



Feidhmeannacht na Seirbhíse Sláinte  
Health Service Executive



INSTITUTE OF OBSTETRICIANS  
& GYNAECOLOGISTS  
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

## CLINICAL PRACTICE GUIDELINE

### THE DIAGNOSIS AND MANAGEMENT OF ECTOPIC PREGNANCY

Institute of Obstetricians and Gynaecologists,  
Royal College of Physicians of Ireland  
and  
Directorate of Clinical Strategy and Programmes,  
Health Service Executive

Version: 1.0

Guideline No: 33

Publication date: November 2014

Revision date: November 2017

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## Key Recommendations

1. Women of reproductive age presenting acutely with gastrointestinal symptoms, particularly diarrhoea, as well as those presenting with abdominal pain and/or vaginal bleeding should have a urinary hCG test.
2. A transvaginal ultrasound service should be provided to all acute hospitals or maternity units for the initial investigation of women with a suspected ectopic pregnancy (EP).
3. If appropriate ultrasound services are not available, referral to an Early Pregnancy Assessment Unit (EPAU) is recommended provided that the woman's condition is stable.
4. Ideally, treatment should be based on a positive identification of the EP.
5. Expectant management is an option in selected women with probable EP who have a small mass with low and falling hCG provided they have minimal symptoms and are compliant with follow-up.
6. Methotrexate (MTX) therapy may be considered for women with an adnexal mass  $\leq$  35 mm whose initial hCG is less than 1500 IU/L, provided they have minimal symptoms and compliance with follow-up is anticipated.
7. A laparoscopic approach is preferred for the surgical management of EP. Either salpingectomy or salpingotomy may be used. Both have a similar outcome regarding future pregnancy success.
8. Salpingectomy is appropriate for women who have a healthy contralateral tube and it may be necessary in cases of uncontrolled bleeding or extensive tubal damage.
9. Salpingotomy has a greater risk of persistent trophoblastic activity requiring follow up with serial hCG monitoring. MTX therapy is appropriate for treatment of persistent trophoblastic activity.
10. A woman diagnosed with ectopic pregnancy, and her partner, need to have the diagnosis and treatment options communicated sensitively and clearly.

## 2. Purpose and Scope

The purpose of this guideline is to improve the management of women who may have an ectopic pregnancy. It is for use by all healthcare professionals involved in women's care and particularly obstetricians, nurses/midwives, sonographers, radiologists and general practitioners who provide care to women in early pregnancy. The guideline should be read in conjunction with Clinical Practice Guideline No. 1 *Ultrasound Diagnosis of Early Pregnancy Miscarriage* and Clinical Practice Guideline No. 10 *Management of Early Pregnancy Miscarriage*. The guideline aids clinical judgment and does not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow the guideline if it is deemed to be in the best interest of the woman.

## 3. Background and Introduction

Worldwide, ectopic pregnancy (EP) remains the leading cause of maternal death in the first trimester (Autry, 2013). The most recent figure for the rate of EP in Ireland is 14.8 per 1,000 maternities (HIPE, 2012). In Ireland, as in most of the developed world, there has been a reduction in mortality from EP reflecting a success story of modern management. A life-threatening surgical emergency in a woman with a positive pregnancy test and haemodynamic shock has been converted to a non-urgent medical condition in many cases. In the US from 1970 until 1992 the mortality rate decreased by 90% despite a simultaneous 6-fold increase in incidence of EP. Death rates from ectopic pregnancy in the UK have almost halved from an estimated 31.2 (95% CI 16.8–57.9) per 100,000 estimated ectopic pregnancies for 2003-05 to 16.9 (95% CI 7.6–37.6) for 2006-08 (The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom, 2011). The major improvement in mortality came as a result of earlier and more accurate diagnosis, made possible by the development of high-resolution ultrasonography and radioimmunoassay for human chorionic gonadotropin (hCG) and also the widespread availability of laparoscopy (Lipscomb, 2010).

Serial hCG measurement is widely used in the diagnosis of early pregnancy complications. In the US this is combined with an aggressive strategy of intervention by uterine curettage to distinguish a non-viable intrauterine pregnancy (IUP) from an EP. Transabdominal scanning by non-specialists is still widely used in emergency room assessment in the US. A different approach has been taken in Europe where Early Pregnancy Assessment Units (EPAU)'s have been introduced to provide specialist assessment. The preferred option for first line investigation of a woman who is symptomatic in the first trimester is transvaginal ultrasound scanning (TVS). In cases of suspected EP serial hCG measurement may be combined with an extended period of observation and follow-up scanning after an interval of a week or more (NICE, 2012). Every Irish maternity unit now has an EPAU with an evolving standardisation of practice along the European model.

Despite improvements in prompt diagnosis of this potentially fatal condition there are avoidable factors in over half of the associated deaths. EP remains responsible for 6% of maternal deaths which mainly occur after an acute initial presentation. Women who present with signs of hypovolemia demand rapid diagnosis and management. Yet in about half of those with EP presenting to emergency departments the diagnosis is missed at first assessment (CMACE, 2011).

