

ECTOPIC PREGNANCY

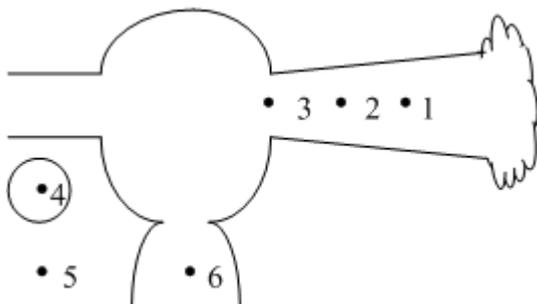
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Document Type	Guideline
Function(s)	Clinical Service Delivery
Health Service Group (HSG)	Women's Health
Department(s) affected	Gynaecology
Patients affected	All gynaecology patients
Staff members affected	All clinicians in gynaecology
Key words	n/a
Author – role only	Clinical Director of Gynaecology
Owner (see ownership structure)	Clinical Director of Gynaecology
Edited by	n/a
Date first published	May 2007
Date this version published	May 2012
Date of next scheduled review	May 2015
Unique Identifier	NMP200/SSG/006

Definition, Incidence and Aetiology

Definition

A pregnancy occurring outside the uterine cavity.



•	Position
1	Ampulla - Commonest site of implantation
2	Isthmus
3	Cornua
4	Ovary
5	Intra-abdominal
6	Cervix

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Definition, Incidence and Aetiology, Continued

Incidence

In most populations 1% of pregnancies will be extra-uterine⁶. The incidence is rising in most countries and in Auckland there is approximately one ectopic pregnancy for every 64 live births. This increased prevalence is associated with a high prevalence of chlamydial infection and pelvic inflammatory disease (PID) The use of more sensitive diagnostic techniques permitting the detection of ectopic pregnancies when previously implantation site would have remained unknown. The more widespread use of assisted reproductive techniques (ART) such as IVF.

Who is at risk?

Women with a past history of:

- Pelvic infection
 - Ectopic pregnancy
 - Tubal surgery/pathology/sterilisation
 - Sub-fertility
 - Current or past IUCD use
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Clinical Features, History and Examination

Clinical features

Clinical features can vary according to the site of the ectopic pregnancy, gestational age and whether rupture of the ectopic has occurred. Many ectopic pregnancies follow a relatively chronic course making clinical diagnosis difficult and sudden collapse associated with tubal rupture is unusual (less than 10% of cases)¹².

Where the finding of a probable ectopic is uncertain because of incongruous ultrasound and an intervention is planned, appropriate checking should occur; e.g. by repeat examination by the same clinician or if immediate treatment is required by another clinician.

History:

- Amenorrhoea: Many patients deny any amenorrhoea and some vaginal bleeding around the time a period is common (probably associated with low progesterone levels).
- Unexpected or continuous light vaginal bleeding in early pregnancy may be present.
- Pelvic/abdominal/shoulder tip pain: Pain is often initially mild and is usually in one or other adnexa. Exacerbations of pain which then settle for several hours or days is common.
- Past history of pelvic inflammatory disease: IUCD use or conception through assisted reproductive technology.

Signs on Examination:

- Minimal to severe abdominal tenderness, guarding or peritonism.
- Cervical excitation.
- Adnexal mass or fullness. It is rare to be able to palpate an ectopic pregnancy on vaginal examination.
- Rarely a collapsed patient.

Diagnosis

Introduction

Increased awareness and diagnostic advances have resulted in the earlier and more consistent diagnosis of ectopic pregnancy, contributing to a decrease in the case fatality rate by 90% over the last 20 years³. It has also permitted a more conservative approach to the management of ectopic pregnancy. The most important advances in diagnosis have been the use of quantitative serum β -hCG measurement and trans-vaginal ultrasound.

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Diagnosis, continued

Serum β -hCG

- 99% sensitivity in detecting pregnancy⁴.
- β -hCG is detectable at the time of a missed menses.
- Abnormal pregnancies are associated with impaired β -hCG production:
 - In normal early intrauterine pregnancies serum β -hCG concentrations double every 48 hours¹¹.
 - An increase in serum β -hCG concentrations of less than 66% in 48 hours is associated with either ectopic or a failing intra-uterine pregnancy in more than 85% of cases⁹.
- Serum β -hCG measurement is the single most important test in women of reproductive age group with abdominal pain.

