Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

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THE MANAGEMENT OF EARLY PREGNANCY LOSS

This is the second edition of this guideline, which was previously published in October 2000 under the same title.

1. Purpose and scope

This guideline reviews recent information related to the diagnosis and clinical management of women with early pregnancy loss, defined as a loss within the first 12 completed weeks of pregnancy. It mainly reviews management of spontaneous miscarriage but is also relevant to women affected by ectopic pregnancy and gestational trophoblastic disease. Specific evidence-based clinical management for both these conditions has recently been reviewed and information has been published in other RCOG Guidelines.[1,2] The management of couples with recurrent miscarriage is addressed in RCOG Guideline No.17, *The Investigation and Treatment of Couples with Recurrent Miscarriage*, 2003.[3] Gynaecologists should be familiar with the various diagnostic tools available to help delineate viable from non-viable pregnancy and ectopic from intrauterine pregnancy. The place of the various diagnostic modalities should be clearly defined within unit-specific algorithms. The full range of therapeutic options (expectant, medical and surgical) should be available to women who miscarry. Apart from certain specific clinical circumstances, women should be able to choose their preferred method of management. Algorithms for therapeutic intervention should outline clear pathways for each of the options available.

2. Background

Miscarriage occurs in 10–20% of clinical pregnancies[4] and accounts for 50 000 inpatient admissions to hospitals in the UK annually.[5] Historically, the majority of women who miscarried underwent 'routine' surgical uterine evacuation; that is, evacuation of retained products of conception (ERPC). In the last 5 years, standard management has changed, with more treatment on an outpatient basis and the development of more refined diagnostic techniques and therapeutic interventions. Miscarriage may be associated with significant psychological sequelae. Evidence suggests that appropriate support and counselling offered to women after miscarriage can have significant beneficial effects. Changes in medical terminology for miscarriage were recommended in 1997[6] but many textbooks and research publications continue to use historical terminology which women are likely to find distressing. Medical terminology used in association with pregnancy loss has been reviewed and appropriate changes recommended. This guideline is primarily aimed at the professionals in many disciplines who support couples at the time of pregnancy loss but we hope that those directly affected by miscarriage will also find it useful.

3. Identification and assessment of evidence

A search of Medline, Embase and Cochrane, 1999–2006, as well as RCOG publications, was undertaken to include relevant systematic reviews, meta-analyses, randomised controlled trials and other clinical trials.

The search words used were 'miscarriage', 'spontaneous abortion', 'uterine evacuation', 'mifepristone', 'prostaglandin (misprostol)' and 'progesterone'.

The definitions of the types of evidence used in this guideline originate from the US Agency for Health Care Policy and Research. Where possible, recommendations are based on, and explicitly linked to, the evidence that supports them. Areas lacking evidence are highlighted and annotated as 'good practice points'.

4. Appropriate terminology

The recommended medical term for pregnancy loss under 24 weeks is 'miscarriage'. The word 'miscarriage' should be used in clinical practice and its' use should be strongly encouraged in textbooks and scientific journals. **C**

New recommendations have been made for use of the terms 'pregnancy of unknown location' and 'intrauterine pregnancy of uncertain viability' (see section 5.2).

When talking to women, the inadvertent use of inappropriate terms such as 'pregnancy **failure**', or '**incompetent** cervix' can contribute to negative self-perceptions and worsen any sense of failure, shame, guilt and insecurity.[7] Evidence level IV

The following terms are recommended:

Previous term	Recommended term[6]
Spontaneous abortion	Miscarriage
Threatened abortion	Threatened miscarriage
Inevitable abortion	Inevitable miscarriage
Incomplete abortion	Incomplete miscarriage
Complete abortion	Complete miscarriage
Missed abortion/	Missed miscarriage
anembryonic pregnancy/	Early fetal demise
blighted ovum (these reflect different	Delayed miscarriage[8]
stages in the same process)	Silent miscarriage
Septic abortion	Miscarriage with infection (sepsis)
Recurrent abortion	Recurrent miscarriage

The European Society for Human Reproduction Special Interest Group for Early Pregnancy has published revised nomenclature for use in early pregnancy loss in order to improve clarity and consistency.[9] The following are some of the pertinent recommendations: Evidence level IV

Term	Definition
Biochemical pregnancy loss	Pregnancy not located on scan
Empty sac	Sac with absent or minimal structures
Fetal loss	Previous CRL measurement with subsequent loss of fetal heart activity (FHA)
Early pregnancy loss	Confirmed empty sac or sac with fetus but no FHA ‹12 weeks
Delayed miscarriage	As 'early pregnancy loss'
Late pregnancy loss	Loss of FHA ›12 weeks
Pregnancy of unknown location	No identifiable pregnancy on scan with positive hCG

The guideline will be particularly useful in aligning terminology used in the literature but, as the authors state, 'a modernised classification system is not able to address every clinical scenario'. Terminology that describes different types of clinical miscarriage (e.g. 'incomplete' and 'missed') remain relevant, as specific medical interventions vary depending on the type of miscarriage.