The development of algorithms for diagnosis and medical management using MTX has allowed one third of EP's to be managed without surgery (Hoover *et al.*, 2010). This results in fewer complications of treatment and lower costs. Surgery, when performed, is more likely to be laparoscopic. By 2007 a woman in the US was twice as likely to have laparoscopic surgery as laparotomy.

## 4. Methodology

Medline, EMBASE and Cochrane Database of Systematic Reviews were searched using terms relating to ectopic pregnancy, diagnosis and management. Searches were limited to humans and restricted to English language articles published between January 2000 and June 2013. Relevant meta-analyses, systematic reviews, interventional and observational studies were included.

The guideline was developed by Professor Michael Gannon. The guideline was peer-reviewed by Dr Anne Bergin (Midwifery), Dr Brian Cleary (Pharmacy), Dr Sam Coulter-Smith (Rotunda), Dr Nadine Farah (Coombe), Ms Síle Gill (Midwifery), Ms Caroline Keegan (Midwifery), Ms Valerie Kinsella (Midwifery), Ms Máiread McGuire (Pharmacy), Dr Mary Moran (Midwifery), Dr Aoife Mullally (Obstetrics), Ms Janet Murphy (Midwifery), Ms Mary O'Reilly (Midwifery) Professor Michael Turner (HSE Director, Clinical Care Programme in Obstetrics and Gynaecology) and Dr Julia Unterscheider (Obstetrics).

The sample Patient Information Leaflet was reviewed by Ectopic Pregnancy Ireland and Miscarriage Association Ireland.

## 5. Clinical guideline

### 5.1 Clinical assessment

About 5% of women with EP present in haemorrhagic shock. Pallor, tachycardia and hypotension should alert the examiner to major abdominal bleeding, regardless of the intensity of abdominal pain. Shoulder pain occurs from irritation of the diaphragm. Vomiting and diarrhoea may be the presenting symptoms of abdominal bleeding.

Women of reproductive age presenting acutely with gastrointestinal symptoms particularly diarrhoea and dizziness, as well as those presenting with abdominal pain and/or vaginal bleeding, should have a urinary hCG test. This readily available test which is highly sensitive and specific for the beta subunit of hCG narrows the differential diagnosis to pregnancy-related problems.

The common presentation of EP - vaginal bleeding and lower abdominal pain in a woman with delayed menses – also occurs in early pregnancy miscarriage. Women who have an EP typically complain of brown vaginal discharge soon after a missed period, sometimes progressing to heavier bleeding similar to a miscarriage. This is often followed by pain associated with tubal distension and intraperitoneal bleeding at the fimbrial end of the tube (Crochet *et al.*, 2013).

Clinical suspicion is the key to identifying women who need prompt and careful evaluation. The risk of EP increases 2-fold for infertility, 3-fold for tubal pathology and 4-fold for documented salpingitis. One third of pregnancies in women who have been sterilised and one half in women with a LNG-IUS are ectopic. The risk of recurrence is approximately 10% for women with one previous EP and at least 25% for women having two or more previous EP's. Women with a history of EP should be given early access to an EPAU in a future pregnancy (NICE, 2012).

### 5.2 Ultrasound scanning

Speculum and bimanual examination are uncomfortable and have a limited diagnostic value. However the widespread availability of TVS allows this modality to be the initial investigation of choice for women with suspected EP. It is desirable that TVS is carried out by an experienced sonographer with good equipment. If appropriate scanning facilities are not immediately available and provided that the woman's condition is stable referral to an early pregnancy unit within 48-72 hours is recommended. Women with an interim diagnosis of pregnancy of unknown location (PUL) with a history of a previous ectopic pregnancy, and women at high risk of ectopic pregnancy (e.g. assisted conception, IUD in situ) should be seen by an obstetrician and a management plan formulated. Women and their partners should be informed that scanning cannot be guaranteed to be 100% accurate in early pregnancy (NICE, 2012).

The presence of an intrauterine gestational sac containing a yolk sac (from 5.5 weeks) or a fetus (from 6 weeks) constitutes an IUP (Barnhart, 2009). Fetal cardiac activity may be apparent from 6.5 weeks. When no IUP is seen on TVS careful examination of the adnexae and cul-de-sac should be carried out. Approximately 60% of EP's are seen as a nonhomogeneous mass adjacent to the ovary, 20% appear as a hyperechoic ring (bagel sign) and 13% have an obvious gestational sac with a fetal pole. Failure to detect either an intra or extrauterine pregnancy by scan in a woman

with a positive pregnancy test is termed a PUL which is an interim diagnosis requiring further investigation (Barnhart *et al.*, 2011).

