

# OBSTETRICS AND GYNAECOLOGY

**CLINICAL PRACTICE GUIDELINE** 

## **Early Pregnancy Complications**

(including miscarriage, pregnancy of unknown location, ectopic and caesarean scar pregnancy):

Management of [NEW]

Scope (Staff): WNHS Obstetrics and Gynaecology Directorate staff  Scope (Area): WNHS Obstetrics and Gynaecology Directorate staff and clinical areas	This document should be read in conjunction with the <u>Disclaimer</u> .							
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The Women and Newborn Health Service (WNHS) endorses the use of this Clinical Practice Guideline in conjunction with the **Royal Australian and New Zealand College of Obstetricians and Gynaecologists** Miscarriage, Recurrent Miscarriage and Ectopic Pregnancy (C-GYN 38) Clinical Guideline(2025):

https://ranzcog.edu.au/wp-content/uploads/Miscarriage-Ectopic-Pregnancy.pdf

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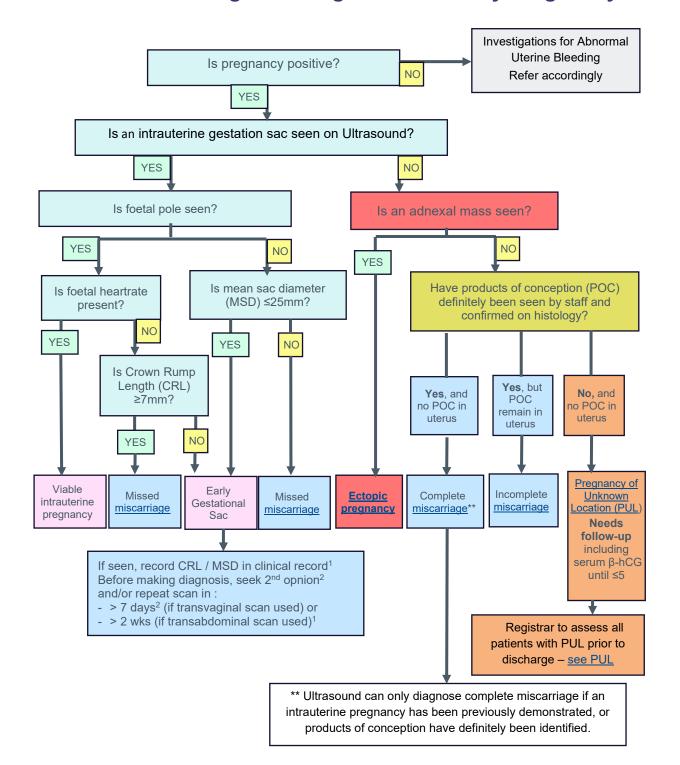
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## Flow Chart 1: Bleeding / Pain Algorithm for Early Pregnancy



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## Early Pregnancy Complications - pain, bleeding and miscarriage

#### Overview

Bleeding and pain are common symptoms during pregnancy. Although many pregnancies will progress normally, pain and bleeding may be the initial signs of pregnancy complications and require a thorough assessment. Early miscarriage affects between 10-25% of known pregnancies depending on the gestation<sup>(1)</sup>.

#### **Current terminology and definitions**

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Miscarriage	Spontaneous pregnancy loss under 20 weeks' gestation.
Second trimester pregnancy loss	Miscarriage at ≥14 weeks & < 20 weeks' gestation.
Complete miscarriage	Expulsion of all products of the pregnancy (fetus / embryo and trophoblast) with resolution of symptoms.
Incomplete miscarriage	Retention of some products of the pregnancy (fetus / embryo / trophoblast), usually accompanied by PV bleeding, though may still be diagnosed after return to normal cycling.
Missed miscarriage	Presence of a complete but non-viable pregnancy without onset of significant symptoms of miscarriage (heavy bleeding or pain); sometimes referred to as asymptomatic pregnancy loss.
Threatened miscarriage	Vaginal bleeding and uterine cramping in the setting of a known pregnancy under 20 weeks' gestation
Septic miscarriage or abortion	Onset of signs and symptoms of infection of pregnancy tissue within the uterus (whether a complete sac or following partial expulsion).
Recurrent Pregnancy Loss	≥2 pregnancy losses.
Induced abortion	Use of a medical or surgical procedure to end a pregnancy.
Embryonic demise	An embryo with no heartbeat in one of 3 situations:  1. Previous scan confirmed heartbeat.  2. CRL >7 mm at first scan.  3. CRL <7 mm at second scan with adequate time interval between scans.
Fetal demise	Absence of heartbeat at CRL >10-week size.
Intrauterine sac	< 20mm mean diameter with no obvious yolk sac or fetus.
Uncertain viability	An intrauterine gestational sac (IUGS) of <25mm in mean diameter with no obvious yolk sac, or the presence of a fetus or fetal echo of <7mm CRL with no fetal heartbeat.
	A repeat scan at a minimum interval of 1 week is necessary <sup>(2)</sup> .

#### **Assessment**

First consider risk factors for haemodynamic instability - presence of heavy bleeding (1 pad/hr for  $\geq$  2 hours), passage of large clots, presyncope, severe pain. These symptoms indicate need for more urgent assessment including observations, IV cannulation, G&H +/- crossmatch, FBP, coagulation studies +/- IV fluids. Serum  $\beta$ -hCG is not an urgent investigation but should be requested at the same time.

#### **History**

- Pregnancy investigations already performed (Urine  $\beta$ -hCG, Serum  $\beta$ -hCG, scans) where, when and what are the results?
- LMP, cycle length & regularity, use of contraceptive hormones just prior to pregnancy
- Timing of first confirmation of pregnancy (by urine or blood) to estimate minimum GA
- Symptoms of active miscarriage extent of bleeding, presence of crampy, period-like pain, passage of large clots or suspected pregnancy tissue, light-headedness.
- Symptoms of ectopic pregnancy bleeding may be lighter but more prolonged (for tubal ectopic), pain may be sharp, unilateral or shoulder-tip, light-headedness.
- Note timing and degree of bleeding
- Note nature of pain, presence of exacerbating or relieving factors
- Risk factors for miscarriage or ectopic age, previous History, caesarean section, pelvic inflammatory disease (PID), delay to conception, fertility assistance (past or current)
- Do they still feel pregnant? Falling β-hCG leads to loss of nausea & breast tenderness
- Patients medical history, surgical history, medications, and Allergies
- Blood group (if known)

#### **Examination**

- Record vital signs and reassess regularly when haemodynamic stability is uncertain
- Shock and syncope may indicate massive haemorrhage due to a ruptured ectopic pregnancy requiring emergency surgery. Cervical shock due to products of conception in the cervix should also be considered.
- Fever may indicate septic miscarriage.
- Record height and weight on medication charts.
- Abdominal palpation location and degree of tenderness, signs of peritonism such as rebound tenderness and rigidity
- Speculum examination (with chaperone) extent of blood loss, alternative origins of blood (vaginal or external cervical), cervical pathology, open cervix, presence of tissue passing through the cervical canal. Removing visible pregnancy tissue can slow the rate of bleeding and reduce the pain.
- Bi-manual pelvic examination (with chaperone) size and location of uterus, presence of adnexal pain or cervical excitation (pain with movement of the cervix).

#### Investigation

IV access (ideally 16G if heavy bleeding); IV fluids if indicated.

- Test β-hCG in urine if any doubt about pregnancy, otherwise Serum β-hCG. Note that when intra-uterine pregnancy has already been demonstrated by ultrasound, Serum βhCG adds little or nothing to the assessment.
- FBC, coagulation studies, UEC (if significant bleeding is present)
- Blood group + Ab screen (and hold if heavy bleeding) Anti-D is given according to the Transfusion Medicine policy - <u>WNHS Transfusion Medicine – Haematology Protocol –</u> Use of RhD Immunoglobulin (RhD Ig) in pregnancy
- Consider serum progesterone after discussion with a senior doctor (Refer to the <u>Pregnancy of Unknown Location</u> section within this guideline)
- Any tissue passed from the cervix should be sent for histopathology to confirm presence of chorionic villi and exclude GTD.
- Note that genetic assessment of miscarried pregnancies (to determine a possible cause) is not undertaken routinely. Cytogenetic analysis of pregnancy tissue following miscarriage is not routinely recommended as there is no increase in genetic abnormalities in those with recurrent miscarriage. Genetic abnormalities may occur relatively more often in sporadic miscarriage but are unlikely to change clinical management in subsequent pregnancies<sup>(3)</sup>.
- Consider/offer screening for STIs based on history.

#### **Imaging**

- Transabdominal +/- transvaginal ultrasound is usually required to complete assessment
  of early pregnancy bleeding or pain, but may not be required immediately if the patient is
  stable
- If the patient is stable and the pregnancy is known to be intra-uterine, the urgency is usually emotional, rather than medical (allowing for the rare situation of heterotopic pregnancy).
  - However, transabdominal PoCUS (Point-of-Care Ultrasound), by credentialled staff, may be sufficient to reassure the patient that a heartbeat (or at the least the pregnancy sac) is still present.
- If no heartbeat is visible, either proceed to transvaginal PoCUS (if appropriate staff are available), refer to Early Pregnancy Assessment Service (EPAS) or refer to Medical Imaging (if timely EPAS appointment is not available). If the patient already has plans for, or has easy access to, a community ultrasound, and would prefer to continue care in the community, this is appropriate. Community ultrasound can be also followed up in EPAS (book as GYN 551).
- If the patient is stable and ectopic is not suspected, but no prior scans have been performed, referral for repeat Serum β-hCG in 48 hours or for imaging if appropriate (Serum β-hCG >1500 or clinically indicated) is recommended.
- If ectopic pregnancy is suspected based on history, examination or findings from previous scans, urgent scan should be undertaken. If the patient is stable this can be done in the morning after an overnight admission. Please refer to the <u>Ectopic</u> <u>Pregnancy section</u> of this Guideline.
- Clinical management of unstable patients may be aided by immediate ultrasound if available (either PoCUS or within Medical Imaging) but appropriate surgical intervention should not be delayed by lack of imaging.

## **Outcomes of Assessment and Management**

## Live intra-uterine pregnancy

#### **Diagnosis**

- Presence of an intra-uterine gestational sac (IUGS) with a live embryo or fetus.
- A heartbeat is usually visible by transvaginal ultrasound in an embryo of 2 mm CRL (5w3d) but may not be visible until 6 mm CRL.
- Transabdominal ultrasound assessment may be hampered by early gestation or other anatomical structures (uterine retroversion, fibroids, abdominal wall scarring, high BMI) but, if a heartbeat is visible, progression to TV assessment is not required unless the pregnancy dating is also in question and TA views are inadequate for this.
- The normal heart rate is often 80-100 bpm at 5w3d, increasing to 160-180+ bpm by 7-8 weeks. Therefore, reference to 'bradycardia' should be made cautiously or not at all under 7 weeks. If there is doubt about the HR, a further scan can be offered in 2 weeks.
- The pregnancy number should be confirmed and, if a multiple pregnancy is present, chorionicity established. In the setting of monochorionic twins, the amniotic (dividing) membranes are not clear until the amniotic fluid begins to expand around each or both twins, at 7-8 weeks.
- If a regular cycle with known LMP is present, the GA should be taken from the LMP (adjusted for cycle length) unless the GA by CRL is at least 5 days different.
- If the LMP is unknown, the cycle irregular, or conception has occurred whilst using contraceptive hormones, the EDD should be based on the CRL.
- IVF dates should be based on age (3 or 5 day) and date of embryo transfer and only adjusted with caution.
- See <u>Pregnancy Due Date Calculator (perinatology.com)</u> for help.

