT.
- The Heparin is continued until 10 days after delivery and the Aspirin is continued until delivery.

- All women require regular assessment in ANC and growth scans at 28 and 32 weeks, if there is evidence of growth restriction then repeat scan at 36 weeks is required.

6.4 Positive Thrombophilia Screen (with 2nd Trimester miscarriage)

- Women with positive thrombophilia screen should be advised to use LMWH (tinzaparin 4500 units s/c per day).It should be started following visualization of fetal heart on USS -6weeks. It needs to be continued until 10 days after delivery and VTE assessment should be made as per MP012 Venous Thrombosis Guideline.
- There is no indication for Aspirin therapy.
- All women require regular assessments in ANC and regular growth scan at 28 and 32 weeks are required (36 weeks scan is required if there is evidence of growth restriction).

6.5 No abnormality detected

- If these women have no detected cause behind their miscarriage, the aim of care should be reassurance.
- They should be advised that there is no place for empirical treatment with Aspirin (with or without heparin)
- They should be offered early contact with EPU at either hospital or serial scans every 2 weeks from 7 weeks onwards until routine antenatal ultrasound screening is commenced.

6.6 Anti D Administration

- For Anti-D administration, please refer to current miscarriage guideline.

References:

Recurrent Miscarriage, Investigation and Treatment of Couples (Green-top Guideline No. 17) 19/05/2011

Appendix A: Genetics Specimen form

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GENETICS SPECIMEN FORM
Genetics Laboratories, 5th Floor, Tower Wing, Guy's Hospital, Great Maze Pond, London, SE1 9RT
http://www.viapath.co.uk/departments-and-laboratories/genetics

MOLECULAR GENETICS: T: 020 7188 1696/2582 F: 020 71887273
CYTOGENETICS: T: 020 71881709 F: 020 71881697
BIOCHEMICAL GENETICS: T: 020 71882591 F: 020 71887275
CLINICAL GENETICS: T: 020 71881364 F: 020 71881369

PATIENT DETAILS

Surname:

First Name:

Previous Name:

DOB: Sex: M / F

Address:

Postcode:

Ethnic Origin:

Hospital Number:

NHS number (mandatory):

Private Patient (please attach invoicing details) ☐

REFERRING HOSPITAL

Consultant:

Full address for return of report including department:

Signed: Date:

Name (PRINT): Tel no:

Fax no:

G.P DETAILS

Name:

Postcode:

SAMPLES

Blood in potassium EDTA (DNA / MLPA / array CGH) ☐

Blood in lithium heparin (Chromosome rearrangements / Biochemical Genetics) ☐

Prenatal sample (Please circle) CVS / AF / POC

Other (Please state) _____

Date and time sample taken:

Please ensure specimens are dispatched to the laboratory promptly after sampling

TESTS REQUESTED
NB For testing for chromosome imbalance (array CGH/chromosome analysis), please provide clinical details on the reverse of this form.

In submitting this sample, the clinician confirms that consent has been obtained:
(a) for testing and possible storage
(b) for the use of this sample and the information generated from it to be shared with members of the donor's family and their health professionals (if appropriate).
Please do NOT send the consent form

CLINICAL DETAILS/REASON FOR REFERRAL
(Please include full details of patient, with pedigree if relevant)
NB For testing for chromosome imbalance (array CGH/chromosome analysis), please provide clinical details on the reverse of this form.

Has this case been discussed with the Genetics Department? If so, with whom?

Is the patient pregnant? Y / N

If YES: how many weeks gestation? _____

All fields above are mandatory. Samples supplied with inadequate or illegible information, will be subject to delay or rejection.

For departmental use only

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NHS Number: _____

CLINICAL INFORMATION – for chromosome imbalance testing
Place an X in the box if statement applies to the subject.

1. Cognitive Development
- Typical ☐
- Delay (Atypical) ☐
- Mild (IQ 50-69; for adults mental age 9-12 yrs) ☐
- Mod (IQ 35-49; for adults mental age 6-9 yrs) ☐
- Severe (IQ 20-34; for adults mental age 3-6 years) ☐
- Profound (IQ <20; for adults mental age <3 years) ☐

2. Specific Developmental Disorder
Speech & language ☐ Reading/spelling ☐ Arithmetic ☐ Motor skills ☐

3. Neurodevelopmental/Behavioural Problems
Autism Spectrum Disorder ☐ ADHD ☐
Tics ☐ Sleep ☐ Feeding ☐ Psychosis ☐ Other Behavioural Problems ☐

4. Neurological Disorders
Vision ☐ Hearing ☐ Abnormal tone Involuntary Movements ☐
Structural brain lesion (eg dysplasia, tumour)
Cerebral Palsy Unilateral ☐ Cerebral Palsy Bilateral ☐
Epilepsy ☐
Age of onset: <3 months ☐ 3-24 months ☐ > 24 months ☐
Seizure type documented: atonic ☐ myoclonic ☐ other ☐

5. Growth abnormalities
At birth: Small for gestational age (<10th centile) ☐ Large for gestational age (>90th centile) ☐
Current: Tall stature (height >95th centile) ☐ Short Stature (height < 5th centile) ☐
Macrocephaly (>95th centile) ☐ Microcephaly (<5th centile) ☐

6. Congenital Malformations/Dysmorphism
Heart disease (eg ASD, VSD) ☐ Renal and Urogenital malformations ☐ Brain malformations ☐
Eye malformations (eg anophthalmia, microphthalmia) ☐ Ear malformations ☐
Cleft Lip ☐ Cleft Palate ☐ Micrognathia ☐
Limb abnormalities (eg short or long bones) ☐ Digital abnormalities (eg syndactaly, polydactaly) ☐
Facial dysmorphism eg hypertelorism ☐

7. Endocrine and metabolic conditions ☐

8. Cutaneous stigmata/skin lesions ☐

9. Hair, nail, teeth abnormalities ☐

10. Other Skeletal abnormalities eg scoliosis ☐

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