### 5.3 Human Chorionic Gonadotropin

Diagnostic accuracy can be improved by measuring the rate of change of serum hCG, which is predictable during the early weeks of a normal IUP. First detectable in maternal serum as early as 8-10 days after ovulation the level of serum hCG rises to between 50 and 100 IU/L by the time of the expected menstrual period. In general, levels double every 1.4 – 2.1 days in early pregnancy and peak at 50,000 - 100,000 IU/L between 8 and 10 weeks gestation. An interval of 48 hours is used to monitor progress in early pregnancy from paired serum hCG levels. If the expected doubling is observed this is a reliable indicator of viability provided an intrauterine sac is seen. A lesser rise is also compatible with normal pregnancy and a minimum increase of 53% in 48 hours was seen in 99% of viable IUP's. Below this level a pregnancy is likely to be nonviable (Barnhart, 2009).

The accumulated experience in ultrasound and hCG assessment has led to a clearer picture of the natural history of EP. Women who present early are more likely to have a rising hCG. In about 20% of EPs the rise in hCG is the same as for a potentially viable IUP (Barnhart, 2009). More than 70% of women with an EP will have a rise in hCG that is slower than the minimal rise for a viable pregnancy or a decline that is slower than the minimal rate of fall in a complete miscarriage. A fall in hCG reflects a natural failure of the pregnancy and in 8% of women with EP the rate of fall is the same as that found after a complete miscarriage, at least 15% over 48 hours. With higher initial levels expect a quicker fall, at least 20% for an initial level of 500 IU/L and 30% for a level of 2000 IU/L or more. The differential for a slowly falling hCG is an EP, a non-viable missed miscarriage or an incomplete miscarriage.

The absolute value of hCG is also useful in diagnosis: above 1,000 – 1,500 IU/L (the discriminatory zone) a viable IUP should be visible on TVS. Although this may be helpful, experience has shown that pregnancies identified by the discriminatory zone are not always ectopic. The majority of non-visualised pregnancies are failed IUP's or incomplete miscarriages with small amounts of retained products or the aftermath of miscarriage when initial levels were high. The discriminatory zone should be interpreted with caution and always in conjunction with the clinical features. When the situation is not acute and the diagnosis is unclear it is usually preferable to continue observation until a positive diagnosis is made (Jurkovic and Wilkinson, 2011).

### 5.4 Expectant Management

Extended observation of women who have an uncertain prognosis in early pregnancy has shown that many EPs resolve spontaneously. Expectant management is an option in selected women with probable EP provided they have minimal symptoms and are compliant with follow-up (Jurkovic and Wilkinson, 2011). In the presence of a nonhomogenous adnexal mass it has been shown that expectant management may have a success rate of over 80% provided that the initial hCG is less than 1,000 IU/L and falling by at least 13% over 48 hours.



Continuing outpatient observation is appropriate if the woman is clinically stable (van Mello *et al.*, 2013). She should be given written information explaining her condition and the possible complications of EP. She should understand the importance of compliance with follow-up and have easy 24 hour access to emergency hospital gynaecological care. Women managed expectantly should be followed at least weekly with serial hCG measurements and TVS to ensure a rapidly decreasing hCG level (ideally less than 50% of its initial level within seven days) and a reduction in the size of an adnexal mass by seven days. As tubal rupture has been reported with low and declining hCG concentrations follow-up should be continued until hCG is at a non-pregnant level (RCOG, 2010).

Considering the potentially serious risks of tubal rupture and haemorrhage and the established safety and effectiveness of medical and surgical treatment of EP, it seems prudent that expectant management should be reserved for asymptomatic patients with very low and falling hCG levels. Any plateau or rise in the hCG measurements should prompt medical or surgical treatment (Jurkovic and Wilkinson, 2011). Expectant management may have to be abandoned in patients who become symptomatic whether or not hCG levels are falling.

## 5.5 Medical Management

Systemic MTX (MTX) is a safe and effective treatment for EP. MTX avoids anaesthesia and is simpler, less invasive and less costly than surgery. MTX is a folic acid antagonist that inhibits DNA and RNA synthesis by inactivating dihydrofolate reductase. Rapidly proliferating tissues such as trophoblast cells are particularly vulnerable to its actions. MTX has a half-life of 8-15 hours.

Women with EP who have minimal symptoms and a low level of hCG should be considered for medical treatment (Mol *et al.*, 2008). MTX therapy can be considered for those whose initial hCG is less than 1,500 IU/L with an adnexal mass not greater than 35 mm (NICE, 2012). Although medical therapy can be successful at higher levels of hCG there is a price to be paid in longer follow-up and a higher rate of surgical re-intervention. A candidate for medical management with MTX should be haemodynamically stable with no evidence of acute intra-abdominal bleeding and not in severe or persistent pain. She should have no contraindication to MTX therapy and should have a reliable commitment to comply with follow-up surveillance (ASRM, 2008).