#### Management

- The patient should be reassured but cautioned that future miscarriage may still occur.
- A copy of the Patient Information document <u>Bleeding and/or pain in early pregnancy</u> should be provided
- Return to routine community care is appropriate in most cases. If there are features
  associated with increased risk of future miscarriage (e.g. recurrent pregnancy loss, large
  peri-gestational haematoma, HR under 80bpm ≥ 7 weeks) referral to EPAS for review in
  1-2 weeks may be offered.
- Advice should be provided to return for assessment in the event of very heavy bleeding or significant pain, not responding to simple analgesics.
- Anti-D is given as per current guidance from Transfusion Medicine WNHS Transfusion
   Medicine Haematology Protocol Use of RhD Immunoglobulin (RhD Ig) in pregnancy
- Progesterone should be recommended for pregnant women with two or more previous miscarriages and with early pregnancy bleeding as it potentially increases the live birth rate and has little to no association with congenital abnormalities or severe adverse events.
  - The duration of treatment should be to 16 weeks' gestation at a dose of 400 mg twice daily of micronised progesterone vaginally. Of note, This indication is not covered by the

PBS; should the patient be discharged from hospital care with a script to fill outside of KEMH or OPH, the patient will incur a cost of about \$10 per day<sup>(1)</sup> which may be a barrier to effective treatment. Subsidised non-PBS costing is accessible to the patient from the KEMH and OPH Outpatient Pharmacies during business hours.

- There is no current convincing evidence of benefit for progesterone therapy for women without a history of miscarriages or for women without bleeding.
- There is no current convincing evidence of benefit for aspirin or anticoagulant therapy in preventing miscarriage.
- Patients with recurrent pregnancy loss (≥2) can be advised to speak to their GP for a referral to a fertility clinic.
- A letter detailing the patient attendance, outcome and a summary of advice provided should be sent to the GP.

## Early intra-uterine pregnancy of unknown viability (IPUV)

#### **Diagnosis**

- First transvaginal scan showing:
  - o IUGS (MSD < 25 mm) with no embryo, regardless of presence of yolk sac
  - o IUGS with embryo <7 mm with no heart motion<sup>(4)</sup>
- Correlation of ultrasound findings with clinical history and dating is important as, in some settings, definitive history allows a diagnosis of non-viable pregnancy from the first scan (see section below on <u>non-viable intra-uterine pregnancy – Diagnosis</u>).
- Typical imaging features of an empty IUGS, include a thick trophoblastic rim and (in very early gestations) eccentric location within the endometrium. In the setting of these features, an IPUV should be diagnosed, not a PUL.

## Management

- It should be acknowledged to the patient that an IPUV is a normal stage of all pregnancies (typically between 4w3d and 5w3d gestation).
- Repeat ultrasound is recommended to confirm viability.
- If IPUV appropriate for gestation, and the woman is clinically stable, recommend seeing GP for repeat USS in the community to confirm viability.
- Referral to EPAS could be considered upon discretion.
- The timing of the next scan is as follows:
  - o For IUGS < 12 mm with no yolk sac: ≥ 2-week interval to next scan
  - o For IUGS < 12 mm with yolk sac: ≥ 11-day interval to next scan
  - o For IUGS ≥ 12 mm: ≥ 7-day interval to next scan
  - For IUGS of any size with CRL < 7 mm: ≥ 7-day interval to next scan</li>
- Anti-D is given as per current guidance from Transfusion Medicine <u>WNHS Transfusion</u>
   Medicine Haematology Protocol Use of RhD Immunoglobulin (RhD Ig) in pregnancy.
- A copy of the Patient Information document <u>Bleeding and/or pain in early pregnancy</u> should be provided.
- If a non-viable pregnancy is the most likely outcome, offer a copy of the Patient Information documents relevant to miscarriage for their consideration prior to the scheduled review appointment:

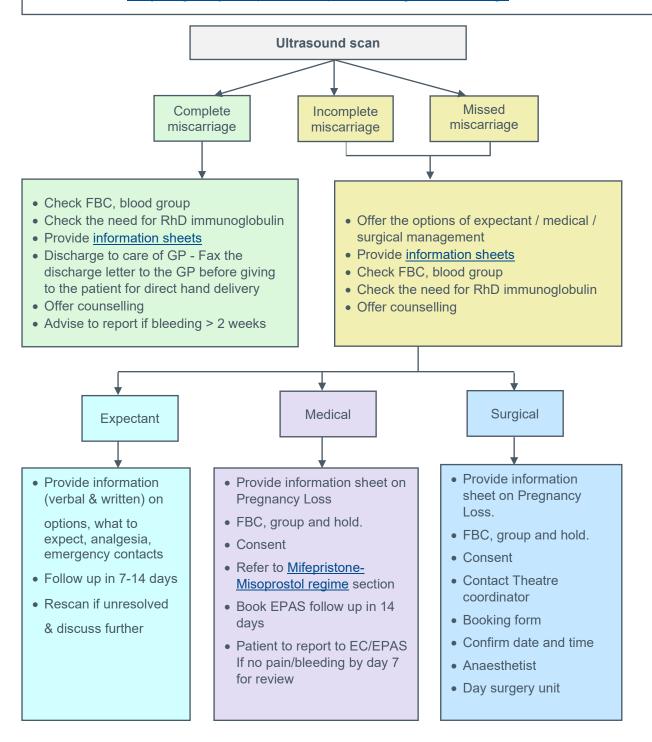
- o Pregnancy Loss in the First 13-weeks of Pregnancy (health.wa.gov.au)
- <u>Pregnancy Loss Medical Management of Early Pregnancy Loss</u> (health.wa.gov.au)

## Non-viable intra-uterine pregnancy: diagnosis

- First transvaginal scan showing<sup>(4)</sup>:
  - o IUGS (MSD ≥ 25 mm) with no yolk sac or embryo
  - IUGS with embryo ≥7 mm with no heartbeat
- Repeat transvaginal scan showing<sup>(4)</sup>:
  - No heartbeat ≥7 days after initial scan showing embryo <7 mm with no heartbeat</li>
  - No yolk sac or embryo ≥7 days after initial scan showing empty sac with MSD ≥12
  - No yolk sac or embryo ≥14 days AND the MSD has not doubled in size after initial scan showing empty sac with MSD <12 mm.</li>
  - No embryo with heartbeat ≥11 days after initial scan showed yolk sac present.
  - o No heartbeat after initial scan showed heartbeat to be present.
- Correlation of ultrasound findings with clinical history and dating is important as, in some settings, definitive history allows a diagnosis of non-viable pregnancy from the first scan. Examples include certainty of conception date, such as with assisted reproductive technologies or previous Serum β-hCG results verifying a minimum gestational age.
- The ultrasound diagnosis should be independently confirmed by a clinician of Registrar grade or above before initiation of treatment. If there is an uncertainty about the diagnosis, the images can be reviewed by the sonologist in session, or another ultrasound can be offered (after discussion with SR/consultant).

## Flow chart 2: Management of Miscarriage Algorithm

\*For miscarriage assessment, examination, investigations, imaging/ultrasound and diagnosis, see earlier section <a href="Early Pregnancy Complications">Early Pregnancy Complications</a> – pain, bleeding and miscarriage within this Guideline.



## Non-viable intra-uterine pregnancy: management

- The diagnosis should be discussed sensitively and appropriate support offered, as miscarriage can have significant psychological effects on both the woman and her partner.
- Options for management are conservative, medical or surgical.
- All options are associated with bleeding, pain, risk of retained tissue and risk of infection.
- Future reproductive outcomes are also similar between groups.
- Expectant management is typically associated with the highest number of review appointments, and surgical management the fewest.
- Surgical management is associated with the risk of surgical complications, including uterine perforation and intrauterine adhesions, which may affect future fertility.
- In most circumstances, all options should be considered, and patient satisfaction is greatest when they are assisted to make their own, informed decision.
- To help determine patient preferences, consider the following discussion points:
  - Have they had previous miscarriages? How were they managed? Any complications? Were they happy with the care received?
  - What worries them most? This may be the pain or prolonged, unpredictable course of conservative or medical management, or fear of surgical complications.
  - Do they feel comfortable waiting for the pregnancy to pass spontaneously, or do they prefer active intervention to expedite the process as soon as possible?
  - Do they have any specific concerns about surgical procedures?
  - What support do they have to help them during periods of pain, or to bring them to hospital for procedures? What support do they have to care for other children?
  - Provide written information, as relevant:
    - Pregnancy Loss: In the First 13 Weeks of Pregnancy (WNHS)
    - Pregnancy Loss: In the Second and Third Trimester (WNHS)
    - Pregnancy Loss: Medical management of early pregnancy loss (WNHS)
    - Miscarriage Treatment options (WA Health Procedure Information sheet, EIDO Healthcare Australia – access external to WA Health is limited)
    - Miscarriage (RANZCOG)
    - Pregnancy Loss (RANZCOG)

## **Miscarriage: Expectant Management**

- The timing to onset of bleeding and completion of miscarriage cannot be predicted.
- Patients should be aware of the risk of heavy bleeding and severe pain, either of which may require further medical assistance.
- A 1–2-week trial of expectant management is a reasonable first-line strategy for most<sup>4</sup>, though some patients may be comfortable with a longer wait for onset of bleeding.
- Expectant management is less likely to be appropriate where there is a higher risk of haemorrhage or in the presence of symptoms which suggest infection.
- Miscarriage completion rates between pregnancy failure and diagnosis are 25-30% at 7 days and 52-59% at 14 days<sup>(6)</sup>.

- Patients should be provided information about what symptoms to expect, and what symptoms warrant medical review.
- Offer analgesia to use at the time of miscarriage.
- Offer histopathology examination to exclude partial molar pregnancy and provide a specimen pot and pre-populated Pathology Request form to the patient for return and testing of pregnancy tissue.
- Refer to EPAS for review at an agreed interval. If there is no need for repeat scan, this
  review can be by telephone initially.
- Advice should be provided on the timing for Anti-D requirement in those who are Rh neg, according to current guidance from Transfusion Medicine - <u>WNHS Transfusion</u> Medicine - Haematology Protocol - Use of RhD Immunoglobulin (RhD Ig) in pregnancy

## **Miscarriage: Medical Management**

#### Mifepristone:

Mifepristone works as an antiprogestogen, blocking progesterone receptors in the endometrium, which leads to embryo detachment, prostaglandin release, and uterine contractions that expel pregnancy tissue. At higher doses, it also acts as a glucocorticoid receptor antagonist, blocking cortisol activity.

#### **Misoprostol:**

Misoprostol is a synthetic analogue of prostaglandin E1. It induces contractions of the smooth muscle fibres in the myometrium and relaxation of the uterine cervix. The uterotonic properties of misoprostol should facilitate cervical opening and evacuation of intrauterine contents.