Evidence level IV

5. Service provision

5.1 What is the ideal setting for assessment of women with a potential diagnosis of early pregnancy loss?

All units should provide a dedicated outpatient early pregnancy assessment service. There are clinical and economic benefits associated with this type of service. C

Management of women with threatened or actual early pregnancy loss can be streamlined, with improvement in the efficiency of the service and quality of care. Admission to hospital can be avoided in 40% of women, with a further 20% requiring shorter hospital stay.[10]

Evidence level IV

5.2 What are the requirements for running an effective early pregnancy assessment unit service?

The National Service Framework recommends that early pregnancy assessment units (EPAU) should be generally available and easily accessible. ✓

The EPAU service should be comprehensive and ideally sited in a dedicated area with appropriate staffing. There should be direct access for GPs and selected patient groups. C

To be effective, an EPAU requires an efficient appointments system, an appropriate setting, ultrasound equipment (including transvaginal probes) and easy access to laboratory facilities for rhesus antibody testing and selective serum human chorionic gonadotrophin (hCG) and progesterone estimation.[11] The service should be available on a daily basis during the normal working week, although many units offer an additional limited service at weekends. Standardised information leaflets, referral and discharge letters should be available and regularly reviewed. Certain patient groups, such as women who have had a previous ectopic pregnancy and those with repeated or recurrent miscarriage, can be offered future access to the service by direct self-referral via the appointments system.

Evidence level IV

6. Diagnosis and investigation

6.1 What is the role of transvaginal ultrasound in the EPAU setting?

EPAUs should have access to transvaginal ultrasound with staff appropriately trained in its use. C

Transvaginal scanning will be required in the majority of women referred to an EPAU. Ultrasound assessment is particularly reliable in confirming the diagnosis of complete miscarriage (positive predictive value 98%).[12] The sonographer should be formally trained in the use of both transabdominal (TAS) and transvaginal ultrasound (TVS) and should ideally produce reports using standardised documentation, as proposed by the Joint Working Party of the Royal College of Radiologists and the Royal College of Obstetricians and Gynaecologists.[13] Ultrasound practice must conform with the recommendations of the British Medical Ultrasound Society. TAS and TVS are complementary and the appropriate modality should be used. The RCOG Special Skills Module, *Ultrasound Imaging in the Management of Gynaecological Conditions,* includes appropriate training for early pregnancy assessment under the guidance of a preceptor.

Evidence level IV

6.2 How should cases of suspected early pregnancy loss be managed in the EPAU?

EPAUs should use and develop diagnostic and therapeutic algorithms of care. In particular, these should be available for the management of suspected ectopic pregnancy, intrauterine pregnancy of uncertain viability and for pregnancy of unknown location. **C**

The use of the term 'indeterminate' is confusing and more specific definitions should be used (specifically 'pregnancy of unknown location' and 'pregnancy of uncertain viability'). ✓

'Indeterminate' is a term used in clinical practice that has led to confusion. Some practitioners have used the term to mean 'pregnancy of indeterminate site' while others mean 'pregnancy of indeterminate viability'. This present revision recommends that 'indeterminate' should no longer be used but should be replaced with the two separate terms below. Both terms should only be used after assessment by TVS.

Evidence level IV

- Pregnancy of unknown location: No signs of either intra- or extrauterine pregnancy or retained products of conception in a woman with a positive pregnancy test.
- Pregnancy of 'uncertain viability': Intrauterine sac (<20 mm mean diameter) with) no obvious yolk sac or fetus

  or

  Fetal echo <6 mm crown–rump length with no obvious fetal heart activity. In order to confirm or refute viability, a repeat scan at a minimal interval of 1 week is necessary.[14]

Even with expert use of TVS using agreed criteria, it may not be possible to confirm if a pregnancy is intrauterine or extrauterine in 8–31% of cases at the first visit. These women should be classified as having a pregnancy of unknown location.[11] In specialised scanning units, the overall incidence of pregnancy of unknown location is as low as 8–10%.

Evidence level IV

In cases of known intrauterine pregnancy, viability will be uncertain in approximately 10% of women at their first EPAU visit.

The number of cases falling into these two groups can be kept to a minimum by using a thorough and critical approach to TVS in conjunction with strict diagnostic criteria.[15] The sonographer should record whether an 'apparently empty' sac is eccentrically placed in the fundus, whether it exhibits a 'double-ring' pattern, and so on. These findings will help to delineate whether this is likely to be an intra- or extrauterine pregnancy.

Evidence level IV

A basic diagnostic algorithm has been appended in this guideline (Appendix 1) that includes the terminology described above, with the aim of encouraging a consistent approach across EPAUs. TVS is only one part of the diagnostic process in the assessment of potential early pregnancy loss. Women should be managed within a unit-specific guideline that includes use of serum hCG assay. Several published guidelines are available on which to base clinical practice.[11,16]

Evidence level IV

6.3 What is the role of serial hCG assessment in predicting pregnancy outcome?

Serial serum hCG assay is particularly useful in the diagnosis of asymptomatic ectopic pregnancy. **B**