Contraindications include:

- pre-existing blood dyscrasias, such as bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anaemia
- serious, acute or chronic infections such as tuberculosis, HIV or other immunodeficiency syndromes
- ulcers of the oral cavity and known active gastrointestinal ulcer disease
- breast-feeding
- concurrent vaccination with live vaccines (<http://www.hpra.ie/homepage/site-tools/search?query=MTX>)

MTX is directly toxic to hepatocytes and is cleared from the body by renal excretion; therefore it should not be used in women with hepatic or renal disease. For women with suspected hepatic or renal disease screening should be performed by liver function tests and serum creatinine (Clark *et al.*, 2012).



The single dose MTX protocol was developed to reduce the incidence of side effects, eliminate the need for folic acid rescue and increase convenience of administration. The single dose MTX has proved successful in treating EP and is the regime favored in the UK (Kirk *et al.*, 2007). The regime involves a single administration of MTX by intramuscular injection with monitoring of hCG levels on day 4 and day 7. The dose of MTX can be calculate in either of two ways. The first method is based on a calculation of 1mg/kg body weight. The second method is based on body surface area. Please see Appendix 2 for calculations. All calculations should be double-checked by two people prior to administration. If the calculated dose is above 100mg, please recheck dose carefully. When MTX is not available on the wards out of hours, and the pharmacy is closed, provisions should be made to ensure that there is no delay in obtaining MTX at the appropriate dose for the patient. Prepacks can be made up that contain 2 x vials of MTX, patient information leaflet and prescribing and administration information.

If there is less than the expected 15% decrease in hCG, the dose of MTX can be repeated. Measure hCG at weekly intervals until non-pregnant levels are reached. At least 15% of medically treated women require a second dose of MTX. Surgery is indicated for failure of satisfactory medical reduction in hCG level.

Almost 75% of women experience abdominal pain following treatment (RCOG, 2010). This may reflect tubal bleeding or tension from a haematoma. Increasing or severe pain should prompt re-evaluation, preferably as an inpatient, to determine if observation and medical treatment can be continued safely. Surgery should be performed for suspected tubal rupture, which may occur in approximately 7% of women.

The use of MTX in a presumed EP which is subsequently identified as a viable intrauterine pregnancy may cause exposure of the fetus during a critical stage of embryogenesis. Great care must be taken to confirm the diagnosis of EP prior to administration of MTX (Nurmohamed *et al.*, 2011). Although MTX may persist in body tissues for extended periods of time after treatment has stopped, there are no reported cases of MTX embryopathy in a baby exposed to MTX from maternal treatment of a prior ectopic pregnancy. However, it is important to advise women who receive MTX that they should wait at least three months before attempting to become pregnant again (Hackmon *et al.*, 2011).

## 5.6 Surgical Management

Surgery is preferable if the hCG level is >1500 IU/L or if there is a visible EP sac with fetal cardiac activity or if there is a mass of greater than 35 mm (NICE 2012). In appropriate cases surgery provides rapid confirmation of the diagnosis with shorter resolution time of the EP thus avoiding prolonged monitoring. Surgery also allows an accurate assessment of the pelvis which is helpful for counselling. It is preferable to demonstrate an EP sac or adnexal mass on TVS prior to surgery.

A laparoscopic approach to the surgical management of EP is preferred. A woman with haemodynamic instability due to intraperitoneal haemorrhage should be treated by the most expedient surgical method to gain rapid haemostasis. Without evidence for an open or laparoscopic approach for a woman in shock, laparotomy has traditionally been favoured (RCOG, 2010). More recent evidence suggests that laparoscopic

treatment is safe and effective for suitably trained and experienced staff (Odenjinmi *et al.*, 2011).

Salpingectomy is recommended for recurrent EP in the same Fallopian tube, extensive damage to the involved tube, uncontrolled bleeding or for women who have completed childbearing. Salpingotomy is preferred in those women who do not have a healthy contralateral tube.

Two recent randomised trials have found no significant difference in fertility between women who had salpingectomy and those who had salpingotomy. The 2-year rates of IUP were 64% and 70% respectively in one reported study (Fernandez *et al.*, 2013) and the 3-year rates were 56% and 61% after salpingectomy and salpingotomy respectively in the second study (Mol *et al.*, 2014). There were no significant differences in recurrent EP's which were 12% vs 8% (Fernandez *et al.*, 2013) and 5% vs 8% (Mol *et al.*, 2014) after salpingectomy and salpingotomy respectively. Persistent trophoblast developed in 7% of the salpingotomy group (Mol *et al.*, 2014), 15 times more than after salpingectomy. Prophylactic use of single shot MTX after salpingotomy significantly lowers the persistent trophoblast rate. However, ten women need to be treated with MTX to prevent one woman with persistent trophoblast. Monitoring serum hCG concentrations seems a better option (Hajenius *et al.*, 2009). A fall of <50% on postoperative day 1 is three times more likely to proceed to persistent trophoblast than a fall of >50%. Serum hCG should be followed weekly until it decreases to a non-pregnant level. Those who have a rise or plateau in hCG indicating persistent trophoblast should be treated with MTX according to the regime outlined above.