- There is ample evidence in the literature for the efficacy of termination of an unwanted pregnancy with the use of Mifepristone and Misoprostol.
  - The process of medical termination of pregnancy can also be applied to medical management of a missed miscarriage, as they are similar processes.
  - It is noted however, that the combination of Mifepristone and Misoprostol is not currently approved for use in the treatment of missed miscarriage.
- Medical treatment with Misoprostol is known to be safe and less costly than surgical management, however less effective in reaching complete evacuation of the uterus.
  - Recently, several trials showed that prompt treatment with the sequential combination of Mifepristone with Misoprostol is superior to Misoprostol alone in reaching complete evacuation.
  - The overall success rate of medical treatment was significantly higher in the Mifepristone-Misoprostol group comparing to Misoprostol-alone group (94.3% vs. 82.5%, RR 1.14, 95% CI, 1.03-1.26; p = 0.008)<sup>(5)</sup>. Accordingly, the rate of surgical treatment was significantly lower in the Mifepristone-group (5.7% vs.14.6%, RR 0.39, 95% CI, 0.16-0.97; p = 0.034)<sup>(8)</sup>. The composite complication rate was similar and lower than 4 percent in both groups.
  - The success rate of the combined method ranges in the literature<sup>(5)</sup> from 73 to 95% as compared to Misoprostol alone 83%. This method of management of

- a missed miscarriage has become standard of care in several Early Pregnancy Services worldwide.
- The combination of the two medications has been shown to have a better efficacy than the use of Misoprostol alone in terms of passing the sac, need for further treatment doses or surgical intervention, and financially than the current commonly used regimen<sup>(5)</sup>. The flow-on effect is the ability to manage a greater number of women who choose medical management of their missed miscarriage.
- This option is suitable for patients who:
  - Have an intrauterine pregnancy
  - Have had a caesarean section
  - Have a multi-fetal pregnancy
  - Are obese
  - Have uterine abnormalities, including fibroids
  - Have positive STI pathology and have commenced treatment
  - Wish to avoid surgical intervention
  - Are currently breastfeeding
  - Have available supports, can access emergency care and be active in postprocedure follow-up

For those women choosing medical management of a <u>missed</u> miscarriage, the recommended regimen is:

 Mifepristone 200 mg oral followed by misoprostol 800 microg(vaginal, buccal or sublingual) 24 to 48 hours later<sup>(1)</sup>

For those women choosing medical management of an <u>incomplete</u> <u>miscarriage</u>, the recommended regimen is:

- Misoprostol 800 microg (vaginal, buccal or sublingual)<sup>(1)</sup>
- Most patients will respond to medical management with onset of cramps and bleeding within 4-12 hours of misoprostol use, though some may commence bleeding following mifepristone, prior to using the misoprostol.
- Management in the outpatient setting is suitable for most patients with CRL under 11-week size (45 mm). Pain and bleeding may be more significant with increasing CRL.
- Advise patients when to return to the KEMH Emergency Centre (EC) in the event of heavy bleeding – i.e. 1 pad/hr for ≥ 2 hours, passage of large clots, syncope/presyncope.
- Patients who elect for medical management with CRL 45mm and above should be offered inpatient admission for monitoring and assessment due to increased risk of significant bleeding and pain.
- Confirm eligibility criteria and check for contraindications to medical management (see next section in guideline).
- Provide information about the expected course, medication side effects and symptoms which warrant earlier medical review than planned.
- Obtain written consent for medical management of miscarriage.
- Offer analgesia and antiemetics.

- Offer histopathology examination to exclude partial molar pregnancy and provide a specimen pot and pre-populated pathology request form to the patient for return and testing of pregnancy tissue.
- Provide Anti-D requirement to those who are Rh neg, according to current guidance from Transfusion Medicine - <u>WNHS Transfusion Medicine - Haematology Protocol -</u> <u>Use of RhD Immunoglobulin (RhD Ig) in pregnancy</u>
- Schedule EPAS telephone consultation (GYN551) 1 week after medication.
  - This appointment is used to confirm response, check wellbeing and progress of symptoms, assess for signs of infection, and answer any questions. If all is progressing as expected at that time, a further GYN551 appointment will be scheduled for 2 weeks after the first phone call (three weeks after the medication). If, after 3 weeks from medication, there is still PV bleeding or a Urine β-hCG test is still positive, a repeat scan appointment at EPAS (GYN530) will be offered.
- Ensure patient has the contact mobile number (0422 779 790) for the EPAS midwives in case they have any **non-urgent** concerns during weekday working hours.

#### **Contraindications to Mifepristone and Misoprostol combination**

- Intrauterine device (IUD) in place if the IUD cannot be removed, a surgical abortion is the recommended safe option.
- Haemorrhagic disorder or treatment with anticoagulants.
- Long-term use of an oral corticosteroid (effectiveness may be reduced by the antiglucocorticoid action of mifepristone).
- A travel time to hospital emergency services with blood transfusion services of more than two hours in the 14 days after taking mifepristone.
- Corticosteroids mifepristone may reduce the activity of inhaled and systemic corticosteroids for 3–4 days after its use due to its antiglucocorticoid effects; monitor symptoms accordingly and consider temporarily increasing corticosteroid dose if needed.

#### Suspicion of ectopic pregnancy

- Refer to the <u>Pregnancy of Unknown Location</u> and <u>Ectopic Pregnancy</u> sections in this Guideline.
- Heavy bleeding (>1 pad/hour for >2h).
- Complete miscarriage.
- Suspicion of Gestational Trophoblastic Disease See also KEMH Clinical Guideline, WNHS Gestational Trophoblast Disease Clinical Practice Guideline
- Suspected or confirmed intrauterine infection.
- Medical conditions such as severe asthma, glaucoma, sickle cell anaemia, moderate to severe hypertension despite treatment, mitral stenosis.
- Hypersensitivity to one or both components.

#### Side effects

Diarrhoea

- Bleeding
- Headache
- Nausea and vomiting
- Dizziness
- Flushing
- Shivering or chills

#### **Risks and complications**

- Retained pregnancy tissue uncommon; occurs in approximately 1 to 4:100 of cases.
- Patients with incomplete early medical miscarriages could be offered surgical evacuation, a repeat dose of misoprostol, or expectant management.
- This decision will depend on their preferences, signs and symptoms, ultrasound findings, clinical stability, and access to surgery.
- Haemorrhage and heavy bleeding Severe haemorrhage requiring medical or surgical intervention occurs in less than 1:100 cases (EBL > 500 ml, or bleeding requiring transfusion).
- Infection Less than 1:100 cases.

## **Miscarriage: Surgical Management**

#### **Key points < 14 weeks gestation**

- 1. The ultrasound diagnosis should be independently confirmed by a Senior Registrar or Consultant before initiation of treatment.
- 2. Counselling should be offered and information sheets given if appropriate.
- 3. Discuss patient's wishes for disposal of the products of conception, recommend histopathological examination.
- 4. The patient should be informed that they will not be able to drive or drink alcohol for 24 hours after the surgical procedure.
- 5. The woman should be informed that arrangements will need to be made in advance for her transport home after discharge and that a responsible adult should remain with her overnight.

#### Indications for surgical management

- Heavy bleeding or pain and prolonged symptoms.
- Patients with an intact gestational sac and no live embryo who have not expelled the products within a reasonable period.
- Where molar pregnancy is suspected.
- Patient choice may not be comfortable waiting for weeks to expel a non-viable pregnancy.

#### **Pre-operative preparation**

Please refer to <u>Table 1 Checklist: Booking elective surgical management of miscarriage</u> (next page).

#### **Intra-operative management**

For women choosing a surgical option, Suction Aspiration (including Manual Aspiration) is the preferred procedure<sup>(1)</sup>.

Dilatation and sharp curettage is avoided as it is associated with an increased risk of intrauterine adhesions. This risk is further increased for any subsequent miscarriage or uterine evacuation procedure<sup>(1)</sup>.

Antibiotic prophylaxis at the time of surgical management of a miscarriage is recommended:

• Give 100 mg oral doxycycline 1 hour before the procedure or earlier (can be given at time of administration of misoprostol)<sup>(1)</sup>.

#### **Post-operative management**

- On transfer to the Day Surgery Unit or inpatient area, record baseline observations
  of respiratory rate, oxygen saturations, heart rate, blood pressure, temperature,
  consciousness and vaginal blood loss.
- 2. Repeat the above after one hour or more frequently as clinically indicated. Offer a light meal / fluid when fully awake.

#### Discharge planning

- Follow up appointment for 2-weeks with her General Practitioner or gynaecology clinic if there have been complications.
- Offer Pastoral Care referral for emotional support and information regarding memorial services if appropriate.
- Provide Anti-D requirement to those who are Rh negative, according to current guidance by WNHS Transfusion Medicine - <u>WNHS Transfusion Medicine</u> – <u>Haematology Protocol</u> – <u>Use of RhD Immunoglobulin (RhD Ig) in pregnancy</u>
- Provide the woman with information sheets for post-operative / pastoral care, as appropriate:
  - Pregnancy Loss: In the First 13 Weeks of Pregnancy OR
  - o Pregnancy Loss: In the Second and Third Trimester (WNHS) support information
  - Pastoral Care Services

#### Discharge criteria

- Vital signs stable for at least one hour.
- Ensure the woman is orientated as to time, place and relevant people.
- Adequate pain control with oral analgesics.
- Self-care should be normalised.
- Minimal nausea, vomiting or dizziness.
- Minimal vaginal bleeding.
- Has passed urine.
- Has a responsible adult to take the woman home.

# Early Pregnancy Complications **Table 1: WNHS checklist for booking surgical management of miscarriage**

	WNHS Checklist: Booking surgical management of miscarriage
1	<ul> <li>Ensure case suitable to be booked</li> <li>☐ Meets criteria for missed miscarriage (CRL 7mm, MSD 25mm etc)</li> <li>☐ If CRL ³ 12 weeks gestation discuss of surgical management of miscarriage appropriateness with senior doctor</li> </ul>
2	Consent patient  ☐ Complete Generic Consent Form MR295 ☐ Risks including uterine perforation, need for repeat procedure, uterine adhesions etc ☐ Add cytogenetics to consent form if indicated (miscarriages, testing desired etc)
3	Book case based on clinical urgency – refer to Emergency Surgery Clinical Practice Guideline  ☐ Contact Theatre Coordinator (*41220 or 0424148574) – to check theatre availability ☐ Complete BASE booking ☐ Include patient weight ☐ Ensure gestation is entered correctly ☐ Please ensure that you clearly state 'miscarriage' and not 'termination' as this impact's equipment
4	Call Duty Anaesthetist (0420302571) if booking is urgent (EC1-3), patient is unstable, or if has medical history requiring pre-op anaesthetic review
5	Inform Consultant rostered to list if case complex  ☐ For EG - repeat procedure for RPOC, morbid obesity, complex patient medically / surgically etc
6	Prescribe pre-op medications including misoprostol / analgesia / antiemetics on DSU medication chart  □ Pre/Post Operative Protocol for Day Surgery Patients MR810.06  □ Misoprostol 400mcg buccal/SL/PV  □ Leave post op medications (back page) for anaesthetic staff to chart
7	If Rh Negative: current Group & Hold is required  □ Dose of Anti-D depends on gestation/pregnancy – refer to Use of RhD Immunoglobulin (RhD Ig) in Pregnancy □ 250IU IM Anti-D on DSU medication chart for a single pregnancy and gestation ≤12 weeks □ 625IU IM if: multiple pregnancy, ≥12 weeks gestation
8	Does not require Group & Hold unless blood group not known or increased risk of complications (i.e. molar pregnancy, endometriosis, cervical stenosis, thrombophilia - speak with senior doctor if these complications apply)
9	Advise all patients to call DSU evening before procedure from 5-7pm to confirm when to attend
10	Ensure a copy of USS report available on the DMR (as often the USS report is not available for the team doing the procedure and it adds time trying to chase and confirm the appropriate diagnosis of missed miscarriage)  ☐ Ask EC ward clerk to action this if required ☐ Include medical history, assessment, and plan in DMR and on EDIS
11	Ask EC clerical staff to contact medical imaging to cancel any further US appointments for the patients
12	<b>Give patient pamphlets</b> for surgical management , pregnancy loss and memento (i.e. felt heart) as appropriate
13	Medical Certificate to patient (patient can usually be back at work in 1-2 days if well)  ☐ Carers day leave for carer for day of surgery.
1. 2.	AM operating theatre list  Fast from midnight. Can drink clear fluids, water, black tea/coffee up to 2 hours pre-op (0600hrs)  If patient on the AM list attend EC ward clerk desk at 0615hrs.
<b>IF P</b> 1. 2.	PM operating theatre list Fast from 0700hrs. Can drink clear fluids, water, black tea/coffee up to 2 hours pre-op (1100hrs) If patient on PM list, attend DSU ward clerk desk at 1100hrs
1. 2.	vise patient: To call DSU the night before admission There is potential for delay on the day, related to more urgent unplanned surgery Pre-op Misoprostol will be given in DSU

## **Pregnancy of Unknown Location**

#### Aim

To provide information on the diagnosis and management of pregnancy of unknown location (PUL) at KEMH.