Clinical Application:

- Diagnosis of pregnancy.
- Serial measurements can be used to assess the viability of a pregnancy.
- To determine the type of sonography to be used.

Caution should be exercised in using serial measurements in very early pregnancy. For viable pregnancies the “doubling-time” for β -hCG concentrations may be occasionally greater than 48 hours. If methotrexate is being considered then a diagnosis of non-viability must be certain.

Ultrasonography (USS)

- Used to confirm or exclude an intrauterine pregnancy. Can be combined with serum β -hCG measurement to produce the concept of a “discriminatory zone”: at a certain concentration of β -hCG a viable intra-uterine pregnancy will always be seen on ultrasound. An intra-uterine pregnancy will be seen at a lower β -hCG concentration with trans-vaginal ultrasound than with abdominal ultrasound. If a patient presents with symptoms suggestive of an ectopic pregnancy, an empty uterus on trans-vaginal ultrasound and a serum β -hCG above the “discriminatory zone” then an ectopic pregnancy is very likely to be present. This may be unreliable in women at high risk of a multiple pregnancy.
 - Discriminatory Zones:
 - β -hCG of > 6000 IU/l – intrauterine gestational sac of a viable pregnancy will be seen with trans-abdominal USS⁹.
 - β -hCG of > 2000 IU/l – viable intrauterine gestational sac or a viable pregnancy will be seen with trans-vaginal USS¹³.

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- Additional USS findings of adnexal mass/significant free fluid in pelvis is suggestive of ectopic pregnancy. If an adnexal gestation sac containing a fetal pole and a visible heart beat is seen (about 10% of ectopic pregnancies) a diagnosis of ectopic pregnancy is certain. The finding of an adnexal mass adjacent to but separate from the ovary makes a diagnosis of ectopic pregnancy very likely. Sometimes the nature of an adnexal mass is difficult to define making diagnosis less certain. In about 70% of ectopic pregnancies an adnexal mass will be seen on trans-vaginal ultrasound at first presentation².

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Diagnosis, continued

- Caution should be exercised when using the concept of a discriminatory zone and the ultrasound finding of an empty uterus if serum β -hCG levels are close to the discriminatory zone. This is particularly true if no ectopic pregnancy is seen and medical therapy is contemplated. There may be a risk of administering methotrexate to women with a very early intra-uterine pregnancy. **Consultant review prior to treatment and the use of a formally reported scan by a Radiologist/Sonographer at National Women's Ultrasound Department is essential.**
- **Heterotopic Pregnancy.** The finding of a viable intrauterine pregnancy is often thought to effectively rule out a diagnosis of ectopic pregnancy. Previously, the incidence of heterotopic pregnancy has been thought to be as low as 1:30 000⁵. The increasing incidence of ectopic pregnancy and the use of ovulation induction drugs and ART has made heterotopic pregnancy more common and should always be considered in such women.
1:100 in ART programmes
1:4000 in general population⁸

Laparoscopy

Careful history, physical examination, β -hCG and ultrasound will in most instances diagnose an ectopic pregnancy. A laparoscopy is usually not indicated as a diagnostic tool. A very early ectopic pregnancy may not be seen at laparoscopy (3% of cases).¹²

Failure to Diagnose an Ectopic Pregnancy

Missing a diagnosis of ectopic pregnancy

On occasions it is not possible to reach a firm diagnosis at initial presentation. The presence of "Trophoblast of Unknown Site" will have been confirmed by serum β -hCG measurement and negative ultrasound findings, but further serum β -hCG measurement and ultrasound evaluation will be needed. This should be done no more than 48 – 72 hours later.

Common reasons for failing to diagnose an ectopic pregnancy are⁶:

Developed by:	Deputy Clinical Director	Classification:	NMP200/SSG/006
Authorised by:	Clinical Director O&G	Date Issued:	Reviewed May 2012

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- A failure to consider EP as a diagnosis.
- A failure to correlate scan findings and β -hCG levels.