The choice of salpingectomy or salpingotomy should take into account both the clinical situation and the woman's preference.

## 5.7 Non-tubal ectopic pregnancies

Ultrasound is an essential tool in the diagnosis of non-tubal EPs. As is the case with tubal EPs expectant or medical management can be employed and is more likely to succeed with a smaller pregnancy and lower baseline hCG. Close monitoring is needed as it may take several months for hCG to return to normal and there is also a slow resorption of pregnancy tissue seen on scan.

### 5.7.1 Interstitial pregnancy

The pregnancy is implanted in the tubal segment which is within the muscular wall of the uterus (Moawad *et al.*, 2010). Pain is more common than bleeding at clinical presentation. A significant number of women have a history of damaged tubes and surgery including salpingectomy (Oliver *et al.*, 2007).

Many are diagnosed at first trimester scanning by the presence of an eccentric gestational sac. A thin surrounding myometrial layer helps to distinguish this from an angular intrauterine pregnancy. A further sonographic sign is the presence of an echogenic line running from the endometrial cavity to the gestational sac.

For failed medical treatment or when rupture is suspected surgery is usually necessary. Laparoscopic linear cornuostomy is carried out in a similar manner to salpingostomy for EP including allowing spontaneous closure of the corneal incision.

Cornual resection is another option that may also be carried out by laparotomy. Post-operative monitoring by hCG should be performed.

### 5.7.2 Cornual pregnancy

This is a pregnancy implanting in the contralateral rudimentary horn of a unicornuate uterus (Mavrelos *et al.*, 2007). Presentation may be delayed and is usually with abdominal pain. About 50% present after rupture and morbidity is high.

The sensitivity of ultrasound diagnosis is low. The appearance is of a gestation sac separate from an empty unicornuate uterus which is identified by the single interstitial tube. The sac is mobile and surrounded by a thick myometrial layer. A vascular pedicle may be seen joining the gestational sac and the lateral aspect of the empty unicornuate uterus. Surgical cornual excision is usually preferred either by laparoscopy or open surgery and avoids the risk of recurrence.

### 5.7.3 Cervical pregnancy

Implantation is within the cervical canal. Common predisposing factors are curettage, caesarean section or cervical surgical procedures. Usually the first complaint is of painless vaginal bleeding and speculum examination may reveal an open external cervical os with a fleshy mass protruding (Fylstra, 2012).

Ultrasound shows a gestation sac distal to a closed internal cervical os. Doppler demonstration of surrounding vasculature helps distinguish a cervical pregnancy from a displaced intrauterine pregnancy. In addition, gentle pressure with the transvaginal probe may elicit the "sliding sign" whereby a miscarrying sac is seen to slide within the cervical canal unlike the cervical pregnancy which is fixed.

Cervical dilation and curettage may provoke bleeding. Infiltration of the cervix with a haemostatic vasoconstricting agent, followed by the placement of cervical sutures to temporarily occlude the descending branches of the uterine arteries followed by suction curettage (without dilation) and post-curettage cervical canal balloon tamponade has proven successful in treating first trimester cervical pregnancies. Another treatment option is uterine artery embolisation which has been used in combination with MTX (Zakaria *et al.*, 2011).

### 5.7.4 Caesarean scar pregnancy

Caesarean scar pregnancy differs from placenta accreta in that the pregnancy is situated outside the endometrial cavity and completely surrounded by myometrium and scar tissue (Ash *et al.*, 2007). It may present as early as 5–6 weeks with light painless bleeding or as an incidental scan finding (Rotas *et al.*, 2006). Depending on its location in the uterine wall growth may be toward the cavity resulting in profuse bleeding or toward the abdominal cavity resulting in severe pain and rupture. There is a substantial risk of catastrophic haemorrhage if the pregnancy continues past the first trimester. The mortality rate of nearly 1 in 500 is more than 10 times that for all EPs (CMACE, 2011).

Diagnosis by TVS relies on an empty uterine cavity and a gestation sac in the anterior uterine isthmus with a thin myometrium between sac and bladder. There is no contact between the sac and the uterine cavity and the cervical canal is empty. Colour flow Doppler may show distinct circular peritrophoblastic perfusion surrounding the gestation sac.

Expectant management carries a significant risk of uterine rupture and hysterectomy. Medical treatment using MTX is an appropriate first line measure. Blind uterine curettage, which may not reach the gestation sac, may result in heavy bleeding and should be discouraged. Surgical removal can be carried out by operative hysteroscopy or laparoscopy, with the choice depending on the location of the pregnancy sac. Open surgical treatment by wedge resection should be considered in women who do not respond to these methods and for women who present after rupture or if facilities and expertise for operative endoscopy are not available.

### **5.7.5 Ovarian pregnancy**

The clinical features are similar to those for tubal EP, current use of an IUD is more likely in cases of ovarian pregnancy (Odejinmi *et al.*, 2009).

