

# Ectopic Pregnancy Management

## 1. Purpose

This guideline outlines the management of women who have a diagnosed ectopic pregnancy. An ectopic pregnancy occurs in about 1 in 60 pregnancies. Combined intra-uterine and extra-uterine pregnancy (heterotopic pregnancy) is rarely encountered (occurs in around 1:40,000 natural pregnancies and substantially more frequently in IVF pregnancies, depending on the number of embryos transferred).

This guideline is related to guideline [‘Pain and Bleeding in Early Pregnancy’](#).

## 2. Definitions

**Ectopic pregnancy** is a pregnancy that is not located in the uterus. The fertilized egg has settled in a location other than the endometrium. The large majority (95%) of ectopic pregnancies occur in the fallopian tube.

**Early Pregnancy Assessment Service (EPAS)** is located in the Women's Emergency Care (WEC). EPAS sees women with and without scheduled appointments during business hours Monday to Friday.

## 3. Responsibilities

**Gynaecology registrar** is responsible for clinical assessment, determining and implementing appropriate management.

**WEC HMO/Registrar** is responsible for providing acute/emergency care if required.

## 4. Guideline

### 4.1 Clinical presentation and diagnosis

(See guideline [‘Pain and Bleeding in Early Pregnancy’](#))

Ectopic pregnancy is suspected when a woman presents with a combination of the following:

- **Clinical:**
  - History of amenorrhea
  - Pelvic pain and/or abnormal bleeding in the first trimester
  - Shoulder tip pain
  - Dizziness or spells of fainting
  - Other evidence of blood in the peritoneal cavity including haemodynamic compromise
  - Adnexal tenderness, cervical excitation, signs of peritonism.
- **Biochemical:**
  - Positive pregnancy test (urine or serum).
- **On transvaginal ultrasound:**
  - Intrauterine gestational sac not seen
  - Ovarian / fallopian mass may be seen (note: an adnexal mass will not be found in a small minority of women with an ectopic pregnancy)
  - Blood in the Pouch of Douglas.

Where clinical and ultrasound findings are not conclusive, diagnostic laparoscopy may be indicated.

### 4.2 Risk factors for ectopic pregnancy

- Women with previous ectopic pregnancy
- Previous pelvic infection or pelvic inflammatory disease
- IUCD in situ
- Previous pelvic surgery – including caesarean section, tubal surgery, appendicectomy
- History of fertility problems – including assisted conception

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- Progestagen only contraception.

## 4.3 Selecting an appropriate management method

When **ectopic pregnancy** is diagnosed or considered likely the gynaecology registrar will:

- Clinically assess the woman, including vaginal examination if planning non-surgical treatment.
- Discuss proposed management with the gynaecology consultant.
- Advise woman of safe treatment options, advantages and disadvantages.
- Ensure woman participates in the selection of the most appropriate treatment.

Treatment of interstitial and non-tubal ectopic pregnancies (such as ovarian, cervical and caesarean section scar ectopics) is not covered here as it needs to be individualized with consultant gynaecological and ultrasonological input. A helpful review was published in 2012 <sup>1</sup>. Treatment may include intrasac injection and/or multiple dose methotrexate (see appendix A for dosage schedule) or other interventions.

Plans for management and follow-up should be clearly recorded in the EPAS record and in any discharge letter from the EPAS.

