

Miscarriage (and *recurrent miscarriage*)

Sadly, miscarriage does happen, and happens unexpectedly.

Diagnosis

Usually, there are symptoms and signs (vaginal bleeding associated with abdominal pain/cramps) that warn you miscarriage is impending. In some cases, miscarriage is diagnosed completely out of the blue during a routine ultrasound scan (USS)- as the patient does not feel anything untoward (perhaps, may be, a reduction in pregnancy symptoms).

Diagnosis, particularly in the latter case, is important as a wrong diagnosis may result in inadvertent termination of a viable early pregnancy.

USS is diagnostic in most cases but care must be exercised when interpreting *early* pregnancy USS report. A certainty of last menstrual period *cannot* be used to date the pregnancy as **late** ovulation (and hence later conception date) may be the reason for a “small, undeveloped” embryo. A blood test requesting serial pregnancy hormone (hCG), noting a reduction in levels may then help to confirm the diagnosis.

Management

Miscarriage is managed expectantly, medically or surgically.

Early pregnancy miscarriage can be managed **non-surgically**. Expectant management may involve a prolonged waiting thus exacerbating the whole negative experience of the miscarriage. The timing of actual miscarriage can be unpredictable and “inconvenient”. By administering oral medicine, the process of expulsion of the products of conception (POC) is expedited and, hopefully, at a more specified time. It usually results in a heavy and painful “period”. A follow up at the clinic is necessary to ensure a complete miscarriage has occurred (that is, a surgical curettage is not required).

Surgical management (evacuation of retained products of conception- ERPC or commonly known as D&C) is preferred in “older” pregnancy that is > 7-9 weeks amenorrhoea as non-surgical management may result in failed treatment or incomplete miscarriage thus requiring an ERPC anyway.

ERPC is performed under general anaesthesia and is relatively safe. There are no long term sequelae on future fertility or pregnancy, unless rare complications such as uterine perforation, infection and adhesion formation (Asherman’s syndrome) arise. Not so rare complications include haemorrhage or incomplete emptying of the POC requiring another procedure. A situation that is to be avoided is performing an ERPC on a suspected intrauterine pregnancy that turned out to be an ectopic pregnancy.

Why did miscarriage occur? What investigation should be requested?

Miscarriage occurs commonly. About 15-20% of all clinical pregnancies end in miscarriage. The rate of miscarriage is higher still if one includes “unknown” pregnancy where women thought she has a “heavier-than-usual” period. In contrast, *recurrent* miscarriage (defined as three or more consecutive early pregnancy losses) is a medical condition (requiring further investigation and treatment) and is seen in 1-3% of couples.

Simple blood tests for maternal health looking for chronic illnesses such as **diabetes, kidney diseases, thyroid diseases and autoimmune disease** should be done.

The *most likely* cause of miscarriage is a **chromosomal disorder**. This can be a random sporadic event or a hereditary recurrent occurrence. To find out if chromosomal abnormalities actually cause the miscarriage, the clinic offers **Anora test** (from USA) on the *products of conception* (POC). The POC (even a small sample from home if the miscarriage occurs there) is sent to USA to determine the chromosomal composition.

Additionally, chromosomal composition of the couple can be examined by means of **blood karyotyping**. This is to examine for **balance translocation** in either husband or wife or both.

Another useful test is to look for **thrombophilia** (acquired and inherited). Thrombophilia is a condition whereby the blood has a greater tendency to clot and somehow results in miscarriage.

For acquired thrombophilia (**antiphospholipid syndrome**), the clinic can test for **anticardiolipin antibody and lupus anticoagulant**.

For inherited thrombophilia, the clinic can test for **factor V Leiden mutation, protein C deficiency, protein S deficiency and antithrombin III deficiency, hyperhomocysteinaemia and prothrombin gene mutation**.

In some cases, the couple are both **carriers of a (same) genetic disease** thus resulting in the foetus being a homozygote (the disease being expressed). The clinic offers screening test (**Horizon** from USA) looking at up to 274 genetic conditions (including common conditions such as **thalassaemia (alpha and beta), cystic fibrosis, fragile X syndrome, congenital adrenal hyperplasia, Tay-Sachs disease, familial hypercholesterolemia, homocystinuria, spinal muscular dystrophy and Duchenne muscular dystrophy**).