Apart from the few cases with a clear cut yolk sac or fetal pole visible in the ovary ultrasound diagnosis is difficult. The ring surrounding an EP usually shows greater echogenicity than the surrounding ovarian tissue unlike the ring of a corpus luteum cyst which is less echogenic. If laparoscopy for suspected EP reveals that the tubes are normal a close inspection of the ovaries should be performed. Typically an ovarian EP has the appearance of a cystic haemorrhagic mass.

Optimum management is resection of the ovarian pregnancy with preservation of healthy ovarian tissue. Follow-up hCG monitoring is recommended. MTX is appropriate for persistent trophoblast and has also been used for primary treatment but is limited in this regard due to the need for laparoscopic and histologic confirmation of diagnosis.

### **5.7.6 Abdominal pregnancy**

Implantation in the Pouch of Douglas is the most common site for abdominal pregnancy. Diagnosis is difficult and is usually made intraoperatively (Oliver *et al.*, 2007).

Primary abdominal pregnancy which presents in the first trimester can be removed laparoscopically with minimal morbidity. Secondary abdominal pregnancies following tubal ectopic rupture are usually advanced at presentation and require an open procedure. If the placenta is firmly attached with no significant bleeding it can be left in situ after trimming the cord and membranes. Postoperative MTX has been used to assist the involution process.

## 5.8 Anti-D Rhesus prophylaxis

Non-sensitised women who are Rhesus negative with a confirmed or suspected ectopic or suspected ectopic pregnancy should be offered anti-D immunoglobulin 250 iu (50 micrograms) as soon as possible (RCOG, 2010).

## 5.9 Counselling

Healthcare professionals providing care for women with early pregnancy loss must be mindful of the emotional impact of pregnancy loss. The unavoidable delay that frequently attends the diagnosis of ectopic pregnancy may cause additional and significant emotional distress. It is important that the purpose of each investigation is clearly explained and the treatment options are unambiguously outlined so that the woman and her partner may understand the treatment choices available to her. The choice of treatment is jointly agreed between the woman and the attending obstetrician. Information is communicated in a sympathetic manner that takes cognisance of the couple's social and cultural needs. At the discretion of the attending obstetrician, or if requested by the couple, a referral for bereavement counselling may be recommended. Staff providing care to women with early pregnancy loss should receive training in communicating bad news.

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## 7. Implementation Strategy

- Distribution of guideline to all members of the Institute of Obstetrics and Gynaecology, to all maternity units and to all acute general hospitals.
- Implementation through HSE Obstetrics and Gynaecology Programme local implementation boards.
- Distribution to other interested parties and professional bodies.

## 8. Key Metrics

- a) Total number of ectopic pregnancies diagnosed
- b) % treated expectantly
- c) % treated with MTX only
- d) % treated laparoscopically
- e) % treated using laparotomy
- f) % requiring MTX for persistent trophoblastic activity
- g) Number of caesarian section scar ectopic pregnancies.

## 9. Qualifying Statement

These guidelines have been prepared to promote and facilitate standardisation and consistency of practice using a multidisciplinary approach. Clinical material offered in this guideline does not replace or remove clinical judgment or the professional care and duty necessary for each pregnant woman. Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion
- Advising women of their choices and ensure informed consent is obtained
- Meeting all legislative requirements and maintaining standards of professional conduct
- Applying standard precautions and additional precautions, as necessary, when delivering care
- Documenting all care in accordance with local and mandatory requirements.

## 10. Appendices

- Appendix 1: List of National Guidelines
- Appendix 2: MTX Regime
- Appendix 3: Sample Patient Information Leaflet

## **Appendix 1: List of associated national guidelines**

Ultrasound Diagnosis of Early Pregnancy Miscarriage (Clinical Practice Guideline No. 1, issued December 2010). [http://www.rcpi.ie/content/docs/000001/647\\_5\\_media.pdf](http://www.rcpi.ie/content/docs/000001/647_5_media.pdf)

Management of Early Pregnancy Miscarriage (Clinical Practice Guideline No. 10, issued April 2012). [http://www.rcpi.ie/content/docs/000001/655\\_5\\_media.pdf](http://www.rcpi.ie/content/docs/000001/655_5_media.pdf)

## Appendix 2: Methotrexate (MTX) Regime

The dose of MTX can be calculated in either of two ways. The first method is based on a calculation of 1 mg/kg body weight. The second method is based on body surface area and is calculated using the following equation.

$$\text{Body Surface Area (m}^2\text{)} = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$$

A body surface area calculator is available in a pack with 2 vials of MTX 50mg/2ml from pharmacy to verify the body surface area. To use this calculator: line up the patients weight and height; the patients' BSA will be shown in the "Adult" window.

It is important to be aware that the two methods of dose calculation give different doses with the body surface area giving the higher dose. The clinician should decide which method of dose calculation is most appropriate for his patient.