Management method	Clinical criteria
<b>Surgical</b>	<p><b>Surgery</b> is the default treatment for ectopic pregnancy, because of the risk of intraperitoneal haemorrhage and rupture of untreated ectopic pregnancy, with associated morbidity and mortality.</p> <p>Indicated if <b>any</b> of the following apply:</p> <ul style="list-style-type: none"> <li>• Not haemodynamically stable</li> <li>• Intraperitoneal bleeding on the basis of clinical or ultrasound findings</li> <li>• Fetal heart activity on ultrasound examination</li> <li>• Adnexal mass measuring <math>\geq 3.5</math>cm by ultrasound</li> <li>• <math>\beta</math>hCG level <math>\geq 3500</math> IU/l</li> <li>• Moderate to severe pelvic pain</li> <li>• Any contraindication to medical management</li> </ul>
<b>Medical</b>	<p><b>Medical management</b> with methotrexate may be considered if diagnostic parameters indicate haemorrhage and rupture are less likely <b>and</b> the woman clearly understands the risks and indicators for seeking urgent care <b>and</b> is willing to attend for regular follow up (usually 1-2 per week for 3 weeks)</p> <p>All the following criteria must also be met:</p> <ul style="list-style-type: none"> <li>• Haemodynamically stable</li> <li>• No or mild pelvic pain; no significant pelvic tenderness on vaginal examination</li> <li>• <math>\beta</math>hCG <math>&lt; 3500</math> IU/L (note: may bleed or rupture at much lower hCG levels.)</li> <li>• Transvaginal ultrasound shows no fetal heart activity, an un-ruptured ectopic mass size <math>&lt; 3.5</math>cm and no significant blood in the peritoneal cavity or pouch of Douglas</li> <li>• Will use reliable contraceptive for 3 months from the last methotrexate dose</li> <li>• Normal LFT, U&amp;E and FBC (no liver, renal or bone marrow impairment)</li> <li>• No known contraindications to methotrexate eg aplastic anaemia, active liver disease, etc. Refer to MIMS if in doubt.</li> <li>• Not currently taking non-steroidal anti-inflammatory drugs(NSAID), diuretics, penicillin and tetracycline group drugs (this is not so critical for the single dose methotrexate regimen).</li> <li>• No co-existing intrauterine pregnancy</li> </ul>

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Management method	Clinical criteria
	<ul style="list-style-type: none"> <li>Not breastfeeding</li> </ul>
<b>Expectant</b>	<p>Consider if failing pregnancy/tubal miscarriage likely and the woman is willing to attend follow up as necessary. This usually means the woman has:</p> <ul style="list-style-type: none"> <li>No pain or tenderness attributed to the ectopic</li> <li>Low/falling hCG levels (usually well below 1,000 IU/l)</li> <li>Ultrasound findings are inconclusive (<b>i.e.</b> location of the pregnancy may not be established with certainty).</li> </ul> <p>See also Guideline: <a href="#">Pain and Bleeding in Early Pregnancy</a></p>

Admission pack should include:

- Printed Methotrexate Treatment Record for Women with Ectopic Pregnancy (MR/53)
- Information for women
- Consent form
- Medication chart.

#### 4.4 Bereavement Support

Where a woman and her partner are particularly distressed by their loss, referral to a bereavement support worker may be appropriate; provide contact details for Women's Social Support Services or Pastoral Care and Spirituality Services.

#### Note:

- The psychological impact of early pregnancy loss may seriously affect women and their partners
- When safe to do so, time should be given for women to make decisions and counselling should be made available
- Evidence has shown that there may be little difference in psychological outcomes when comparing surgical and medical methods of managing ectopic pregnancy.

#### 4.5 Surgical Management

##### Treatment schedule:

The Gynaecology registrar will:

- Explain treatment to the woman (and partner) and provide information booklet on ectopic pregnancy
- Obtain written informed consent
- Arrange date and time for surgical management including booking of Operating Theatre and inpatient bed
- Request/arrange pre-treatment bloods (i.e.  $\beta$ hCG, group and hold, FBC)
- Prescribe Anti-D for Rhesus negative women according to the guideline: [Anti-D Immunoglobulin Use in Maternity Patients](#).

##### Surgical methods:

If the woman is:

- Haemodynamically stable, a laparoscopic approach is preferable to an open approach
- Not haemodynamically stable:
  - surgical management should be performed even before blood and fluid losses have been replaced
  - resuscitate

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- secure immediate IV access
- send blood for FBC and cross match 4 units of blood
- inform Operating Theatre, anaesthetist and on-call gynaecology consultant, stressing the urgency of the situation.

*Salpingectomy* is often performed, particularly if:

- The tube is severely damaged
- There is uncontrolled bleeding
- There is a recurrent ectopic pregnancy in the same tube
- There is a large tubal pregnancy of >5cm
- The woman has completed her family.

*Laparoscopic salpingotomy* should be considered as the primary treatment if the woman has contralateral tube disease and desires future fertility.

If a family wants to bury the products of conception at home:

- Ensure the remains are not placed in formalin
- Consult a bereavement worker
- Discuss with Anatomical Pathology staff.
- Refer to the [Bereavement Response Manual](#) (available as a PDF) which can be found in the Women's Intranet-only Policy and Procedure Manual: linked to any of the Reproductive Loss procedures.