Implications of missed ectopic

- Loss of opportunity to implement more conservative management.
- May require salpingectomy or laparotomy.
- Blood transfusion
- Death

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Failure to Diagnose an Ectopic Pregnancy, Continued

Pregnancy loss counseling

Pregnancy loss counseling is to be offered in all cases of expectant management, before administration of methotrexate, and in cases of surgical management when it is appropriate because the woman is asymptomatic.

This may require the on call social worker to be called.

Treatment/Management Guidelines

Expectant / Conservative Management

May be considered if the serum β -hCG concentration is less than 1000 IU/l.

Medical Management

Intra-muscular Methotrexate

Surgical Management

- Laparotomy or laparoscopy
- Salpingotomy – opening the tube and removing trophoblast
- Salpingectomy – removing the tube

The words salpingostomy and salpingotomy are used interchangeably.

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Expectant Management of Ectopic Pregnancy and Trophoblast of Unknown Site

Criteria for expectant management

- Minimal symptoms.
- No significant free fluid in Pouch of Douglas.
- β -hCG < 1000 IU/l.
- Patient able to understand and attend for follow-up

Follow-up

Patients should have a repeat serum β -hCG measurement and trans-vaginal ultrasound at 48-72 hours. As many as 60% of ectopic pregnancies in women with serum β -hCG concentration less than 1000 IU/l will resolve spontaneously^{7 10}. However, some women will experience pain associated with tubal abortion and there is a risk of tubal rupture even at low β -hCG levels.

- If β -hCG levels are rising then medical or surgical treatment should be considered.

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Expectant Management of Ectopic Pregnancy and Trophoblast of Unknown Site, continued

Trophoblast of unknown site

In women with serum β -hCG levels less than the discriminatory zone for trans-vaginal ultrasound (see page 5) and negative ultrasound findings a diagnosis of trophoblast of unknown site is made. Many of these women will have failing intra-uterine pregnancies and serum β -hCG levels will usually start to fall rapidly. Others will have extra-uterine pregnancies that may eventually be detected on a subsequent ultrasound. Follow-up with trans-vaginal ultrasound and serum β -hCG measurement at 48-72 hours is required. Once β -hCG levels are falling rapidly, unless new symptoms develop further ultrasonography is no longer necessary.

Medical Treatment of Ectopic Pregnancy

Criteria for medical therapy

- Haemodynamically and clinically stable.
- No significant free fluid in Pouch of Douglas.
- Gestation sac <5cm in adnexa.
- Normal blood count, liver enzymes, serum creatinine.
- β -hCG < 5000 IU/l.
- Desire for future fertility (methotrexate is still an option for women who don't wish to have further children).
- Patient able to understand and attend for follow-up

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- Patient informed (by medical officer/consultant) regarding possible adverse actions.

Drug used

Methotrexate (a single intra-muscular dose initially – repeated doses may be necessary – see protocol)

Dose

50 mg/m² of patient body surface area (typically 75mg to 95mg) calculated using nomogram. (See Administration of Methotrexate later in policy)

Side effects

- Stomatitis - common
- Gastritis, nausea - common
- Leucopenia - rare
- Thrombocytopenia - rare
- Raised liver enzymes - rare
- Alopecia- very rare

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Medical Treatment of Ectopic Pregnancy, continued

Contra-indications

Methotrexate therapy should not be used in the presence of :

- Hepatic dysfunction: AST > 2x normal.
- Abnormal renal function: Serum creatinine level elevated
- Blood dyscrasia: Leucocyte count < 3000 cells/cc.
Platelet count < 100,000/cc.
- Active peptic ulcer disease.
- Presence of fetal cardiac activity.
- Any active liver/renal disease.

Protocol

<i>Methotrexate Treatment for Unruptured Ectopic Pregnancy</i>		
Day	Tests	Therapy
0	β -hCG, FBC, AST, Creatinine, Group and hold, rhesus status, transvaginal scan	Methotrexate
4	β -hCG	

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7	β -hCG, AST, FBC	
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Repeat doses of intramuscular methotrexate may be given, if β -hCG levels are rising or plateauing.

All women that have Methotrexate need to have an USS (ultrasound scan) the day of Methotrexate administration at National Women's Hospital by a certified sonographer or radiologist. A second opinion from another consultant or discussion with the radiologist reporting on the USS is wise if diagnosis is not certain.