## **Key Points**

- 1. PUL is a classification, not a final diagnosis, and only applies to a patient with a positive Serum  $\beta$ -hCG and no identifiable pregnancy on transvaginal ultrasound.
- 2. Patients presenting to KEMH EC with a positive (+ve) Serum β-hCG, symptoms of PV bleeding or abdominal pain, and unsited pregnancy from any prior imaging, must have a transvaginal pelvic ultrasound scan (TVUS) either completed or booked at their first presentation, unless the Serum β-hCG is known to have fallen by > 50%.
- 3. The outcome in patients initially classified as PUL is as follows:
  - a. Intrauterine pregnancy (IUP) (viable or non-viable)
  - b. Resolving PUL
  - c. Ectopic pregnancy (9)
- 4. Consider serum progesterone level to aid diagnosis. If patients are taking progesterone supplements, serum progesterone level is of no benefit.
- 5. Repeat serum  $\beta$ -hCG 48 hrs after positive baseline serum  $\beta$ -hCG.
- 6. A single cut-off level for Serum  $\beta$ -hCG or progesterone cannot be interpreted clinically in isolation<sup>(8)</sup>.
- 7. Specialist review, close follow-up and serial Serum  $\beta$ -hCG monitoring is essential until resolution.
- 8. Triage of PUL using a mathematical risk prediction model (e.g. M6P, 2 step triage strategy) has been demonstrated to be a useful decision support tool<sup>(10-12, 21, 22)</sup> see M6P Calculator section of this Guideline.
- 9. Individualise care according to clinical circumstances

#### **Background**

Pregnancy of unknown location is a term used to describe the following clinical scenario:

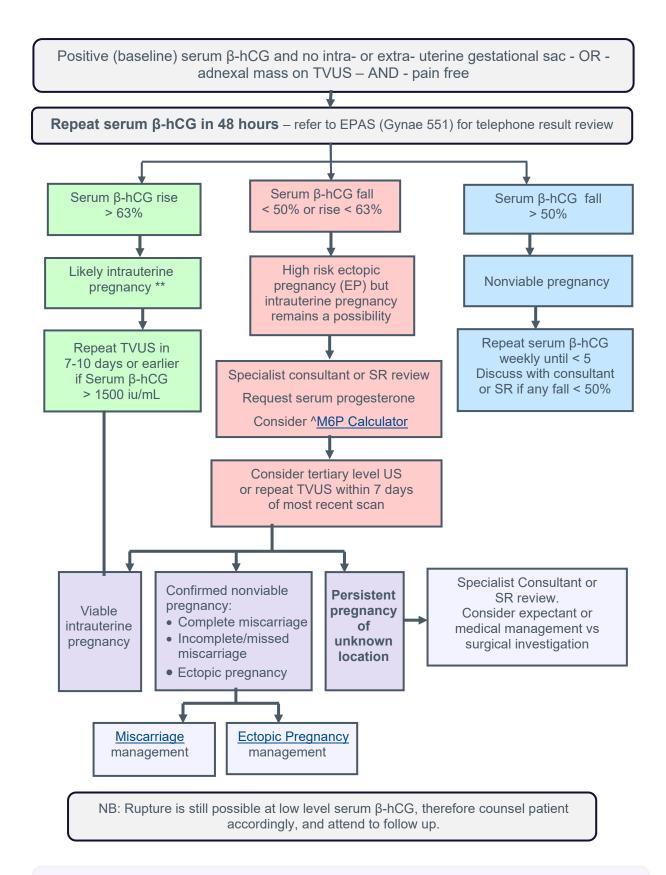
- Positive pregnancy test
- No evidence of intrauterine or ectopic pregnancy on TVUS
- Haemodynamically stable patient

Pregnancy of Unknown Location is not a final diagnosis, but an entity that requires continued evaluation until a final diagnosis is obtained<sup>(10, 11)</sup>.

Although the natural history of most PUL's is an eventual IUP (either viable or non-viable), up to 20% may represent ectopic pregnancy

The serum biomarkers (Serum  $\beta$ -hCG)+/- progesterone can be used to guide management<sup>(13)</sup>.

## Flow Chart 3: Management of Pregnancy of Unknown Location



**Acknowledgement :** Flowchart 2: Investigation and Follow-Up of Pregnancy of Unknown Location (PUL), SA Health Perinatal Practice Guideline – Bleeding in Early Pregnancy: Ectopic pregnancy, Miscarriage and PUL (V1.3, 14/02/2023), ISBN number: 978-1-76083-123-3, <a href="www.sahealth.sa.gov.au">www.sahealth.sa.gov.au</a>. Algorithm edited to inform WNHS model of care.

#### Beta human chorionic gonadotropin (serum β-hCG)

- Serum β-hCG first becomes positive at 9 days post conception
  - Serum β-hCG greater than 5 IU/L is defined as 'positive' (13)
- For a potentially viable IUP up to 6–7 weeks gestation
  - Mean doubling time for serum β-hCG is 1.4–2.1 days (14)
  - 85% show serial serum β-hCG rise of at least 66% every 48 hours<sup>(15)</sup>
  - o 15% show serial serum β-hCG rise between 53–66% every 48 hours (16)
  - The slowest recorded rise over 48 hours is 53% (16)
- A single serum β-hCG value:
  - o Cannot be used to exclude intra or extrauterine pregnancy
  - Does not differentiate between a viable and nonviable pregnancy (17)

## Transvaginal pelvic ultrasound scan (TVUS)

An intrauterine pregnancy (IUP) is usually visible on TVUS when the mean sac diameter (MSD) is  $\geq$  3 mm<sup>(14)</sup> and the QBhCG is greater than 1500 IU/L.

#### **Discriminatory zone**

Defined as the serum  $\beta$ -hCG level above which a gestational sac should be visualised on USS if an IUP is present<sup>(18)</sup>.

This serum level is defined at 1500 IU/L for TVUS at WNHS.

#### **Progesterone**

- Normally serum progesterone levels increase over pregnancy
- A decline between 6 and 8 weeks of gestation, with a nadir at week 7, corresponds to the luteal-placental shift<sup>(19)</sup>
- Levels may be influenced by maternal age, body mass index (BMI) and parity
- Levels are reflective of pregnancy viability, not location<sup>(20)</sup>
- If the initial progesterone level is less than or equal to 2 nmol/L
  - A non-viable pregnancy is likely (intra- or extra- uterine)
  - O An ectopic pregnancy cannot be excluded. A proper safety netting plan is required for outpatient care with serum  $\beta$ -hCG surveillance plan till serum  $\beta$ -hCG < (negative).
  - $\circ$  The risk of ectopic pregnancy is <2%<sup>(13)</sup>.
  - Tracking until serum β-hCG is negative should be undertaken, with reduced frequency of testing. Patients with increasing symptoms of ectopic should return for review.
- Serum progesterone is processed at QEII campus and takes longer to process.
   Review of results at next clinical encounter is appropriate.

## M6P Calculator for Pregnancy of Unknown Location (PUL)

#### **PUL Calculator link: link**

\* Remember to document the risk score in the patient's clinical record \*

M6 risk-prediction model is part of a two-step protocol using an initial progesterone level of  $\leq 2$  nmol/L and serial serum β-hCG levels to identify probable failing pregnancies, and to assist the triage performance for stratifying women with a pregnancy of unknown location (PUL) as being at low or high risk<sup>(12)</sup>.

#### This calculator estimates the probability of:

- Failed Pregnancy of Unknown Location (FPUL)
- Intrauterine Pregnancy (IUP)
- Ectopic Pregnancy (EP)
- It is based on the M6P risk prediction model, Van Calster et al. (2016) (link)<sup>12</sup>

#### **Patient Eligibility**

Only use this tool for patients who are:

- currently Pregnancy of Unknown Location (PUL)
- haemodynamically stable
- not already diagnosed or treated for EP
- not clearly intrauterine or ectopic on scan

#### **Required Laboratory results**

- 1. Initial serum β-hCG (Day 0) in IU/L
- 2. 48-hour serum β-hCG (Day 2) in IU/L
- 3. Initial progesterone in nmol/L (multiply ng/mL x 3.18 if needed)

#### Steps to use

- 1. Enter values in columns Initial serum β-hCG, 48h serum β-hCG, and Progesterone
- 2. Spreadsheet will auto-calculate probabilities for IUP, FPUL, and Ectopic

#### **How to interpret Ectopic Probability**

- EP Probability < 5% → Low-risk
- EP Probability 5–20% → Moderate-risk
- EP Probability > 20% → High-risk

#### **Key reminders**

- Document the risk score in the patient's clinical record
- Use the M6P Calculator tool to support not replace clinical judgement and shared decision-making.

#### Additional considerations

- Progesterone (P4) is used in early pregnancy in assisted reproductive technology (IVF/ICSI) and can impact level. Check with patient.
- Incidence of ectopic pregnancy is increased in assisted reproductive technology (ART) pregnancies, 0.8 to 8.6%<sup>(58)</sup>.
- Ultrasound department can assist with review of imaging from community overnight or the following day, if asked.

- Please call sonologist in session (ext 82842) or sonographer mobile.
- All referrals to EPAS for scans require an ultrasound request form submitted on CPOE.
- If EPAS is full, send CPOE request, stating that no timely EPAS appointments are available and stating date that scan is required. Medical Imaging will contact the patient with a time to attend. Do not instruct patient to attend Medical Imaging before this.
- Monitoring of serum β-hCG levels after initial assessment in haemodynamically stable patients is undertaken through EPAS midwife phone clinic (GYN551) unless the timing of required review falls out of office hours.
- Patients with persistently low positive serum β-hCG, or an unexplained elevated serum β-hCG warrant a considered review and further investigations. Patients with unexplained elevated serum β-hCG may be referred to the <u>Western Australian Trophoblastic Centre</u> (WATC) Multidisciplinary Case Conference for advice on investigations and management (See also <u>KEMH Clinical Guidelines</u>, <u>O&G</u>: <u>Gestational Trophoblast Disease</u>)

#### Red flags

- Consider risk factors for ectopic e.g. IVF pregnancy, previous ectopic, history of chlamydia etc.
- A patient with positive pregnancy test and signs of peritonitis or instability should prompt escalation to a senior doctor for consideration of diagnostic laparoscopy.