## On discharge after surgery:

The Gynaecology registrar will:

- Provide contact numbers / appointments for Women's Social Support Services / Pastoral Care & Spirituality Services and information booklet on ectopic pregnancy.
- Advise woman:
  - To see GP in one week for removal of sutures
  - What to expect (in terms of pain, bleeding etc).
  - To take simple analgesia for pain
  - To contact the registrar of the unit that operated on the patient or WEC if concerns regarding pain or bleeding
- Ensure contraceptive plan is in place
- Ensure clinical review is planned to discuss relevant issues regarding future fertility and pregnancy care; offer appointment to gynae post-operative clinic
- Complete discharge summary and ensure that woman's GP is informed.

## Follow up and monitoring in special circumstances:

Post-salpingotomy or if doubt remains about diagnosis or completeness of removal:

- Notify EPAS of follow up plan and which unit is responsible for the patient (ext 3643, leave message including UR number)
- Day 3  $\beta$ hCG and clinical review by gynaecology registrar if symptoms or results indicate
- Day 7  $\beta$ hCG and clinical review by gynaecology registrar if symptoms or results indicate
- If  $\beta$ hCG plateaus or rises, consider medical treatment.
- Repeat ultrasound examination should only be considered if more than a week post-op and must be discussed with the ultrasound consultant.

## 4.6 Medical management (methotrexate)

The Gynaecology registrar will:

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- Discuss with the gynaecology consultant on call any case where medical management is recommended
- Document in the medical record discussion with consultant, and the unit responsible for the care of the patient.
- Complete and file in the woman's medical record the printed form: Methotrexate Treatment Record for Women with Ectopic Pregnancy (MR/53).

## Treatment schedule<sup>2,3</sup>:

The Gynaecology registrar will:

- Explain treatment to the woman (and partner), provide information booklet on ectopic pregnancy and contact details for EPAS and WEC; include discussion of methotrexate side effects
- Collect pre-treatment bloods (ie.  $\beta$ hCG, U&E, LFT, FBC)
- Prescribe Anti-D for Rhesus negative women according to the guideline: [Anti-D Immunoglobulin use in Maternity Patients](#).
- Obtain woman's weight and height and calculate body surface area (Mosteller method)<sup>4</sup>  

$$BSA (m^2) = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$$
<https://www.amh.net.au/online/misc/bodysurfaceareacalculator.php>
- Obtain written informed consent
- Arrange admission onto the ward (chemotherapy day centre) for administration of methotrexate
- Prescribe a single dose of methotrexate (written up as the total dose of methotrexate in mg). Calculate the dose based on 50mg per m<sup>2</sup> body surface area (round up or down to the nearest 10mg). [Dose will usually be between 70 and 110mg]. Refer to [Appendix 2](#).

## Discharge arrangements:

The Gynaecology registrar will:

- Arrange follow up on day 4 and day 7 (methotrexate given on day 1). The receiving registrar must hand over to the registrar of the treating unit, who is responsible and accountable for ensuring that appropriate follow up occurs, including medical review of the patient and further test results.
- Notify EPAS of treatment and next follow up to ensure patient is entered on the ectopic register (call ext 3643, leave message including UR number)
- Provide contact numbers / appointments for Women's Social Support Services / Pastoral Care & Spirituality Services
- Advise woman of the following:
  - she may experience some pain in the abdomen as the pregnancy resolves
  - she may take simple analgesia – if ineffective, contact EPAS (during hours) / WEC (after hours)
  - avoid vaginal intercourse until clinician satisfied that there is minimal risk of rupture of the ectopic
  - monitoring is needed to assess any changing symptoms and signs, as bleeding or rupture of the ectopic pregnancy may still occur
  - contraception should be recommended for 3 months
  - avoid alcohol for 7 days
  - avoid herbal remedies and vitamin preparations containing folate
- Complete discharge summary and notify the woman's GP.