The majority of women attending an EPAU can be managed using urine-based hCG tests. Modern monoclonal antibody based kits can detect hCG at 25 iu/l, a level reached 9 days post-conception (day 23 of a 28-day cycle).[17] Unit-specific discriminatory zones for serum hCG should be defined to help exclude possible ectopic pregnancy. At levels above 1500 iu/l, an ectopic pregnancy will usually be visualised with TVS.[11] However, the importance of levels that plateau below 1000 iu/l must be recognised. In these cases, pregnancy of unknown location and miscarriage are both possible outcomes. The potential for rarer diagnoses, such as gestational trophoblastic disease or cranial germ cell tumour, must be considered although, in these cases, serum hCG levels are likely to be greater than 1000 iu/l.[11] In a study of 152 women with a history and TVS findings suggestive of complete miscarriage, serial hCG assessment revealed a 5.9% incidence of ectopic pregnancy.[18]

Evidence level III

Early ectopic pregnancy can be difficult to diagnose and the RCOG Study Group concluded that access to serial serum hCG estimation is essential, with results available within 24 hours.[6] Staff must be familiar with what is an acceptable normal rise in 48 hours. Although a doubling of hCG titre is often expected, this can vary depending on gestation.

Serum hCG levels need caution in interpretation. In cases of twin pregnancy or heterotopic pregnancy, a suboptimal rise may be misleading.

Women with miscarriage or ectopic pregnancy who are managed expectantly may also require serial serum hCG monitoring.

6.4 Does serum progesterone assay have a role in predicting pregnancy outcome?

Serum progesterone can be a useful adjunct when ultrasound suggests pregnancy of unknown location. TVS, serial serum hCG levels and progesterone may all be required in order to establish a definite diagnosis. **B**

When ultrasound findings suggest pregnancy of unknown location, serum progesterone levels below 25 nmol/l are associated with pregnancies subsequently confirmed to be non-viable.[11,19–22] However, care must be taken in terms of active intervention and uterine evacuation should not be undertaken based on a low initial progesterone. Viable pregnancies have been reported with initial levels less than 15.9 nmol/l. In the presence of pregnancy of unknown location, a serum progesterone less than 20 nmol/l predicts spontaneous pregnancy resolution with a sensitivity of 93% and specificity of 94%. One advantage is that the need for formal uterine evacuation can be reduced if a policy of expectant management is adopted. Levels above 25nmol/l are 'likely to indicate' and above 60 nmol/l are 'strongly associated with' pregnancies subsequently shown to be normal. Overall, it is not possible to define a specific discriminatory value for a single serum progesterone result that will allow absolute clinical confirmation of viability or non-viability.

6.5 Should all women with early pregnancy loss receive anti-D immunoglobulin?

Non-sensitised rhesus (Rh) negative women should receive anti-D immunoglobulin in the following situations: ectopic pregnancy, all miscarriages over 12 weeks of gestation (including threatened) and all miscarriages where the uterus is evacuated (whether medically or surgically). **B**

Anti-D immunoglobulin should only be given for threatened miscarriage under 12 weeks gestation when bleeding is heavy or associated with pain. It is not required for cases of complete miscarriage under 12 weeks of gestation when there has been no formal intervention to evacuate the uterus. **C**

Discharge documentation from the EPAU should clearly state whether or not anti-D was required/ given. ✓

Several routine antenatal blood tests may be checked in the EPAU. Knowledge of Rh antibody status is not required for **all** women with threatened or actual miscarriage. For many women, the risk of Rh sensitisation is negligible. However, Rh status should be available promptly for certain groups, to allow appropriate administration of anti-D immunoglobulin in non-sensitised Rh negative women.[23] The specific groups are highlighted in the recommendations for this section. Anti-D immunoglobulin should be given in any case where there is clinical doubt and when the uterus is evacuated either surgically or medically.

Evidence level IV

7. Treatment

7.1 Which women should be screened for genital tract infection?

Screening for infection, including *Chlamydia trachomatis*, should be considered in women undergoing surgical uterine evacuation. C

Consider vaginal swabs to exclude bacterial vaginosis if clinically indicated. ✓

Women with *C. trachomatis*, *Neisseria gonorrhoea* or bacterial vaginosis in the lower genital tract at the time of induced abortion are at an increased risk of subsequent pelvic inflammatory disease.[24] Until further research is published, it is recommended that women undergoing surgical evacuation should at least be screened for *C. trachomatis*.

Evidence level IV

7.2 Should prophylactic antibiotics be given prior to surgical evacuation?

There is insufficient evidence to recommend routine antibiotic prophylaxis prior to surgical uterine evacuation. A

Antibiotic prophylaxis should be given based on individual clinical indications. ✓

A randomised trial of prophylactic doxycycline in curettage for incomplete miscarriage did not demonstrate an obvious benefit but the study was of insufficient power to detect a clinically meaningful change in infectious morbidity. Until further research is available, antibiotic prophylaxis should only be given based on individual clinical indications.