All women must receive counselling (from a pregnancy loss counsellor or nurse certified as qualified) prior to methotrexate administration.

Administration of IM Methotrexate

Before Administering

This procedure is a delegated consultant responsibility that is only undertaken by nurses who have been designated to do so following training.

- Patient must be informed of the actions, side effects, contraindications and treatment process.
- Formal pre-decision counselling must be undertaken before administration of Methotrexate. (Counsellors are available through on call – out of hours and weekends and must be called to see patient.)
- Ensure patient has the information pamphlet. Before ordering the drug, the patient's verbal consent is to be obtained by the nurse on the register after detailed explanations. Verbal consent is to be documented.
- Ensure all blood tests are done. These must be checked by the Registrar in conjunction with their supervising consultant and they must ensure that the results meet the criteria stated in this policy.
- The clinician administering the Methotrexate should know the following:
 - the usual range of drug doses, the recommended dose is 50mg (m²)
 - the method of administration

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- possible effects - both acute & delayed
- nursing management monitoring
- patient self care skills required.
- The clinician administering the medication is to ensure that the correct follow-up has been arranged for the patient.

Note: Nurses who are pregnant or trying to conceive should not administer Methotrexate as it is teratogenic.

Equipment Required

- latex gloves
- long sleeved cuffed gown
- incontinent sheet
- prepared injection from Cytotoxic Pharmacy
- Cytotoxic information sheet
- Cytotoxics waste bin

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Administration of IM Methotrexate, continued

Process

The following describes the process to follow:

- Confirm patient has consented to the procedure and received pre-decision counselling.
- Assemble equipment.
- Explain procedure to the patient.
- Identify patient at the bedside. This is to be done by two (2) registered nurses, one of whom is on the Limited Cytotoxic Register.

Must check patient:

- Verbally
- wristband
- cytotoxic drug sheet
- label on syringe
- Ensure patient is comfortable and relaxed.

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- Wash hands, don gloves and gown. Place incontinent sheet under the site where the IM injection is to be given.
- If there are any bubbles in the syringe leave the needle cap on while expelling the air to prevent aerosoling.
- Administer Methotrexate using aseptic IM technique according to recommended best practice.
- Dispose of equipment according to cytotoxic waste guidelines. Wash hands.
- Observe patient for signs of reaction
- Advise patient regarding follow-up and ensure that she has the patient information leaflet

Note: Using single IM dose significantly reduces incidence of side effects, but patient must be told of possible side effects.