## Follow up and monitoring:

- Day 1: Day the first dose of methotrexate is given
- Day 4: Clinical review by gynaecology registrar (or delegate),  $\beta$ hCG (expected to rise), discuss with unit consultant gynaecologist if necessary

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- Day 7: Clinical review by gynaecology registrar (or delegate), FBC,  $\beta$ hCG, LFTs, U&E
- Day 14:  $\beta$ hCG in EPAS, other tests (eg FBC) if clinically indicated, clinical review by gynaecology registrar if indicated by symptoms or blood results
- Weekly follow up in EPAS until  $\beta$ hCG is  $<5$  IU/L -  $\beta$ hCG can take several weeks to fall, clinical review by gynaecology registrar if indicated by symptoms or blood results.
- If  $\beta$ hCG does not fall by  $>15\%$  between days 4 – 7:
  - discuss with unit consultant gynaecologist; consider whether surgery is indicated
  - consider second dose of methotrexate (Day 7) (required in  $\sim 15\%$  of cases)
  - management should be guided by clinical findings such as peritoneal irritation and vital signs in association with the  $\beta$ HCG. Women with evidence of rupture or significant pelvic/abdominal tenderness should be discussed with a consultant gynaecologist and are likely to require surgical treatment
  - repeat ultrasound examination is usually unhelpful in these circumstances (the ectopic mass and some free fluid will probably be seen). Some pain is to be expected and is not in itself an indication for ultrasound examination: referral for ultrasound examination in these circumstances should be discussed with a consultant ultrasonologist.

## If second dose is administered:

- Day 7: confirm normal LFT. Injection should be given in opposite gluteal from first injection
- Day 11:  $\beta$ hCG and clinical review by gynaecology registrar
- Day 14: FBC,  $\beta$ hCG, LFTs, U&E and clinical review by gynaecology registrar
- Women with evidence of rupture or significant pelvic/abdominal tenderness should be discussed with a consultant gynaecologist and are likely to require surgical treatment.

## On completion of treatment:

- Ensure contraceptive plan is in place
- Ensure clinical review is planned to discuss relevant issues regarding future fertility and pregnancy care; offer appointment to gynae post-operative clinic
- Dictate a letter to the woman's GP.

## 4.7 Expectant management

The Gynaecology registrar will:

- Explain management plan to the woman (and partner) and provide written information including EPAS and WEC contact details;
- Prescribe Anti-D for Rhesus negative women according to the guideline: [Anti-D Immunoglobulin Use in Maternity Patients](#).
- Arrange follow up on day 4 and day 7 (day 1 being day of diagnosis and treatment plan), in conjunction with EPAS/gynaecology registrar. The receiving registrar who has admitted the patient needs to hand-over to the registrar of the receiving unit. The latter is accountable for clinical follow up. Notify EPAS of treatment and next follow up to ensure patient is entered on the ectopic register (call ext 3643, leave message, including UR number, if no answer)
- Provide contact numbers / appointments for Women's Social Support Services / Pastoral Care & Spirituality Services (as appropriate - refer to section: 4.4 Bereavement support)
- Advise woman of the following:
  - she may experience some pain in the abdomen as the pregnancy resolves
  - she may take simple analgesia – if ineffective, contact EPAS (during hours) /WEC (after hours)
  - avoid vaginal intercourse until clinician satisfied that there is minimal risk of rupture of the ectopic



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- monitoring is needed to assess any changing symptoms and signs, as bleeding or rupture of the ectopic pregnancy may still occur
- Complete discharge summary and notify GP.

## Follow up and monitoring:

- Day 1: Day on which diagnosis is made and follow up planned
- Day 4: Clinical review by gynaecology registrar (or delegate),  $\beta$ hCG, discuss with consultant gynaecologist if necessary
- Day 7: Clinical review by gynaecology registrar (or delegate),  $\beta$ hCG
- Day 14:  $\beta$ hCG in EPAS, clinical review by gynaecology registrar if indicated by symptoms or blood results
- Weekly follow up in EPAS until  $\beta$ hCG is  $<5$  IU/L:  $\beta$ hCG can take several weeks to fall, clinical review by gynaecology registrar if indicated by symptoms or blood results.
- If  $\beta$ hCG does not fall at each visit discuss with consultant gynaecologist; consider whether surgery or methotrexate is indicated.

## On completion of treatment:

The Gynaecology registrar will:

- Ensure contraceptive plan is in place
- Ensure clinical review is planned to discuss relevant issues regarding future fertility and pregnancy care; offer appointment to gynae post-operative clinic
- Send a letter to the woman's GP.