## **Ectopic pregnancy**

- 1. Ectopic pregnancy should be considered in all pregnant women who present to the Emergency Centre with abdominal pain and/or vaginal bleeding<sup>(23)</sup>.
- 2. Untreated ectopic pregnancy can rupture and cause intra-abdominal bleeding<sup>(24)</sup>.

#### Background

Ectopic pregnancy occurs when the developing blastocyst becomes implanted at a site other than the endometrial cavity. The most common extra-uterine location is the fallopian tube, <sup>62</sup> which accounts for 91-95% of all ectopic pregnancies<sup>(25)</sup>. Other locations include caesarean/hysterotomy scar (<6.1%), ovarian (1-6%), rudimentary horn of a unicornuate uterus (2%), cervix (<1%), and abdomen (0.9-1.4%)<sup>(25)</sup>. Contemporary management, associated with earlier diagnosis of tubal ectopic pregnancy, involves (where possible) a conservative approach that attempts to save the fallopian tube, rather than salpingectomy<sup>(26,27)</sup>.

Ectopic pregnancy is an important cause of maternal morbidity and mortality<sup>(28,29,52)</sup>. Although deaths associated with ectopic pregnancy have declined with earlier and improved diagnosis<sup>(52)</sup>, the majority (80%)<sup>(25)</sup> of maternal first trimester deaths, and 10-15% of all pregnancy related deaths, are related to haemorrhage from ectopic pregnancy<sup>(29)</sup>.

#### Incidence

Of all reported pregnancies, 1 to 2% are ectopic<sup>(23, 28,30-32)</sup>. The prevalence of ectopic pregnancy among women who go to an emergency department with first trimester bleeding, pain, or both, ranges from 6 -16%<sup>(33)</sup>. Over the past three decades the rate of ectopic pregnancy increased by a factor of three to six and has remained stable<sup>(28)</sup>.

#### Risk factors

Risk factors are only found in approximately 50% of cases<sup>(28)</sup> – refer to Table 1 below.

Table 2: Ectopic pregnancy risk factor and odds ratio

Degree of additional risk	Risk factor	Odds ratio <sup>34</sup>
	Previous ectopic pregnancy <sup>(23,28)</sup>	9.3 - 47
	Previous tubal surgery <sup>(23,28,29,35)</sup>	6.0 - 11.5
High	Failed tubal ligation <sup>(23,28)</sup>	3.0 - 139
	Documented tubal damage or pathology <sup>(23)</sup>	3.5 - 25
	Pregnancy with IUCD(23,28,29)	1.1 - 45
	History of infertility <sup>(29,35)</sup>	1.1 - 28
	Previous pelvic <sup>(28,29)</sup> / genital infection <sup>(23,35)</sup>	2.1 - 3.0
Moderate	Cigarette smoking <sup>(23,28,29,35)</sup>	2.3 - 3.9
	Multiple sexual partners <sup>(23)</sup>	1.4 - 4.8
	Assisted reproductive technology <sup>(28,29)</sup>	2.3 - 3.9
	Previous pelvic/ abdominal surgery	0.93 - 3.8
Low	Early age at first sexual intercourse <sup>(35)</sup>	1.1 – 2.5
	Vaginal douching	1.1 – 3.1

• Other factors include increased maternal age<sup>(28,35)</sup>, and in-utero exposure to diethylstilbestrol<sup>(22,29)</sup>.

#### **Signs and Symptoms**

#### **Symptoms**

Clinical manifestations typically appear six to eight weeks after the last normal menstrual period, but can occur later, especially if the pregnancy is not in the fallopian tube. Normal pregnancy symptoms (e.g., breast tenderness, frequent urination, nausea) are often present in addition to the symptoms described below<sup>(5)</sup>.

The typical triad of symptoms are:

- Bleeding (75% of patients)
- Abdominal pain (80-90% of patients)
- Amenorrhoea<sup>(28,29)</sup>.

When the patient's pain is disproportionately more severe than her bleeding, then ectopic pregnancy is likely. If the bleeding is more severe than the pain, then intrauterine pregnancy is more likely<sup>(28)</sup>.

#### But

- No symptoms before incidental diagnosis 1/3 women
- No symptoms before rupture<sup>(29)</sup> 9%
- Amenorrhoea is not universal
- Other presenting symptoms include dizziness/fainting, shoulder tip pain, passage of tissue or gastrointestinal symptoms<sup>61</sup> like diarrhoea or pain on defaecation<sup>(5)</sup>.

#### **Signs**

The physical examination is often unremarkable in a woman with a small, unruptured ectopic pregnancy.

Findings on physical examination may include<sup>(5)</sup>:

- Lower abdominal / pelvic / adnexal tenderness or mass<sup>(23)</sup>
- Cervical motion tenderness<sup>(32)</sup>
- Signs of shock
  - o Pallor, tachycardia, hypotension, shock, collapse, orthostatic hypotension<sup>(5,23)</sup>.

#### Investigation and diagnosis

The recommended diagnostic tests include:

- Transvaginal ultrasound scan alone (TVS)
- Diagnostic algorithms (TVS + serum β-hCG)<sup>(32)</sup>.

The combination of tests with ultrasound scan +/- serum  $\beta$ -hCG estimation will permit a definitive diagnosis in the majority of cases at a very early stage of pregnancy, thereby permitting treatment options less invasive than surgical excision<sup>(36,37)</sup>. Although progesterone concentrations can be used to predict a viable intrauterine or failed pregnancy, they do not assist clinicians to locate a pregnancy of unknown origin<sup>(28,32)</sup>. Currently, other diagnostic tests (e.g. Doppler or 3D ultrasound, magnetic resonance imaging) have not demonstrated improvement in current diagnosis sensitivity or specificity, and do not provide additional clinically useful information<sup>(28)</sup>.

#### **Pelvic Ultrasound Scan**

Transvaginal ultrasound examination (**TVS**) is the most useful and primary investigation for determining the location of a pregnancy<sup>(23)</sup>. If an ectopic pregnancy is present, the use of TVS should visualise 73-93% of cases<sup>(28)</sup>. Visualisation of an adnexal mass separate from the ovary, on TVS, has been shown to have high sensitivity (84.4%) and specificity (98.9%) for diagnosing ectopic pregnancy<sup>(23)</sup>.

The most appropriate diagnostic criteria include a combination of (28):

- Positive pregnancy test
- Empty intrauterine cavity
- Complex adnexal mass +/- extrauterine gestation sac(28).

Other ultrasound features that may be suggestive of ectopic pregnancy are (28):

- Bagel sign (a fluid filled adnexal mass surrounded by a hyperechogenic ring)
- Pseudo sac (collection of fluid within the endometrial cavity) usually located in the mid cavity and conforming to the contour of the cavity, unlike an IUGS embedded in the decidua.
- Pelvic free fluid<sup>(28)</sup>.

Note: If the woman declines the TVS, offer a trans-abdominal ultrasound scan and explain how findings will be limited, with the low specificity of the test making an ectopic diagnosis difficult<sup>(5)</sup>.

#### Diagnostic algorithms (TVS + serum $\beta$ -hCG)

Ultrasound is inconclusive in 8-31% of women, in whom one or more measurements of serum  $\beta$ -hCG concentration is necessary to guide the assessment<sup>(23)</sup>.

- TVS + discriminatory zone serum β-hCG titre
- TVS + serial serum β-hCG +/- discriminatory zone serum β-hCG.

#### Discriminatory zone QBhCG:1500 IU/L

It is defined as the serum  $\beta$ -hCG level above which a gestational sac should be visualised by ultrasound examination if an intrauterine pregnancy is present<sup>(28)</sup>. At KEMH, this serum  $\beta$ -hCG level is 1500 with TVS (the level is higher [6500 IU/L] with transabdominal ultrasound). The absence of an IUGS at serum  $\beta$ -hCG concentrations above the discriminatory zone strongly suggests an ectopic pregnancy<sup>(28)</sup>.

#### Serum β-hCG above the discriminatory zone (>1500 IU/L)

If no intra or extra uterine pregnancy is visualised on ultrasound scan in the Emergency Centre/EPAS clinic, a consultant review or a formal USS in the department should be organised.

The diagnosis of ectopic pregnancy is less certain if no complex adnexal mass can be visualised, since there is variability in the level of expertise among sonographers. Furthermore, a serum  $\beta$ -hCG greater than 1500 IU/L without visualisation of intrauterine or extrauterine pathology may represent a multiple gestation, since there is no proven discriminatory level for multiple gestations. For these reasons, in the absence of features suggestive of ectopic pregnancy on formal USS, the next step is to repeat the TVS examination and serum  $\beta$ -hCG concentration 48 hrs later in EPAS.

• If an intrauterine pregnancy is still not observed on TVS, then the pregnancy is abnormal.

- A rise or plateauing in the serum β-hCG concentration in the absence of ultrasound evidence of intrauterine pregnancy is diagnostic of ectopic pregnancy.
- A falling serum β-hCG concentration is most consistent with a failed pregnancy (intrauterine or extrauterine). Expectant management will be an option if the patient is stable, there is no fetal cardiac activity, and levels are dropping steadily<sup>(25)</sup> (ideally less than 50% of its initial level within seven days). These patients should be observed closely for rupture or clinical deterioration<sup>(25)</sup>. Weekly serum β-hCG concentrations should be monitored until the result is 5 or less for pregnancy.

#### Serum $\beta$ -hCG below the discriminatory zone

A negative ultrasound examination at serum  $\beta$ -hCG levels below the discriminatory zone (1500IU/L) is consistent with an early intrauterine pregnancy (viable or nonviable) or an ectopic pregnancy. A serum  $\beta$ -hCG concentration less than 1500 IU/L should be followed by repetition of serum  $\beta$ -hCG in 48hrs to follow the rate of rise (>63% in 48h)

- If the serum β-hCG rises normally, then a TVS should be performed when serum β-hCG reaches or is expected to reach the discriminatory zone.
- If the serum β-hCG concentration does not rise appropriately, then the pregnancy is abnormal. The clinician can be reasonably certain that a normal intrauterine pregnancy is not present.
- A falling serum β-hCG concentration is most consistent with a failed pregnancy (intrauterine or extrauterine). Expectant management is an option if the patient is stable and the levels are dropping steadily<sup>(25)</sup> (ideally less than 50% of its initial level within seven days). Weekly serum β-hCG concentrations should be monitored until the result is 5 or less.