Evidence level Ib

7.3 When should surgical uterine evacuation be used?

Surgical uterine evacuation should be offered to women who prefer that option. Clinical indications for offering surgical evacuation include: persistent excessive bleeding, haemodynamic instability, evidence of infected retained tissue and suspected gestational trophoblastic disease. C

Surgical uterine evacuation (ERPC) has been the standard treatment offered to women who miscarry. Until recently, up to 88% of women who miscarried were offered ERPC. This was based on an assumption that retained tissue increases the risks of infection and haemorrhage and would not be passed spontaneously. It remains the treatment of choice if there is excessive and persistent bleeding, if vital signs are unstable or in the presence of retained, infected tissue. Studies suggest that these complications affect less than 10% of women who miscarry.[25] At least 34% of women express a 'strong' preference for a surgical approach to uterine evacuation.[26]

Evidence level IV

7.4 How should surgical uterine evacuation be performed?

Surgical uterine evacuation for miscarriage should be performed using suction curettage. **A**

Consideration should be given to offering surgical evacuation techniques under local anaesthesia or sedation for those women who prefer that approach. **C**

Vacuum aspiration has been used as the method of choice for management of miscarriage where there is an intact intrauterine sac. A Cochrane review concluded that vacuum aspiration is preferable to sharp curettage in cases of incomplete miscarriage. Two trials were included. Vacuum aspiration was associated with statistically significantly decreased blood loss (mean difference –17 ml, 95%CI –24 to –10ml), less pain (RR 0.74, 95% CI 0.61 to 0.90) and shorter duration of procedure (mean difference –1.2 minutes, 95% CI –1.5 to –0.87 minutes).[27] Routine use of a metal curette after suction curettage is not required. Use of oxytocin is associated with a statistically significant (but not clinically significant) difference in median blood loss (17.6 ml versus 24.5 ml).[28] Where infection is suspected, delaying surgical intervention for 12 hours is recommended to allow intravenous antibiotic administration.

Evidence level Ia

Reported serious complications of surgery include perforation, cervical tears, intra-abdominal trauma, intrauterine adhesions and haemorrhage. The incidence of serious morbidity using a similar surgical technique in induced abortion is 2.1%[29] with a mortality of 0.5/100 000.[30]

Evidence level III

The advantages of prostaglandin administration prior to surgical abortion are well established, with significant reductions in dilatation force, haemorrhage and uterine/cervical trauma. There is no randomised evidence to guide practice in cases of first-trimester miscarriage, particularly in the presence of an intact sac. Practitioners may consider oral or vaginal cervical preparation based on individual patient circumstance.

Curettage under local anaesthesia is well described. It is rarely used in the UK but is used commonly in the USA[31] and many European, Asian and African countries. In a UK study of 58 women with incomplete and missed miscarriage, uterine evacuation was achieved in all cases using a manual vacuum aspiration technique under systemic analgesia or patient-controlled anaesthesia. Levels of patient satisfaction and acceptability were high.[32] The technique is appropriate for some women and its wider use should be considered.

Evidence level III

7.5 What are the alternatives to surgical uterine evacuation for miscarriage?

Medical methods are an effective alternative in the management of confirmed first-trimester miscarriage. **A**

Protocols should be developed locally with selection criteria, therapeutic regimens and arrangements for follow-up. ✓

To avoid unnecessary anxiety, women should be informed that bleeding may continue for up to 3 weeks after medical uterine evacuation. ✓

Medical evacuation is an alternative technique that complements but does not replace surgical evacuation. Its availability has led to an improvement in choice for women who miscarry.[33] In a partially randomised study comparing surgical and medical evacuation, 20% of women expressed a strong preference for medical management.[34] The main reasons given for their choice were 'avoidance of general anaesthesia' and the feeling of being 'more in control.'

Evidence level Ib

Various medical methods have been described using prostaglandin analogues (gemeprost or misoprostol) with or without antiprogesterone priming (mifepristone).[34–43]

Evidence level Ib

Efficacy rates vary widely from 13% to 96%, influenced by many factors. These include the type of miscarriage, sac size and whether follow-up is clinical or involves ultrasound. Total dose, duration of use and route of administration of prostaglandin are also important factors. Higher success rates (70–96%) were associated with incomplete miscarriage,[26,35] high-dose misoprostol (1200–1400 micrograms),[26,41] prostaglandins administered vaginally[39,43] and clinical follow-up without routine ultrasound.[26,34,35]

Evidence level Ib

Misoprostol is a cheap, highly effective prostaglandin analogue that is active orally and vaginally. Evidence varies in some studies, with one randomised controlled trial suggesting that the vaginal route may be more effective[39] and two further randomised controlled trials suggesting that the oral, sublingual and vaginal routes may be equally effective.[44–46] In one study of 80 women, missed miscarriages were managed with either oral or sublingual misoprostol and showed success rates of 87.5% (95%CI 74–95%) in both groups.[44] The second randomised controlled trial of 200 women, managed with either oral or vaginal misoprostol, also showed no significant difference in successful outcome (oral 89% versus vaginal 92.9%).[45]

Evidence level Ib

In missed miscarriages (closed cervix and intact sac), effective regimens involve a higher dose of prostaglandin with longer duration of use[32] or, alternatively, priming with antiprogesterone.[26,34] One study used TVS features 12 hours after medical evacuation for missed miscarriage, to try to predict successful outcome ('no further intervention required').[46] The absence of a gestational sac was the main criterion that predicted successful outcome (86%).

Evidence level Ib

Incomplete miscarriage is usually managed with prostaglandin alone. One randomised trial showed no statistical difference in efficacy between surgical and medical evacuation for incomplete miscarriage and for early fetal demise at gestations less than 71 days or sac diameter less than 24mm.[42] Patient acceptability for both methods was equal. There was a reduction in clinical pelvic infection after medical evacuation (7.1 versus 13.2%, $P < 0.001$). With increasing gestation and sac size, acceptability of medical methods fell to 85%.