Prevention and Treatment of miscarriage

Miscarriages that are caused by chromosomal disorders (which are the majority of cases) cannot be treated or prevented. Arbitrary treatment with bed rest or drugs is unlikely to alter the outcome.

Known effective treatment to prevent miscarriage is **low dose aspirin** plus/minus **low molecular heparin** but *only* in cases of thrombophilia disorders. Improved liveborn rate was noted if the treatment is given to recurrent first trimester miscarriage caused by acquired thrombophilia (antiphospholipid syndrome) and second trimester miscarriage caused by inherited thrombophilia.

Treatment (surgical) for anatomical abnormalities (fibroid, uterine septate, bicornuate uterus, Asherman's syndrome) will be discussed at length in the clinic.

Obtaining a good control of chronic illnesses (diabetes, hyper/hypo-thyroidism, kidney and autoimmune) is essential in reducing the risk of miscarriage as well as the risk of developing abnormalities in the baby.

Avoidance of harmful agents to the foetus is obvious and the list includes smoking, alcohol intake, illicit drug use, some infections, certain medications and irradiation. Known harmful infections from food ingestion include listeriosis and toxoplasmosis. Other harmful infections, acquired by air-borne or physical contacts, are herpes, rubella, parvovirus, chickenpox, cytomegalovirus, parvovirus, syphilis, chlamydia and HIV. The clinic offers tests for these, where appropriate; as well as providing immunisation, if applicable.

There is a body of evidence that supports “**tender loving care** (TLC)” as adequate treatment for miscarriage of unknown cause, as successful pregnancy outcome can be achieved by up to 50-60%.

It is noted that women who have experienced miscarriages (or recurrent miscarriages) are particularly emotional and perhaps even depressed and desperate. TLC may not be adequate even after prolonged counselling. Empirical treatment with evidence-limited treatment such as hCG injection and progesterone supplementation may be considered, with cautious, bearing in mind the RCOG’s view being: “the use of empirical treatment in women with unexplained recurrent miscarriage is unnecessary and should be resisted”.

Causes	Investigations	Treatment
Chromosomal abnormalities	To detect chromosomal abnormalities on <i>products of conception</i> by Anora (USA). Karyotyping <i>parental</i> blood.	None available
Antiphospholipid syndrome	Lupus anticoagulant and anticardiolipin antibodies	Low dose aspirin and low molecular heparin
Anatomical / structural	Ultrasound scan, laparoscopy, hysteroscopy, hysterosalpingography.	Corrective surgery where appropriate
Infection	Blood tests.	Immunisation where applicable. ??Role of antibiotic prophylaxis.
Chronic illness	Blood tests.	Good control
Inherited thrombophilia	Factor V Leiden mutation; deficiencies in antithrombin III, protein S and protein C; homocysteine, prothrombin gene mutation.	Possibly, low dose aspirin and low molecular heparin
Inherited diseases (autosomal recessive and X-linked conditions)	Carrier screening test by Horizon (USA).	Genetic counselling.
Unexplained recurrent miscarriage	Diagnosed after having done all the above tests.	Supportive

Footnote:

Other quotations from the Royal College of Obstetricians and Gynaecologists (RCOG) are reproduced for your consideration. Check out “Greentop guideline no 17” on <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg17/>

“Pregnant women with antiphospholipid syndrome should be considered for treatment with low-dose aspirin plus heparin to prevent further miscarriage.”

“There is insufficient evidence to evaluate the effect of progesterone supplementation in pregnancy to prevent a miscarriage in women with recurrent miscarriage.”

“There is insufficient evidence to evaluate the effect of human hCG supplementation in pregnancy to prevent a miscarriage in women with recurrent miscarriage.”

“There is insufficient evidence to evaluate the effect of heparin in pregnancy to prevent a miscarriage in women with recurrent first-trimester miscarriage associated with inherited thrombophilia”.

“Heparin therapy during pregnancy may improve the live birth rate of women with second-trimester miscarriage associated with inherited thrombophilias.”

“Women with unexplained recurrent miscarriage have an excellent prognosis for future pregnancy outcome without pharmacological intervention if offered supportive care alone in the setting of a dedicated early pregnancy assessment unit.”

“The use of empirical treatment in women with unexplained recurrent miscarriage is unnecessary and should be resisted.”

Useful links

www.rcog.org.uk

www.miscarriageassociation.org.uk