#### Serial Serum β-hCG

More than one measurement of serum  $\beta$ -hCG is needed if TVS + Discriminatory zone serum  $\beta$ -hCG is inconclusive. Studies in viable intrauterine pregnancies have reported the following changes in serum  $\beta$ -hCG  $^{(36)}$ :

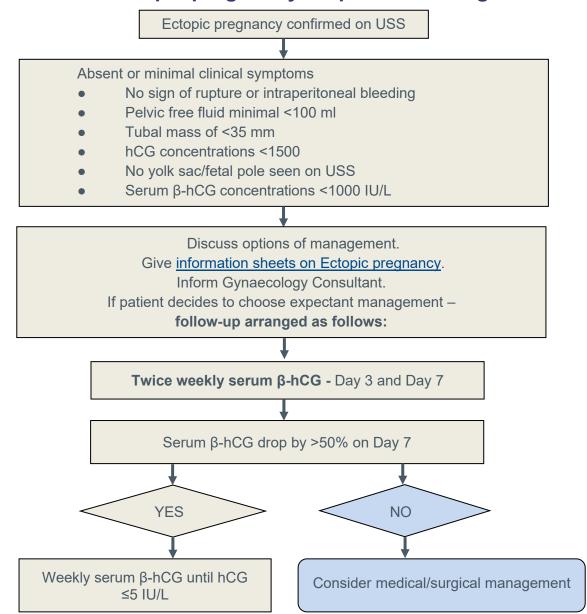
- The mean doubling time for serum  $\beta$ -hCG ranges from 1.4 to 2.1 days in early pregnancy<sup>(32)</sup>.
- In 85% of viable intrauterine pregnancies, the serum β-hCG concentration rises by at least 66% every 48 hours during the first 40 days of pregnancy; only 15% of viable pregnancies have a rate of rise less than this threshold<sup>(36)</sup>.
- The slowest recorded rise over 48 hrs associated with a viable intrauterine pregnancy was 53%<sup>(28,32,36)</sup>.

## Patient information for ectopic pregnancy

Provide written information, as relevant:

- <u>Ectopic Pregnancy</u> (WNHS)
- Methotrexate for Ectopic Pregnancy
- Ectopic Pregnancy (RANZCOG)

## Flow chart 4: Ectopic pregnancy: Expectant management



## **Ectopic pregnancy: Expectant management**

#### **Background**

Ectopic pregnancy can be a gynaecologic emergency requiring urgent treatment. In selected patients, in which the risk of tubal rupture is minimal, expectant management may be appropriate after discussion with the gynaecology consultant on call.

Historically, observation studies reported success rates of 48-100%<sup>(38)</sup>. The criteria between these studies varied considerably. A recent study has reported success rates from 77% when patients were treated expectantly, compared with medical management<sup>(38)</sup>. The success rates of expectant management have been reported to be inversely related to lower serum  $\beta$ -hCG levels at diagnosis of ectopic pregnancy. Success rates when the initial serum  $\beta$ -hCG level was <1000mlU/ml has been found to be between 80-90% by two different studies. In addition, a rapidly decreasing serum  $\beta$ -hCG level appears to predict a favourable outcome<sup>(39,59)</sup>. Higher serum  $\beta$ -hCG levels have been related to lower success rates with expectant management, with one study reporting only 21% of cases were successful when the initial serum  $\beta$ -hCG was >1500mlU/ml<sup>(40,41)</sup>. Other studies, that focused on declining serum  $\beta$ -hCG levels rather than an absolute value, found that, in 25% of ectopic pregnancies with declining serum  $\beta$ -hCG levels, almost 70% will resolve without any treatment<sup>(39)</sup>. Fertility rates have not been found to be significantly different between medical and expectant management<sup>(41)</sup>.

An initial serum  $\beta$ -hCG level of <1000mIU/ml has been demonstrated to be the best, single factor in predicting a successful outcome with expectant management<sup>(40)</sup>. Trans-vaginal ultrasound has also been found to be a useful tool in predicting success<sup>(42)</sup>. Cacciatore et al found trans-vaginal ultrasound had an 84% sensitivity and 100% specificity in predicting the resolution of ectopic pregnancy by serial ultrasounds demonstrating decreasing ectopic size<sup>(39)</sup>. The lack of an identifiable extra-uterine gestational sac on trans-vaginal ultrasound increased the odds of a spontaneous resolution by 5.6 times<sup>37</sup>. Expectant management for atypical ectopic gestations is not recommended due to a lack of available literature<sup>(39)</sup>.

The use of more stringent selection criteria results in an increase in the efficacy of expectant management<sup>(41)</sup>. In expectant management, no treatment is given and the patient is followed twice weekly with serial serum β-hCG measurements and weekly by transvaginal examinations to ensure a rapidly decreasing serum β-hCG level (ideally less than 50% of its initial level within seven days) and a reduction in the size of adnexal mass by seven days<sup>(39)</sup>. Thereafter, weekly serum β-hCG measurement is advised until serum β-hCG levels are  $\leq$ 5 IU/L.

## Inclusion criteria for expectant management

- Absent or minimal clinical symptoms
- No sign of rupture or intra-peritoneal bleeding
- Pelvic free fluid minimal (<100ml)</li>
- Tubal mass of 35mm
- No yolk sac/fetal pole seen
- serum β-hCG concentrations <1500 IU/L

The risk of rupture in a patient with an ectopic pregnancy exists until the serum  $\beta$ -hCG level has fallen to  $\leq 5$  IU/L.

It often involves multiple visits for follow up, of which the physician and patient must be well motivated to accept.

#### **Contraindications**

Expectant treatment should not be attempted or should be abandoned in patients with known or suspected ectopic pregnancy with the following characteristics:

- Haemodynamically unstable
- Signs of impending or ongoing ectopic mass rupture (i.e. severe or persistent abdominal pain or >300 ml of free peritoneal fluid, or fluid outside the pelvic cavity)
- A serum β-hCG that is greater than 1500 IU/ml, is increasing, or is not declining
- The patient is unwilling or unable to comply with monitoring or lives rurally

#### Follow-up

- Twice weekly serum β-hCG measurements
- Expect to have a level less than 50% of its initial level within seven days.
- Thereafter, weekly serum β-hCG measurements until the levels are ≤ 5 IU/L
- Weekly Trans-vaginal Scans
- When the expected results (as mentioned above) are not achieved in a week, consider medical/surgical management.

## **Ectopic pregnancy: Medical management**

#### **Aim**

To outline the medical management of tubal ectopic pregnancy.

#### **Background**

Routine use of an ultrasound scan for patients who present with early pregnancy symptoms, such as pain or bleeding, facilitates an early diagnosis of ectopic pregnancy. Medical treatment can be administered in most cases.

Methotrexate is the drug used for medical management at KEMH.

Methotrexate is a folic acid antagonist (anti-metabolite) which prevents the growth of rapidly dividing cells including trophoblasts and fetal cells by interfering with DNA synthesis. The dose of methotrexate used to treat ectopic pregnancy is relatively low, safe and well tolerated<sup>(43)</sup>.

#### Candidates for medical treatment - inclusion and exclusion criteria

#### Inclusion criteria (24,45)

- Haemodynamically stable.
- Indications
  - o Unruptured tubal or other ectopic pregnancy.
  - Persistent trophoblast after salpingotomy.
- Serum β-hCG < 5000 IU/L</li>
- Size of ectopic mass < 3.5cm
- Normal LFT's, U & E's, and FBC62
- Patient compliance for regular follow ups (average follow up 35 days)<sup>(24)</sup>

#### Exclusion criteria (24,31,45,46)

- Clinically unstable
- Severe or persistent abdominal pain or evidence of significant haemoperitoneum on ultrasound scan (>300mL)

- The presence of cardiac activity Coexistent viable intrauterine pregnancy (heterotopic pregnancy)
- Ectopic mass >3.5 cm (not an independent predictor of treatment success)
- Barriers to consistent safe patient care, for example non-adherence with plan of care, living distance too far from metropolitan health services
- Clinically significant renal, hepatic or haematological impairment
- Known hypersensitivity to methotrexate
- Breast feeding
- Immunodeficiency / concurrent use of corticosteroids

#### Management

#### Pre-treatment checks

- Discuss the options for treatment: expectant / medical / surgical
- Provide the patient with information leaflets.
- FBC, U&Es, LFTs, serum β-hCG, Group & Hold
- Satisfy inclusion and exclusion criteria
- Obtain written consent
- Calculate the Patient Body Surface Area from height and weight (see <u>Table 5</u>)
- Prescribe methotrexate as per the dosage regimen (see <u>Table 6</u>)

#### **Methotrexate administration**

- <u>Methotrexate</u> is given as an outpatient treatment. Patients do not need to be admitted to a ward after methotrexate administration for observation.
- The KEMH Clinical Guideline: Pharmacy: <u>Cytotoxic and Hazardous Medications</u> must be followed when handling methotrexate.
- Methotrexate prefilled syringes are available as various doses in EC and the WA
   Trophoblastic Centre imprest medication store. Please refer to <u>Methotrexate Imprest</u>

   Locations on Formulary One for more detail.
- It may be acceptable to round the calculated patient dose up or down to the nearest 5mg.
- Intramuscular methotrexate administration is the predominant and preferred route for treatment of tubal pregnancy although it can also be given by direct local injection into the ectopic pregnancy sac transvaginally ultrasound guided or laparoscopically<sup>(45)</sup>.
- Methotrexate is given intramuscularly in the buttock or lateral thigh. The empty syringe
  or needle should be placed in a separate purple Sharps Safe, labelled "Cytotoxic waste
  for special incineration".
- Monitor the patient in the emergency centre for 30 minutes for the immediate hypersensitivity reactions. Check for any local reaction. If local reaction is noted, consider antihistamine or steroid cream (very rare).
  - Side effects usually present 2-7 days after the administration of the drug.
- Provide patient copy of information sheet, as appropriate <u>Methotrexate for Ectopic</u> Pregnancy.

#### Methotrexate dosage regimen

- In this commonly used protocol, Day 1 is the day of methotrexate treatment.
- On Days 4 and 7, a serum β-hCG concentration is checked and if the decrease in serum β-hCG is less than 15 percent between Days 4 and 7, a second dose of methotrexate is administered.
- A 15% decrease in serum  $\beta$ -hCG between day 4 and day 7 is a good indicator of the likely success of methotrexate<sup>(47)</sup>.

Table 3: Methotrexate single / variable dose regimen

Day	Management
1	Serum β-hCG, FBC, U&Es, LFTs, G&H
1	Intramuscular methotrexate 50 mg/m <sup>2</sup>
4	Serum β-hCG
	Serum β-hCG, FBC, U&Es, LFT
	• If serum β-hCG decrease > 15 % day 4-7, repeat serum β-hCG weekly
7	• 2 <sup>nd</sup> dose of methotrexate 50mg/m² if serum β-hCG decrease < 15 % day 4-7
	Repeat FBC and AST if further methotrexate is required <sup>(45)</sup>
	Serum β-hCG, FBC, U&Es, LFT
	• If serum β-hCG decrease > 15 % day 7-14, repeat serum β-hCG weekly
14	• 3 <sup>rd</sup> dose of methotrexate 50mg/m² if serum β-hCG decrease < 15% day 7-14
	Repeat FBC and AST if further methotrexate is required <sup>(45)</sup>
Monitoring	The serum β-hCG is followed weekly until the level is ≤5 mIU/L.
Lanarasaany if	

#### Laparoscopy if...

- three doses have been given and there is a <15% serum β-hCG decline from day 14 to 21.
- severe abdominal pain or signs suggestive of tubal rupture.