Evidence level Ib

Medical evacuation has potential economic benefits for the NHS, with an average cost saving of £50/case.[47] Successful evacuation can be achieved with medical methods and selection criteria should be developed in individual units.

Evidence level Ib

Medical management may be undertaken successfully on an outpatient basis. Consideration should be given to offering this approach, depending on the clinical situation and patient choice.[48] In one randomised controlled trial comparing medical and surgical approaches, medical management with misoprostol achieved uterine evacuation in 84% of cases.[49,50] An observational study confirmed that women would prefer misoprostol over surgical curettage if complete evacuation rates exceeded 65%.[50]

Evidence level Ib

An increase in pain and bleeding with medical methods may be a negative factor influencing acceptability.[51] However, higher levels of patient acceptability have been reported with medical versus surgical methods.[43] Bleeding can continue on each day for the 14 days following medical evacuation [52] and for up to 21 days.[42]

Evidence level Ib

The published literature on a wide range of therapeutic regimens is summarised in Appendix 2.

Expectant management is another effective method to use in selected cases of confirmed first-trimester miscarriage.

A

Expectant management is an effective and acceptable method to offer women who miscarry. Patient counselling is particularly important for those women **with an intact sac** who wish to adopt an expectant approach. They should be aware that complete resolution may take several weeks and that overall efficacy rates are lower. They may wish to consider a medical approach or to commence expectant management with the option of surgical evacuation at a later date if required. Expectant management for incomplete miscarriage is highly effective.

Evidence level Ib

Observational and controlled trials of expectant compared with surgical or medical management also show wide variations in reported efficacy (25–100%).[53-62] Similar factors affect the success rates. These factors include the type of miscarriage, duration of follow-up and whether ultrasound or clinical assessment was used for review. A low serum progesterone level can be used to predict those pregnancies which are most likely to resolve spontaneously.[63]

Evidence level Ib

Ultrasound criteria used to define 'retained products' varies between studies. One study included patients with an 'AP tissue diameter of 15–50 mm' with ultrasound review at 3 days (efficacy 71%),[53] while another included all those with an 'AP tissue diameter < 50 mm' and reviewed patients clinically on three occasions up to 6 months (efficacy 100%).[55] The mean anteroposterior (AP) diameter of tissue in those managed expectantly in the latter study was only 11 mm, which would have been defined as 'complete miscarriage' by the former study and therefore would have been excluded. When ultrasound assessment of the uterine cavity shows heterogenous shadows with a maximum AP diameter of 15 mm or less, genuine retained products are less likely to be confirmed histologically. [12] These could, of course, include some cases of 'incomplete miscarriage' but are best managed conservatively as there is a trend towards a lower complication rate compared with surgical management (3.0 versus 5.8%, $P = 0.06$).[57]

Evidence level Ib

Several randomised trials have compared expectant with medical or surgical management. In a trial with 122 women, efficacy rates were confirmed at 6 weeks of 47% (expectant) and 95% (surgical).[59] After 7 days, 37% of women managed expectantly had achieved a complete miscarriage. A meta-analysis of 13 trials comparing expectant with medical management[61] showed that the type of miscarriage was a significant factor affecting the efficacy with an expectant approach. For missed miscarriage, complete evacuation rates for expectant versus surgical management were 28% (49/173, range 14–47%) and 81% (242/298, range 60–83%), respectively. For women with incomplete miscarriage, the rates were 94% (31/33, range 80–100%) and 99% (75/76, range 99–100%).

Evidence level Ia

Concerns have been raised about the infective risks of non-surgical management[56] but published data suggest a reduction in clinical pelvic infection and no adverse affects on future fertility.[26,55,64]

Evidence level Ia

Future work aims to clarify which cases of miscarriage are most likely to resolve spontaneously. This involves the use of novel serum markers including insulin growth factor-binding protein 1 (IGFBP-1), inhibin A and inhibin pro a-C R1 to try to predict which pregnancies will resolve spontaneously.[65]

Evidence level Ib

Medical and expectant management should only be offered in units where women can access 24-hour telephone advice and emergency admission if required.

✓

Expectant management is often followed by minimal bleeding, as any retained tissue will usually undergo resorption. Occasionally, the passage of tissue may be associated with heavy bleeding. In cases of missed miscarriage, managed using antiprogesterone/prostaglandin combinations, one-third of women will bleed or miscarry in the priming phase after antiprogesterone.[26] It is

Evidence level IV

important that all women undergoing medical or conservative management have direct telephone access to ward staff for advice and support. Emergency beds must be available should they require admission.

Evidence level IV

7.6 What are the advantages of arranging histological examination of tissue passed at the time of miscarriage?

Tissue obtained at the time of miscarriage should be examined histologically to confirm pregnancy and to exclude ectopic pregnancy or unsuspected gestational trophoblastic disease. **C**

Heath *et al.* suggested that there is no obvious benefit in routine histological investigation of tissue obtained from cases of pregnancy termination and miscarriage.[66] However, within a subgroup of 468 undergoing surgical evacuation for miscarriage, there were two cases of ectopic pregnancy diagnosed 25 and 28 days post-evacuation (an incidence of 0.42%). Neither was suspected on scan but histology had reported 'decidua only'. In view of the maternal risks associated with ectopic pregnancy and molar pregnancy, it is recommended that practitioners should always consider sending tissue obtained at the time of uterine evacuation (medical or surgical) for histological examination. This may confirm the diagnosis of miscarriage and can help to exclude ectopic pregnancy or gestational trophoblastic disease.[6]

Evidence level IV

Women who miscarry at home and are admitted to hospital should be advised to take with them any tissue passed so that histological examination can be arranged. Alternatively, the attending practitioner should arrange for the appropriate examination.