## Appendix 3. Sample Patient Information Leaflet

This information leaflet is intended for women who are suspected of having, or are confirmed to have, an ectopic pregnancy.

### ***What is an ectopic pregnancy?***

The normal process of pregnancy usually begins when the sperm and egg meet in the fallopian tube. It is in the fallopian tube that fertilisation takes place. Within a week of fertilisation the fertilised egg moves into the womb (uterus) but if this does not happen, the fertilised egg will implant in the fallopian tube or, less commonly, elsewhere such as the ovary or the abdomen. Very rarely it may implant in the cervix (neck of the womb). Ectopic Pregnancy occurs in approximately 1.5-2% of pregnancies and may be psychologically devastating for a woman and her partner.

### ***What causes an ectopic pregnancy?***

The precise cause of ectopic pregnancy may not be known. However, certain women are at greater risk of experiencing an ectopic pregnancy and these include women who have a history of;

- pelvic infection
- abdominal surgery
- previous ectopic pregnancy
- an Intrauterine Contraceptive Device (IUCD) in situ at the time of conception
- become pregnant while taking the progesterone only pill
- assisted In Vitro Fertilization (IVF) pregnancy.

### ***What are the symptoms of ectopic pregnancy?***

The most common symptom is abdominal pain. Not all women are aware that they are pregnant when they experience abdominal pain and may associate the pain with gastro-intestinal upset. Some women experience pain while passing urine which may lead them to suspect a urinary tract infection. There may also be vaginal bleeding, spotting or a brownish discharge after a missed period. If there is a likelihood that pregnancy has occurred, a pregnancy test will alert to the possibility of an ectopic pregnancy. However, the first pregnancy test may not always be positive and when ectopic pregnancy is suspected the test will be repeated next day. Nausea and pain at the tip of the shoulder may also be experienced. Most women attend their family doctor because of some, or many, of the above symptoms. Rarely, a woman may faint or collapse and should this happen she must be brought immediately to the nearest hospital. It is possible though rarely occurs that a woman who has had a tubal ligation (sterilisation) may experience an ectopic pregnancy.

### ***How is an ectopic pregnancy diagnosed?***

A woman with a suspected ectopic pregnancy will be referred ideally to the Early Pregnancy Assessment Unit (EPAU) in a maternity hospital or to the Emergency Department out of Hours in an acute hospital with a gynaecological service. The doctor or midwife will take a detailed medical history and perform a pregnancy test even if a test has already been performed by the woman herself or by her GP. The doctor will examine the abdomen and may do a vaginal examination and/or a speculum examination. As ectopic pregnancy is difficult to diagnose a transvaginal scan will, in most cases, be performed. A transvaginal scan involves inserting a probe about the width of a tampon into the vagina to allow the doctor or sonographer to look at the womb, ovaries and fallopian tubes. However, if the pregnancy is ongoing

for less than 6 or 7 weeks this examination may not be able to confirm an ectopic pregnancy and may need to be repeated some days later. The earlier a woman is in her pregnancy the more difficult it is to diagnose an ectopic pregnancy. If a woman is not acutely ill it may be recommended that the repeat scan is delayed for a day or two. To assist in the diagnosis a blood test measuring hCG (the pregnancy hormone) will be carried out and if necessary repeated at intervals.

### ***What is the management for ectopic pregnancy?***

The choice may be based on the woman's symptoms. It may take a few days to confirm the diagnosis but when this happens the doctor will discuss and recommend one of three treatment options. If at all possible, that is if pain and other symptoms are not severe, 'expectant management' will be recommended. If symptoms are more severe 'medical management' will be considered. 'Surgical management' will be required for women experiencing very severe symptoms e.g. internal bleeding, severe pain or if a fetal heartbeat has been identified in a pregnancy outside the womb.

### ***What is expectant management?***

Expectant management is essentially a 'wait and see' management option as up to 40% of women will not need to have either medical or surgical intervention. This option is suitable for women who have mild or no symptoms and have no vaginal bleeding. The lower the pregnancy hormone, the more likely it is that the pregnancy will end naturally. If this is the case a woman is advised to go home and return to the hospital for a blood test and a transvaginal scan at regular intervals for two to four weeks. Before going home, a woman will be provided with verbal and written information about her treatment plan. If pain increases or if bleeding becomes heavier it will be necessary to return to hospital where the doctor will advise if medical or surgical treatment has become necessary.

### ***What is involved in medical management?***

Medical management avoids anaesthesia and is less invasive than surgery and does not require an overnight stay in hospital. A medication called methotrexate (MTX) is administered by intramuscular injection. In a small percentage of women a second injection may be required some days later. Nearly 75% of women treated with MTX will experience some abdominal pain. However, if the pain increases or if bleeding occurs it is advisable to return to hospital to determine if surgical treatment will be necessary.