Table 4: Body surface area (57)

Weight	Height (cm)													
(kg)	70	80	90	100	110	120	130	140	150	160	170	180	190	200
10	0.42	0.46	0.50	0.54										
15	0.49	0.54	0.59	0.64	0.69	0.73	0.77							
20	0.56	0.62	0.67	0.72	0.78	0.83	0.87	0.92	0.97					
30	0.66	0.73	0.80	0.86	0.92	0.98	1.04	1.10	1.15	1.21	1.26			
40					1.04	1.11	1.17	1.24	1.30	1.37	1.43	1.49		
50							1.29	1.36	1.43	1.50	1.57	1.63	1.70	
60							1.40	1.47	1.55	1.62	1.69	1.77	1.84	1.91
70								1.57	1.65	1.73	1.81	1.89	1.96	2.04
80									1.75	1.83	1.92	2.00	2.08	2.15
90										1.93	2.01	2.10	2.18	2.27
100										2.02	2.11	2.20	2.28	2.37
110											2.19	2.29	2.38	2.47
120	_										2.28	2.37	2.47	2.56
130					_			_			2.35	2.45	2.55	2.65

Table 5: Dose of methotrexate in milligrams (50MG/M<sup>2</sup> Body Surface Area)

Weight		Height (cm)											
(kg)	70	80	90	100	110	120	130	140	150	160	170	180	190
10	21	23	25	27									
15	24.5	27	29.5	32	34.5	36.5	38.5						
20	28	31	33.5	36	39	41.5	43.5	46	48.5				
30	33	36.5	40	43	46	49	52	55	57.5	60.5	63		
40					52	55.5	58.5	62	65	68.5	71.5	74.5	
50							64.5	68	71.5	75	78.5	81.5	85
60							70	73.5	77.5	81	84.5	88.5	92
70								78.5	82.5	86.5	90.5	94.5	98
80									87.5	91.5	96	100	104
90										96.5	100.5	105	109
100										101	105.5	110	114
110											109.5	114.5	119
120					·						114	118.5	123.5
130											117.5	122.5	127.5

#### Post treatment management

- Serum β-hCG: weekly serial serum β-hCG follow up needed until ≤5 IU/L
- USS: There appears to be no clinical benefit from routine serial ultrasound examinations<sup>(55)</sup>. After treatment, the ectopic pregnancy is often noted to increase in size and may persist for weeks on serial USS examinations. This could represent a haematoma, rather than persistent trophoblastic tissue, and is not predictive of treatment failure. However, USS evaluation for peritoneal free fluid is indicated for patients with severe abdominal/ pelvic pain<sup>(45)</sup>.
- Advise the patient to:
  - Avoid vaginal intercourse until serum β-hCG is <5 IU/L</li>
  - Avoid pregnancy for three months due to the risk of teratogenicity with methotrexate
  - Avoid pelvic exams during surveillance of methotrexate therapy due to the risk of tubal rupture
  - Avoid sun exposure to limit risk of methotrexate dermatitis
  - o Avoid foods and vitamins containing folic acid
  - Paracetamol with or without codeine is recommended for pain relief
  - Avoid nonsteroidal anti-inflammatory drugs, as the interaction with methotrexate may cause bone marrow suppression, aplastic anaemia, or gastrointestinal toxicity.

#### **Efficacy**

- Overall success is 88-90% with a single/variable dose regimen.
- 14% of patients on single / variable dose regimen will require a second dose and less than 1% of women will require more than two doses<sup>(54)</sup>.
- When evaluating treatment, studies have found that a decline in serum β-hCG on day 0-4 is predictive of an 88% success rate in medical management. A rise in serum βhCG on day 0-4 is a less reliable indicator, indicating that there is a 42% probability of treatment success<sup>(48)</sup>.

#### **Side Effects**

#### **Drug related**

Adverse reactions to methotrexate are usually mild and self-limited. Approximately 30% of patients in the single dose protocol will have side effects<sup>(54)</sup> the most common are stomatitis and conjunctivitis. Rare side effects include gastritis, enteritis, dermatitis, pneumonitis, alopecia, elevated liver enzymes, and bone marrow suppression. All side effects resolve as methotrexate exposure wanes<sup>(44)</sup>.

#### Separation pain

Up to 75% of patients may complain of pain on days 2-7 after receiving the medication<sup>(54)</sup>. The pain may be due to tubal miscarriage or tubal distension from haematoma formation and can usually be managed with simple analgesia. Nonsteroidal anti-inflammatory drugs should be avoided because a clinically significant drug interaction with methotrexate may occur in some patients taking both drugs.

Occasionally pain may be severe, but patients with severe pain, who are haemodynamically stable, often do not need surgical intervention<sup>(49)</sup>. Patients with severe pain should be closely observed for haemodynamic changes which may accompany a tubal rupture, and undergo ultrasonography to assess for intraabdominal free fluid. If tubal rupture is suspected, immediate surgery is required.

#### Subsequent reproductive performance

- There is no evidence of adverse effects of methotrexate treatment of ectopic pregnancy on future pregnancies<sup>(43,46)</sup>.
- Treatment with methotrexate does not appear to compromise ovarian function<sup>(41)</sup>.
- Ectopic pregnancy is caused by abnormal tubal function due to clinical or subclinical endosalpingitis which is bilateral and irreversible. Hence there is a risk of recurrent ectopic pregnancy and subfertility for patients who have had an ectopic pregnancy irrespective of the type of treatment they received to treat their first ectopic pregnancy. This highlights the need for patients with a history of ectopic pregnancy to have fertility follow up if they plan to conceive<sup>(43)</sup>.
- The incidence of recurrent ectopic pregnancy is approximately 15% and rises to 30% following two ectopic pregnancies. The risk of recurrence appears to be the same for both medical and surgical treatments<sup>(41)</sup>.
- Observational studies have shown a subsequent intrauterine pregnancy rate of 58 89 %<sup>(50)</sup>.

#### Single/variable versus multiple dose regimen

- Similar success rates for single/variable dose and multiple dose regimens.
- More side effects/less patient satisfaction with multiple dose regimens.
- No difference in the rate of future tubal patency, intrauterine pregnancy or recurrent ectopic
- Single/variable dose regimen is less expensive, needs less intensive monitoring and does not require folinic acid rescue.

#### **Medical versus surgical treatment**

- Approximately 35% of patients with ectopic pregnancy will satisfy the criteria for medical management<sup>(56)</sup>.
- In these patients, systemic treatment with variable dose methotrexate regimen is as effective as laparoscopic salpingotomy (82 – 95% MTX Vs 80-92% Salpingotomy).
- Similar post treatment tubal patency and intrauterine pregnancy rates.
- Similar risk of recurrent ectopic pregnancy.
- More side effects with medical treatment especially so with multiple dose regimen.
- The period of post treatment monitoring is longer for medical treatment.

Anti-D is given as per current guidance from Transfusion Medicine – <u>WNHS Transfusion</u> Medicine – Haematology Protocol – Use of RhD Immunoglobulin (RhD Ig) in pregnancy

In patients who are eligible for either medical or surgical treatment, the choice of therapy should be guided by the patient's preference after a detailed discussion of risks, benefits, outcomes, and monitoring requirements of both medical and surgical approaches.

## **Ectopic pregnancy: Surgical management**

#### Aim

Outline the surgical management of tubal ectopic pregnancy.

#### **Background**

Surgical management remains the first line treatment in ectopic pregnancy when a patient's condition is unstable. It should also be considered where there are contraindications to medical and expectant management options. Immediate surgical intervention is indicated in situations where the patient is haemodynamically unstable. Laparoscopic surgery has many benefits over 'open' surgery including less adhesion formation, shorter hospital stay, lower cost, less blood loss, less analgesia and better cosmetic result<sup>(1,51)</sup>. Haemoperitoneum is not a contraindication for performing laparoscopic surgery<sup>(1,51)</sup>.

There is limited research demonstrating a proven significant advantage of salpingostomy compared to salpingectomy. Risks associated with salpingostomy include persistent trophoblastic tissue and a small risk of bleeding postoperatively<sup>(23)</sup>. In the presence of a healthy contralateral tube there is no clear evidence that salpingostomy should be used in preference to salpingectomy<sup>(59)</sup>. When there is a desire for future fertility and the contralateral tube looks abnormal, laparoscopic salpingostomy should be considered<sup>(59)</sup>. Mandatory follow up with serum  $\beta$ -hCG serial monitoring is required where salpingostomy has been performed<sup>(59)</sup>. Fertility rates have been found to be comparable between salpingostomy or salpingectomy in the situation of a normalcontra lateral tube<sup>(41)</sup>. Pregnancy rates following surgery or methotrexate treatment have not been found to be significantly different<sup>(41)</sup>.

#### **Key points**

- 1. Surgical treatment becomes a necessity when a patient is:
  - Haemodynamically unstable
  - Confirmed impending or established rupture of the ectopic pregnancy
  - Co-existing intrauterine pregnancy
  - Contraindication of medical treatment
- 2. In a patient who is haemodynamically unstable, initiate immediate resuscitation and the most efficient surgical procedure to reduce further blood loss<sup>(58)</sup>. Transfer to theatre should not be delayed by attempts to establish a normal circulating plasma volume.
- 3. A laparoscopic approach to the surgical management of tubal pregnancy in the haemodynamically stable patient is preferable. Experienced operators can manage patients laparoscopically, even those with a significant haemoperitoneum.
- 4. Laparoscopic salpingectomy is the standard procedure. However laparoscopic salpingostomy should be considered when managing tubal pregnancy in the presence of contra lateral tubal pathology and the desire for future fertility<sup>(59)</sup>. . Follow up for salpingostomy should include mandatory serial serum  $\beta$ -hCG given the risk of incomplete removal of ectopic pregnancy<sup>(24)</sup>.

#### Follow up

- 1. All patients investigated for possible ectopic pregnancy should be advised to seek medical attention immediately if symptoms change.
- 2. Negative laparoscopies and tubal sparing surgeries should be followed up with serial serum β-hCG until <5.

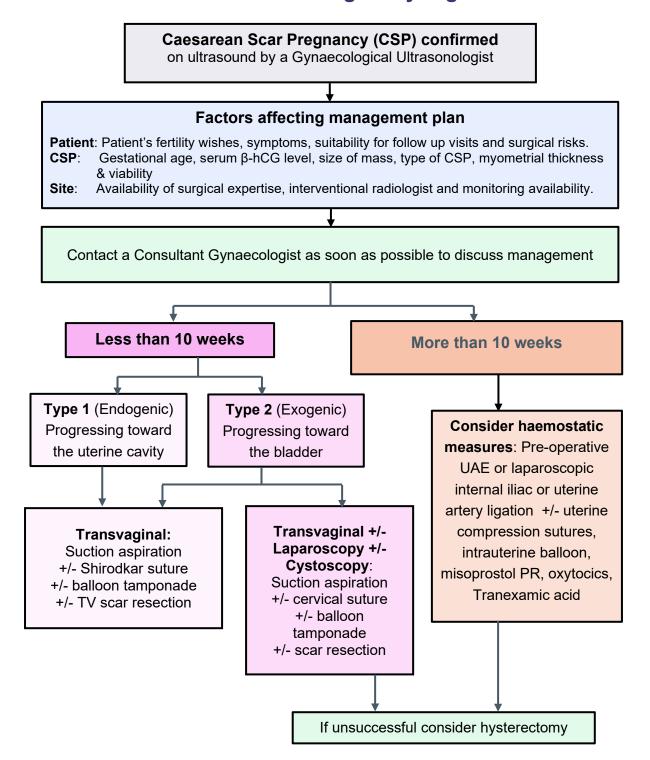
- 3. Ensure Anti D immunoglobulin is given to all non-sensitised patients who are Rhesus Negative, as per current guidance from Transfusion Medicine <u>WNHS Transfusion</u> Medicine Haematology Protocol Use of RhD Immunoglobulin (RhD Ig) in pregnancy.
- 4. If histology confirms no pregnancy tissue, the case should be reviewed by a consultant and the patient advised for follow up.
- 5. All patients treated for ectopic pregnancy should be counselled regarding the risk of recurrence.