## 5. Evaluation, monitoring and reporting of compliance to this guideline

Compliance to this guideline will be monitored, evaluated and reported through periodic clinical audit.

## 6. References

- 1 Fylstra DL. Ectopic pregnancy not within the (distal) fallopian tube: etiology, diagnosis, and treatment. *Am J Obstet Gynecol* 2012; 206: 289-99.
- 2 ACOG Practice Bulletin Number 94: Medical Management of Ectopic Pregnancy. *Obstet Gynecol* 2008; 111 (6): 1479-85,
- 3 Stovall TG, Ling FW. Single-dose methotrexate: an expanded clinical trial. *Am J Obstet Gynecol.* 1993 Jun;168(6 Pt 1):1759-62; discussion 1762-5.
- 4 Pai MP. Drug Dosing Based on Weight and Body Surface Area: Mathematical Assumptions and Limitations in Obese Adults. *Pharmacotherapy* 2012;32(9):856–868.
- 5 Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy: a meta-analysis comparing “single dose” and “multidose” regimens. *Obstet Gynecol* 2003; 101:778-84
- 6 Royal College of Obstetricians and Gynaecologists - RCOG (2012) Ectopic pregnancy and miscarriage: Diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage (NICE Guideline) <http://guidance.nice.org.uk/CG154/Guidance/pdf/English>
- 7 Hajenius PJ, Mol F, Mol BWJ, Bossuyt PMM, Ankum WM, Van der Veen F. Interventions for tubal ectopic pregnancy. *Cochrane Database of Systematic Reviews* 2007, Issue 1. Art. No.: CD000324. DOI: 10.1002/14651858.CD000324.pub2. <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000324.pub2/abstract>
- 8 Mc Guire BW, Sia LA, Leese PT, Gutierrez ML, Stokstad ELR. Pharmacokinetics of leucovorin calcium after intravenous, intramuscular, and oral administration. *Clinical pharmacy* 1998;7 52-58

## 7. Legislation/Regulations related to this guideline

Not applicable.

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### 8. Appendices

Appendix 1: [Methotrexate multi-dose regimen](#)

Appendix 2: [Methotrexate single-dose regimen](#)

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## Methotrexate Multi-dose Regime



### Methotrexate Multi-dose Regime

Treatment of interstitial and non-tubal ectopic pregnancies (such as ovarian, cervical and caesarean section scar ectopics) needs to be individualized with consultant gynaecological and ultrasonological input.

There is no authoritative therapeutic guideline for multidose regimens, but the following regimen may be suitable<sup>2,5</sup> if the consultant decides treatment should include a multi-dose regimen.

Regimen	Monitoring
Administer methotrexate, <b>1 mg/kg IM</b> , on <b>alternate days</b> (days 1,3,5,7) – <b>maximum 4 doses</b> , according to HCG levels	BHCG weekly until <5 IU/L
Administer leucovorin calcium 7.5mg oral tablets or 6 mg IM on alternate days – days 2,4,6,8	Initial blood count platelets and liver enzymes; repeat day 7
Continue until BHCG drops by >15% in 48hrs OR 4 doses methotrexate given	

# Methotrexate Single-Dose Regime



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## Methotrexate Single-dose Regime

### Body Surface Area Table (m<sup>2</sup>)

Weight (kg)	Height (cm)						
	140	150	160	170	180	190	200
40	1.24	1.30	1.37	1.43	1.49		
50	1.36	1.43	1.50	1.57	1.63	1.70	
60	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

[https://www.amh.net.au/online/misc/body\\_surface\\_area\\_calculator.php](https://www.amh.net.au/online/misc/body_surface_area_calculator.php)

“Methotrexate dose (mg) based on BSA (m<sup>2</sup>)

	Body surface area (m <sup>2</sup> )									
	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2		
Dose (mg)	70	70	80	80	*90	*90	100	100		

A single dose of methotrexate (in mg) is calculated based on body surface area (m<sup>2</sup>) multiplied by 50mg (round up or down to the nearest 10mg)

**Stocked strengths of methotrexate:** 50, 70, 80 and 100mg.

**\*90mg NOT available in the inpatient - please round up or down to nearest available dose. If that particular dose needed 24 hours' notice is required- “**