Information on the sensitive disposal of fetal remains can be obtained from the RCOG Good Practice Guideline No. 5, *Disposal Following Pregnancy Loss Before 24 Weeks of Gestation*,[67] the Stillbirth and Neonatal Death Society's (SANDS) *Pregnancy Loss and the Death of a Baby: Guidelines for Professionals* (1995) and the Institute of Burial and Cremation Administration (IBCA) *Policy Document: Disposal of Fetal Remains* (2001). The Royal College of Nursing guidance, *Sensitive Disposal of all Fetal Remains, Guidance for Nurses and Midwives* is also available at: www.rcn.org.uk/members/downloads/disposal_fetal_remains.pdf.

8. Psychological aspects of early pregnancy loss

8.1 Is there potential benefit from support and follow-up after pregnancy loss?

All professionals should be aware of the psychological sequelae associated with pregnancy loss and should provide support, follow-up and access to formal counselling when necessary. Appropriate support can result in significant positive psychological gain. **A**

Plans for follow-up should be clearly recorded in the discharge letter from the EPAU or ward. ✓

A system must be in place for informing all relevant primary care professionals (including the community midwife) in cases of pregnancy loss. ✓

The negative psychological impact of early pregnancy loss can be both severe and protracted and affects both women and their families.[68-70] Many of the specific issues that women think are important are discussed by Moulder.[71] Information should be made available which highlights the options available for appropriate and sensitive disposal of fetal tissue. This is highlighted in RCOG Good Practice Guideline No. 5.[67] Each couple will have different needs and these should be identified to facilitate their grieving process.

Evidence level III

A randomised trial assessing the effects of caring-based counselling on women's emotional wellbeing in the first year after miscarriage found a significant beneficial effect with reduction in overall emotional disturbance, anger and depression.[72] A continuing awareness of the potential effects of miscarriage is required, with a willingness to involve appropriate support and counselling services when needed. The needs of the partner should also be considered. The opportunity for follow-up should be offered to all women after pregnancy loss but unfortunately this does not always occur. In a recent national audit study, 38% of women reported that there had been no offer of or arrangement for follow-up.[73] Follow-up can involve any member of the multidisciplinary team based in hospital or community practice.

Evidence level Ib

8.2 Should we encourage patient choice in deciding which intervention to use to achieve uterine evacuation?

In terms of therapeutic intervention, patient choice should be encouraged, as it is associated with positive quality-of-life outcomes.

A

Objective assessment of psychological morbidity in a controlled trial of expectant versus surgical management of miscarriage revealed no differences related to the procedure itself.[74] However, women with miscarriage who chose their own treatment had the best health-related quality-of-life (HRQL) assessments compared with women who were randomised to one or other treatment modality.[75] This confirms the importance of allowing and encouraging patient choice in the management of early miscarriage.

Evidence level Ib

9. Auditable standards

- Patient satisfaction with elements of the EPAU service.
- Appropriate use of anti-D prophylaxis.
- Appropriate screening for genital tract infection.
- Appropriate use of serial serum hCG/serum progesterone assessment.
- Uptake rates for medical, surgical and expectant interventions.
- Complications of the various interventions (including failure rates).
- Involvement of patient in choice of treatment.
- Number of visits required to reach definitive diagnosis.
- Standards of documentation.

SUPPORT GROUP/WEBSITE INFORMATION

Association of Early Pregnancy Units. Website: **www.earlypregnancy.org.uk**.

Miscarriage Association (Registered Charity No. 1076829) c/o Clayton Hospital, Northgate, Wakefield, West Yorkshire WF1 3JS. Telephone: 01924 200799.