## **Ectopic pregnancy: Caesarean Scar Pregnancy**

#### **Key points**

- 1. Women presenting with caesarean section scar pregnancies (CSP) are recommended to have counselling by a senior clinician experienced in managing CSP. The patients should be informed that these pregnancies are high risk, associated with a high likelihood of miscarriage, placenta accreta spectrum, preterm birth, significant haemorrhage, uterine rupture, hysterectomy, perinatal death and maternal death. There may be different outcomes with Type I and Type II CSP, which need to be discussed.
- 2. Those risks increase as the gestational age increases, therefore if the patient opts for surgical or medical management, early intervention is preferred.
- 3. Establish an accurate diagnosis early via ultrasound (see <u>Ultrasound diagnostic criteria</u> below). Ultrasounds performed external to KEMH should be confirmed by a KEMH Sonologist
- 4. **Expectant management** of a live scar ectopic pregnancy is not recommended as it is associated with a high complication rate including placenta accreta spectrum and hysterectomy. However, if the patient continues with pregnancy, after appropriate counselling, the patient should be referred to the Placenta Accreta Team early, the GP should be informed, and the patient should be safety netted.
- 5. **Surgical management** is preferable over medical management, as it has a higher success rate and a lower complication rate.
  - Consent for surgery should be done by a Senior Doctor include the risk of laparoscopy, laparotomy and hysterectomy.
  - Consider inpatient admission for assessment and monitoring in symptomatic patients.
  - Surgical management should be discussed directly with the operating consultant.
     Suction aspiration alone has a 48-72% success rate and ideally should be performed in conjunction with ultrasound and in combination with other haemostatic measures (high cervical suture, intrauterine balloon, uterine artery embolism (UAE), misoprostol PR, oxytocics, Tranexamic acid) which have been shown to increase the success rate up to >95%.
  - Operative laparoscopy and/or hysteroscopy can be considered where expertise permit.
  - If mifepristone is considered prior to surgery, it must only be used as an inpatient and not as an outpatient. [RCA Recommendation]
- 6. Surgical options are dependent on the type and gestation of CSP (Refer to the Caesarean Scar Pregnancy Flowchart).
- In KEMH, the most common and successful management for early gestations is suction aspiration in combination with Shirodkar absorbable cervical cerclage.
- For later gestations, consider additional haemostatic measures e.g. pre-op Uterine Artery Embolisation (see <u>Checklist of arrangements for arterial embolisation</u> section below for arrangements), or laparoscopic ligation of uterine +/- internal iliac arteries or uterine compression sutures.
- 7. **Medical management** (methotrexate) alone is associated with a low success rate (75% in the literature but only 53-62% in the last two KEMH reviews) and prolonged follow up (median 15.5 weeks, range 6-24 weeks in KEMH).
  - Local methotrexate has a 65% success rate with a 13% complication rate, but the success rate increases to 84% with similar complication rate when it is administered locally in conjunction with potassium chloride (KCI) injection and needle aspiration.

## Flow Chart 5: Caesarean Scar Pregnancy Algorithm



#### Ultrasound diagnostic criteria

- 1. Empty uterine cavity and closed, empty cervical canal.
- 2. Gestational sac or solid mass of trophoblast located anteriorly at the level of the internal os or embedded at the site of the previous lower uterine segment caesarean scar.
- 3. Thin or absent myometrium between the gestational sac and the bladder.
- 4. Presence of functional trophoblast/placental circulation on colour Doppler.
- 5. Negative sliding organ sign

#### Ideal ultrasound report information

- 1. Size of gestational sac.
- 2. Size of whole mass inclusive of sac and surrounding trophoblast.
- 3. Presence of yolk sac, fetal pole (including cardiac activity) and CRL.
- 4. Thickness of myometrium between trophoblast and bladder.
- 5. Degree of distortion to anterior serosal contour.
- 6. Communication with the uterine cavity.
- 7. Degree of peri-trophoblastic vascularity.

#### **Checklist of arrangements for arterial embolisation**

- 1. Ring Sir Charles Gairdner Hospital (SCGH) and ask for the interventional radiologist-SCGH direct line is 6001.
- 2. Get a time for the procedure from the interventional radiologist.
- 3. Inform the patient and explain the embolisation procedure. Ensure that she consentsformal consent form will be conducted at SCGH.
- 4. Ensure patient is stable for transfer- have current FBC, coagulation, G&H and consider sending patient with anaesthetic escort, obstetric escort (Senior Registrar (SR) /Registrar) with blood if concerns about bleeding.
- 5. An obstetric medical escort should always go with the patient (generally Registrar or SR), even when the patient is stable.
- 6. Inform Anaesthetic Consultant at KEMH of the transfer.
- 7. Inform KEMH Hospital Clinical Manager of the transfer.
- 8. Inform the SCGH surgeons on-call of the transfer:
  - They may not need to be involved as the patient routinely returns to KEMH after the
    procedure. However, if the patient does require admission, the patient will be
    admitted at SCGH under the general surgical team, so they need to know.
- 9. Inform the Consultant in the Emergency Department (ED) at SCGH that the patient will be coming through their ED (so the triage person is aware). The patient will not stop in ED but the department needs to know they will be coming through.
- Ensure Adult Special Care Unit (ASCU) staff have the patient prepared for transfer with a nurse escort.
- 11. Generally, the notes will go with the patient.
- 12. Write a referral letter to the interventional radiologists which is comprehensive in case the patient needs admission- put nominated Consultant at KEMH to be contacted should there be issues with the patient and a contact number.
- 13. Write a radiology form for arterial embolisation.
- 14. Get a taxi voucher from the Nurse Manager so that the escort and the obstetric (plus or minus the anaesthetic personnel) can return to KEMH.
- 15. Call the ambulance as CAT 1 (or delegate the task). It is vital that it is delegated as a CAT 1 transfer, otherwise the ambulance will not come promptly- thereby will be in a queue which could be long, and the radiologist impacted by delayed care when the patient does not arrive promptly.
- 16. Once you have called a CAT 1 ambulance, be aware they will arrive in 5-10 minutes so be ready to go.

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#### Related policies

#### Legislation

- Abortion Legislation Reform Act 2023
- Criminal Code Act Compilation Act 1913 S199
- <u>Health (Miscellaneous Provisions) Act 1911;</u>

Policies: Department of Health Western Australia

• MP 0175/22 WA Health Consent to Treatment Policy;

#### Related WNHS procedures, guidelines and forms

- Obstetrics and Gynaecology Clinical Practice Guideline:
  - Blood Group Management & Clinically Significant Antibodies: RhD Negative & Positive: Rh(D) Immunoglobulin
  - Gestational Trophoblastic Disease
  - Restricted Area Guideline <u>Abortion and Pregnancy Loss Medications</u>
     (<u>Mifepristone and Misoprostol</u>) (access for WA Health employees through HealthPoint/SharePoint only)
- Transfusion Medicine Protocol: Use of RhD Immunoglobulin (RhD Ig) in pregnancy
- Pharmaceutical and Medicines Management:
  - o ADULT Medication Monograph Methotrexate
  - Guideline Cytotoxic and Hazardous Medications
- Allied Health: Pastoral Care guidelines
- Form: Generic Consent Form MR295

#### Resources

- WNHS Pastoral Care Services: <u>King Edward Memorial Hospital Pastoral care, spiritual care and chaplain (health.wa.gov.au)</u>
- WNHS Patient Brochures:
  - Death of your Baby
  - Ectopic Pregnancy
  - Methotrexate for Ectopic Pregnancy
  - Medical Management of Early Pregnancy Loss
  - Pastoral Care Services
  - o Pregnancy Loss: In the First 13 Weeks of Pregnancy
  - o Pregnancy Loss: In the Second and Third Trimester
  - o Pregnancy Loss: Medical management of early pregnancy loss (WNHS)
- WA Health EIDO Australia Library Informed Consent Procedure Information Sheets:
  - Miscarriage (Treatment Options) (OG17)
  - Surgical Management of miscarriage (OG15)
  - Surgery for Ectopic Pregnancy (OG28)
  - o <u>Termination of Pregnancy</u> (OG10)
- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Patient Information:
  - o Ectopic Pregnancy
  - o Miscarriage
  - Pregnancy Loss

Keywords	Early pregnancy complications, early pregnancy bleeding, early pregnancy pain, pregnancy bleeding algorithm, miscarriage, misoprostol, pregnancy loss, pregnancy failure, medical management of miscarriage, surgical management of miscarriage, suction aspiration, manual aspiration, early pregnancy assessment service, EPAS, complete miscarriage, incomplete miscarriage, missed miscarriage, expectant management of miscarriage, pregnancy of unknown location, PUL, intra-uterine pregnancy of unknown viability, IPUV, Non-viable intra-uterine pregnancy, Progesterone, hCG, QBhCG, quantitative hCG, Beta hCG, βhCG, amenorrhoea, pregnancy loss, ectopic pregnancy, ectopic, tubal ectopic, early gestational sac, intra-uterine gestational sac, IUGS, viability of pregnancy, yolk sac, salpingectomy, salpingostomy, laparoscopy, EC, emergency centre, referral from GP, POC, products of conception, methotrexate, caesarean scar pregnancy, caesarean section scar, caesarean scar, CS pregnancy, CSP								
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Early Pregnancy Complications

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NSQHS Standards Applicable:	Std 1: Clinical Governance  Std 4: Medication Safety		ng for Safety g and Responding to Acute							
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#### **Version History**

Number	Date	Summary
1.0	September	First version.
	2025	Initial content for ectopic and caesearean scar pregnancy extracted from the WNHS Obstetrics and Gynaecology Pregnancy Care: First Trimester Complications Clinical Practice Guideline, and WNHS Miscarriage Clinical Practice Guideline.
		Major content consultation, review and update by senior medical subject matter experts within WNHS.
		Introduction of new 'Pregnancy of Unknown Location' (PUL) content as per SAC1 CIMS recommendation, including introduction of the M6P PUL calculator, using a risk-prediction model as part of a two-step protocol using an initial progesterone level of ≤ 2 nmol/L and serial serum βhCG levels to identify probable failing pregnancies, and to assist the triage performance for stratifying women with a PUL as being at low or high risk.  Review and update of Caesarean Scar Pregnancy content as recommendation from a SAC1 CIMS recommendation. Specific
		instruction within guideline: If mifepristone is considered prior to surgery, it must only be used as an inpatient and not as an outpatient.
		Miscarriage guideline content has been amalgamated into this Early Pregnancy Complications guideline and has been removed from the WNHS restricted guideline section (within the WNHS Intranet) – supported by the WNHS Clinical Governance Committee 26/11/2025. Restriction from the public domain was required prior to the Abortion Legislation Reform Act 2023 (WA) where previously, prescription authority regarding restricted viewing of medical termination of pregnancy pharmacotherapy regime.

The health impact upon Aboriginal people has been considered, and where relevant incorporated and appropriately addressed in the development of this policy.

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