### ***What is involved in surgical treatment?***

Hospital admission is necessary when surgical treatment is required. Ideally admission to a gynaecological ward will be arranged. As with many surgical procedures a woman will be given an anaesthetic. The operation will be performed through 'key-hole surgery' (laparoscopy). Two small incisions are made close to the umbilicus (belly button) and the ectopic pregnancy is removed. In some, but not all cases, the fallopian tube will be saved. If the pain is very severe and if there is internal bleeding a more invasive surgical procedure called a laparotomy will be performed. This involves only one but a wider incision in the lower abdomen. Provided the fallopian tube is not damaged it will be preserved during the operation.

### ***Does a woman have any say in the treatment she receives?***

Yes. The doctor will discuss the management options with each woman and, where appropriate, her partner or family. Treatment recommendations will be based on the results of each woman's investigations and her treatment preference. The diagnosis



and all management options should be discussed on an on-going basis with the woman and, if appropriate, those supporting her. The only occasion when a choice is not offered is when a woman presents in an emergency situation where there is severe pain and internal bleeding. If a woman has any questions or concerns she should not hesitate to ask questions.

The advantages and disadvantages of the three treatment options are outlined below. In addition to having one of these treatments women with a Rhesus Negative blood group may be advised to have an Anti-D Rhesus injection.

### Treatment options

Risks	Advantages	Disadvantages
Expectant Management	No hospital stay No anaesthetic No risk from surgery Saves affected tube	Longer follow up May not be successful May still need medical or surgical treatment
Medical Management	No overnight stay in hospital No anaesthetic No risk from surgery	Longer follow up Side effects of drug May still need surgery No guarantee that the affected tube will be saved
Surgical management	Quickest and most effective treatment	Hospital admission Risk of surgical complications 2-4 weeks recovery time for 'key-hole' surgery 4-6 weeks recovery time for abdominal surgery Medication as used for the medical management of ectopic pregnancies may still be necessary

### ***How long will it take to recover?***

The loss of a baby can be a devastating experience for a couple. Physical recovery may take up to 10 weeks but emotional recovery may take much longer. An appointment will be made to meet the hospital's bereavement specialist should the woman or her partner wish to do so. Pregnancy loss may become an overwhelming emotional experience after discharge from hospital in which case it is advisable to use the telephone numbers listed below or to contact your GP.

### ***Does an ectopic pregnancy affect fertility?***

When a fallopian tube is removed and provided the second tube is healthy, fertility is only slightly reduced. It is important to seek antenatal care early during the next and later pregnancies. The GP will refer a woman with a history of an ectopic pregnancy to an Early Pregnancy Assessment Unit where she will have an early scan to confirm

the pregnancy is in her womb. This is important because women who have had an ectopic pregnancy are at a slightly higher risk of having a second ectopic pregnancy.

**How soon can I try for another baby?**

The length of time to physically and emotionally recover from an ectopic pregnancy will vary between individuals. Some couples will feel ready to conceive sooner than others. It is recommended that women treated with MTX should avoid pregnancy for 3 months. In all other cases pregnancy is best delayed until after the next period or until a woman feels ready to try again. Future pregnancies will in all likelihood be more stressful and it is advisable that a woman and her partner feel emotionally ready. In the meantime a woman’s GP will advise on the method of contraception that is best for her. Ectopic Pregnancy Ireland ([www.ectopicireland.ie](http://www.ectopicireland.ie)) provides information and support to those who have been affected by an ectopic pregnancy. All volunteers have first-hand experience of ectopic pregnancy and can be contacted by telephone: 089 436 5742 or by email [info@ectopicireland.ie](mailto:info@ectopicireland.ie). The Miscarriage Association of Ireland ([www.miscarriage.ie](http://www.miscarriage.ie)) also provides a support service for couples who have experienced an early pregnancy loss. The association can be contacted by telephone: 01 873 5702 or by email [info@miscarriage.ie](mailto:info@miscarriage.ie).

**Is there anything one should do in advance of becoming pregnant?**

It is important to enjoy a well-balanced diet, take regular exercise and take folic acid supplements daily prior to and during pregnancy. Folic acid enriched foods will not provide an adequate amount of folic acid for women preparing for or during early pregnancy. Cigarettes and alcohol are best avoided prior to and during pregnancy. Information on folic acid and healthy eating can be found at <http://www.hse.ie/eng/search?q=pregnancy%20diet>.

**Useful telephone numbers**

Hospital Telephone Number: \_\_\_\_\_

Gynaecological Ward: \_\_\_\_\_

Early Pregnancy Assessment Unit: \_\_\_\_\_

Ectopic Pregnancy Ireland (EPI): [www.ectopicireland.ie](http://www.ectopicireland.ie)

EPI Telephone Number: 089 436 5742

EPI email: [info@ectopicireland.ie](mailto:info@ectopicireland.ie)

Miscarriage Association of Ireland (MAI): <http://www.miscarriage.ie/>

MAI Telephone Number: 01 873 5702

MAI email: [info@miscarriage.ie](mailto:info@miscarriage.ie).