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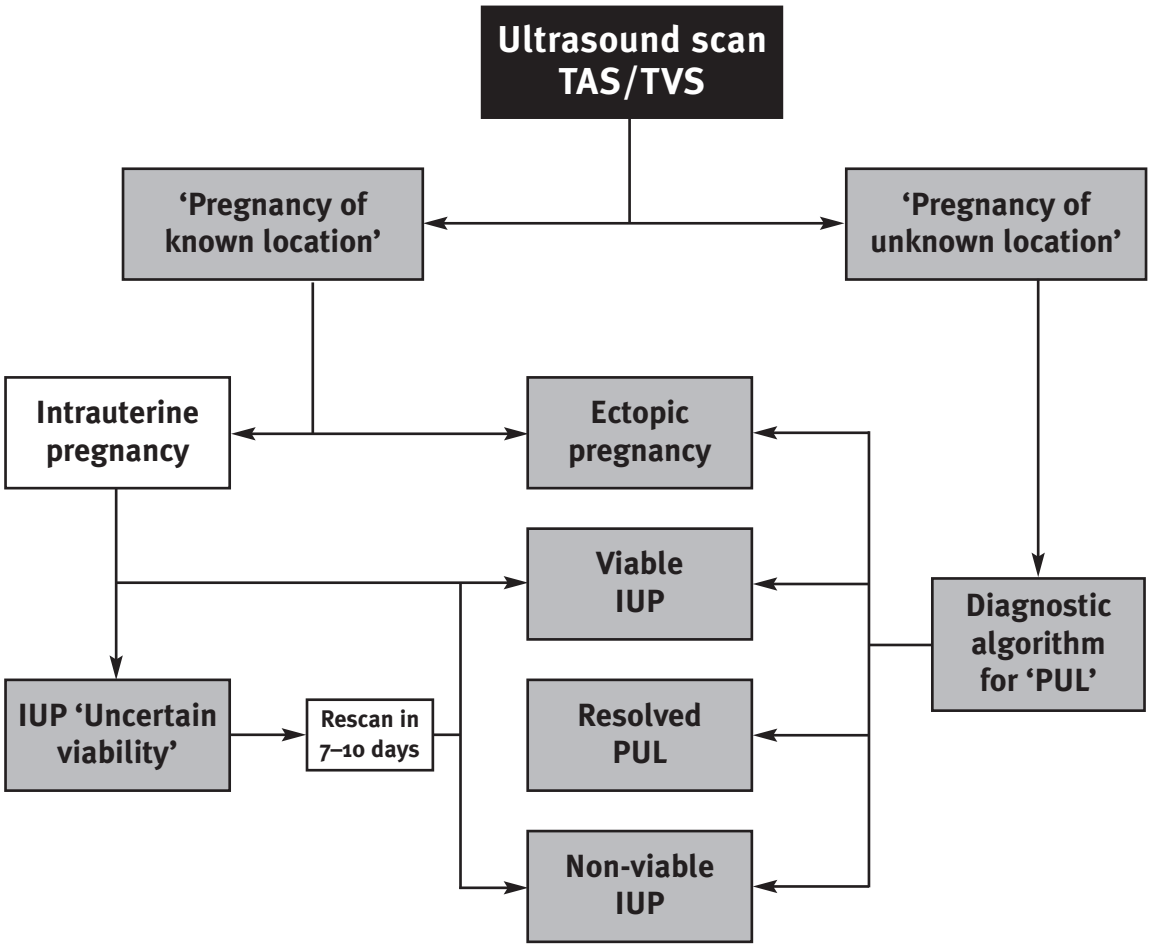
APPENDIX 1.
Basic diagnostic algorithm for early pregnancy loss



KEY

IUP Intrauterine pregnancy
PUL Pregnancy of unknown location
TAS Transabdominal scan
TVS Transvaginal scan

APPENDIX 2.
Summaries of studies evaluating therapeutic regimens and outcome for early pregnancy

Ref.	Year	Women (*n*)	Treatment	Success rate	Adverse effects
36	1994	132	1 mg vaginal gemeprost 3-hourly until products were passed. Max. 5 doses	60/132 (45%), of which 2 later underwent ERPC	Reported adverse effects of gemeprost: abdominal pain (24.2%), nausea (17.4%), diarrhoea (11.3%), postural hypotension (1.4%), drowsiness (0.7%)
38	1995	141	400 micrograms oral misoprostol 4-hourly × 3 doses	88/141 (62%); 53/141(38%) had evidence of retained POC and underwent ERPC	
41	1997	225	1200 micrograms oral misoprostol divided into 3 doses/day for up to 2 days	107/225 (48%) within 24 hours; 148/214 (69.6%) over 48 hours	Of the 225, 2 required ERPC for excessive bleeding, 2 developed fever. At follow-up, 1 had ectopic, 3 underwent ERPC for continuing bleeding, 2 had pelvic infection treated with antibiotics: complication rate 6/217 (3%)
39	1997	20	Randomised to 400 micrograms oral misoprostol (12/20) or 800 micrograms vaginal misoprostol (8/20). This was repeated 24 hrs later if GS still present on TVS		Common adverse effects: nausea, vomiting, diarrhoea
52	2004	80	800 micrograms vaginal misoprostol randomised to dry or moistened (with 2 ml saline). Max. 2 doses	62/80 (85%) had complete miscarriage without ERPC. No difference between dry/moistened misoprostol groups	
37	1995	50	Randomised to 1 dose 400 micrograms oral misoprostol or ERPC	Misoprostol group 3/23 (13%) ERPC group 26/27 (97%)	Significant fall in Hb in misoprostol group after treatment. No significant difference in ERPC group
42	2001	80	Randomised to 1 dose 800 micrograms vaginal misoprostol or ERPC	Missed miscarriage 20/26 (77%) Incomplete 13/14 (93%) 40/40 (100%) ERPC	Nausea significantly more common in ERPC group. ERPC group had shorter duration of pain but required more analgesia. 2 in ERPC group had offensive discharge and were given antibiotics by GP
34	1992	60	600 mg oral mifepristone followed 48 hours later by 600 micrograms oral misoprostol then another 200 micrograms oral misoprostol 2 hours later	56/59 (95%) – 8/59 (14%) after mifepristone alone 43/59 (73%) after misoprostol 600 micrograms 5/59 (8%) after second misoprostol dose 3/59 (5%) failed and had ERPC	Antiemetics required by 5 and 7 reported diarrhoea

Ref.	Year	Women (*n*)	Treatment	Success rate	Adverse effects
32	2004	58	Manual vacuum aspiration with 800 micrograms vaginal misoprostol at least 3 hours prior to the operation to ripen the cervix	57/57 (1 who chose general anaesthetic was excluded from study)	1/57 had postoperative intrauterine infection with group B streptococcus that responded to antibiotics
50	2006	64	Informed that misoprostol available immediately in outpatient setting, that it consisted of 4 x 200-microgram tablets administered vaginally by speculum repeated after 1 day if evacuation not complete. Also informed of adverse effects, off-label use and analgesia; risk of complications of ERPC; performed under general anaesthesia. Success of ERPC set at 100% and initially 100% for misoprostol, reduced in 5% steps to 10%. Women asked at each step whether they preferred misoprostol or ERPC		
35	1993	44	0.5 mg IM sulprostone or 400 micrograms oral misoprostol (after sulprostone was withdrawn by manufacturer)	41/43 (95%)	
47	1996	437	Medical management: missed/anembryonic 200 mg mifepristone followed 36–48 hours later by 3 sequential doses oral misoprostol; incomplete 2 sequential doses oral misoprostol. Surgical management: ERPC	Medical management 171/186 (92.5%) relative to 98.4% Incomplete miscarriage 100%	
51	1997	29	Randomised to ERPC (12/29) or medical management (17/29). Medical management for incomplete miscarriage 1 mg gemeprost pessary. Missed miscarriage, 200 micrograms mifepristone followed by 1 mg gemeprost 36–48 hours later		Surgical group had less pain, decreased duration and severity of bleeding and fewer hospital attendances but greater drop in Hb concentration than medical group. One complication occurred in each group: surgical 1 uterine perforation, medical 1 laparoscopy to exclude ectopic converted to laparotomy to investigate blood in pouch of Douglas (no pathology found)

Ref.	Year	Women (*n*)	Treatment	Success rate	Adverse effects
45	2004	200	4 × 200 micrograms misoprostol orally (101) or vaginally (99). 2 days later if substantial debris remained in uterus on ultrasound option given of ERPC or waiting for a further 5 days to give additional time for evacuation	Oral group 89/100 (89%) Vaginal group 91/98 (92.9%)	Pain/cramps, heavy bleeding, diarrhoea, fever/chills, vomiting
40	1997	31	400 mg oral mifepristone followed by 400 micrograms oral misoprostol 36 hours later	16/31 (52%)	4/31 (13%) had emergency ERPC for severe pain or bleeding. 1 required treatment for PID after ERPC
46	2005	44	600 micrograms vaginally 4-hourly. Max. 3 doses	4/44 (9%) ERPC on day 1 due to visible gestation sac. 38/44 (86%) by 21 days	2/44 (5%) ERPC for symptoms before follow-up
44	2003	80	Randomised to 600 micrograms sublingual or vaginal misoprostol 3-hourly, max. 3 doses	35/40 (87.5%) in both groups. 82.5% (sublingual group) and 75% (vaginal group) reported passage of POC within 24 hours	Nausea, vomiting, diarrhoea, dizziness, fatigue, lower abdominal pain, headache, chills, fever (≥ 38ºC). Diarrhoea and fatigue significantly more common in sublingual group
48	2002	50	Randomised to 800 micrograms misoprostol or placebo administered vaginally. Repeated at 24 hours if no satisfactory response	Misoprostol: 21/25 (84%) with 10/25 (40%) after 1 dose. Placebo: after 1 week 4/25 (16%) had complete evacuation and 2/25 (8%) had incomplete evacuation	Misoprostol group: 1 had severe gastrointestinal adverse effects and 2 had severe pain not relieved by codeine. 4/25 (16%) later required ERPC for prolonged or heavy bleeding or persistent positive pregnancy test
43	1998	25	200 micrograms vaginal misoprostol 4-hourly to total dose of 800 micrograms or passage of POC	22/25 (88%): 5/25 (20%) after 1 dose; 13/25 (52%) after 2 doses; 4/25 (16%) after 3 doses; 0/25 after 4 doses. 3/25 (12%) failed after 4 doses and had ERPC	1 ERPC after passage of POC for heavy bleeding
49	2005	652	Randomised to 800 micrograms vaginal misoprostol on day 1 (repeated on day 3 if POC still present) or ERPC (57% manual, 43% electric vacuum aspiration) ratio 3:1	Misoprostol: 412/488 (84%); 346/488 (71%) after 1 dose ERPC: 143/148 (97%)	Significant drop in Hb > 3 g/dl more common in misoprostol group (5% vs. 1%). Misoprostol group more likely to report nausea, vomiting, abdominal pain and more severe pain

APPENDIX 3

Classification of evidence levels

Ia Evidence obtained from meta-analysis of randomised controlled trials.

Ib Evidence obtained from at least one randomised controlled trial.

IIa Evidence obtained from at least one well-designed controlled study without randomisation.

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grades of recommendations

A Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)

B Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)

C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

Good practice point

✓ Recommended best practice based on the clinical experience of the guideline development group.

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