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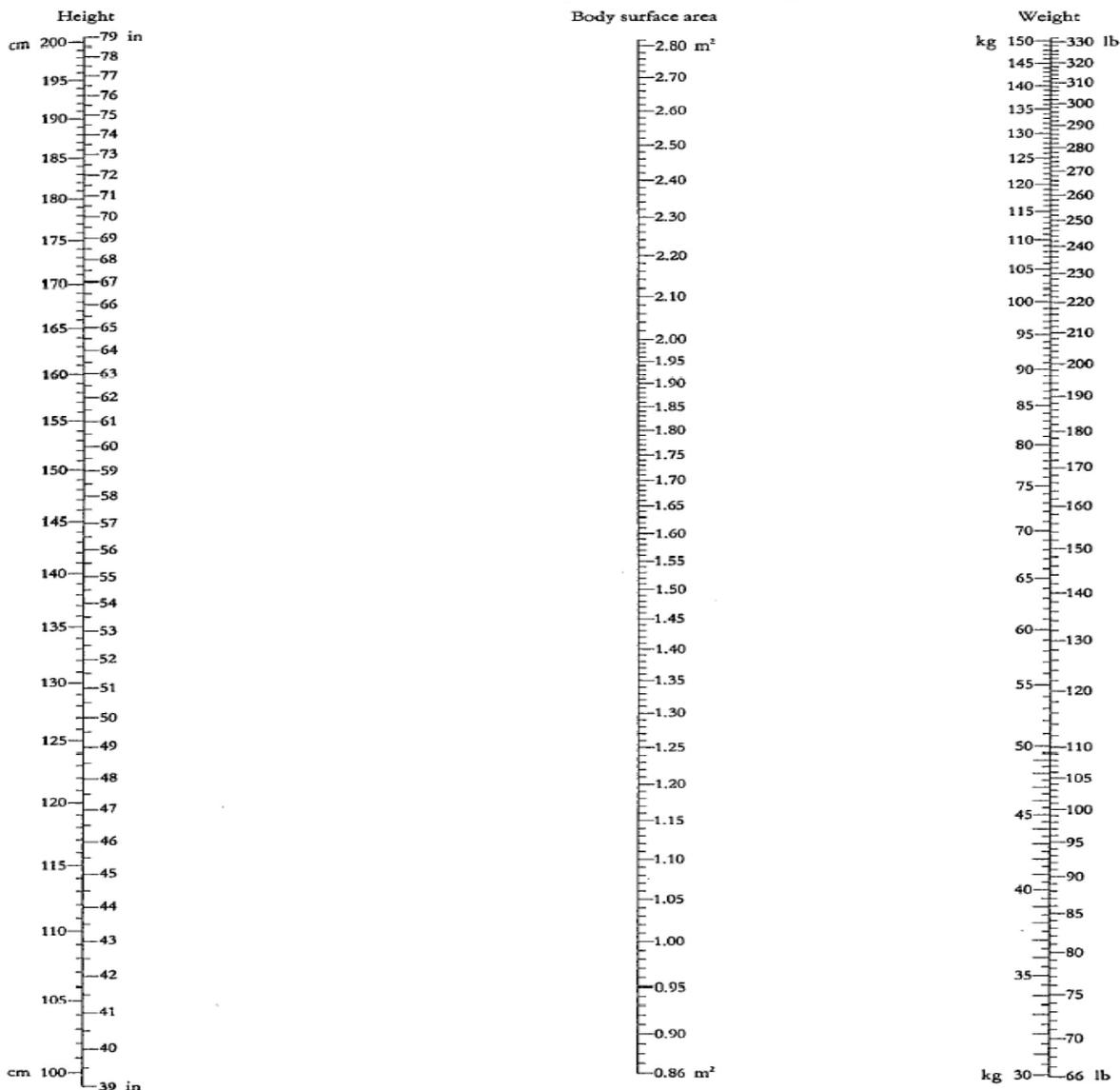
Administration of IM Methotrexate, continued

Body Surface Area of Adults

Nomogram

For determination of body surface area from height & weight; a straightedge placed from the patient's height (left column) to her weight (right column) will give her body surface area (middle column).

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From the formula of Du Bois and Du Bois, *Arch. intern. Med.*, 17, 863 (1916): $S = W^{0.425} \times H^{0.725} \times 71.84$, or $\log S = \log W \times 0.425 + \log H \times 0.725 + 1.8564$ (S = body surface in cm², W = weight in kg, H = height in cm)

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Administration of IM Methotrexate, continued

Note:

Pre-treatment counselling by the pregnancy loss counsellor / on call social worker should be offered at all times

A significant fall in β -hCG may not happen on day 4 but at least 15% decline in β -hCG titre should occur between days 4 - 7 otherwise a second dose of methotrexate (50 mg/m²) should be given 1 week after the first dose. Patients with declining β -hCG titres by day 7

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are monitored weekly until the β -hCG titre is less than 5 IU/l. A third dose of methotrexate is given only if there is a plateauing or increase in two consecutive weekly β -hCG titres.

Abdominal pain is common and can be expected 3 to 7 days after the start of treatment. Women should be encouraged to return to the ward for re-assessment. A full clinical assessment including a full blood count and transvaginal scan and then discussion with the consultant on-call is essential.

Patients should refrain from alcohol, sexual intercourse and vitamin pills containing folic acid until serum β -hCG titres are less than 5 IU/l.

Patients should be advised to use either oral contraceptives or barrier contraception for at least 2 months after completion of therapy.

Surgical Treatment of Ectopic Pregnancy

Laparoscopic management of ectopic pregnancy

Laparoscopy is now increasingly used to treat as well as diagnose ectopic pregnancy. Both salpingotomy and salpingectomy can be performed.

The use of operative laparoscopy permits earlier discharge and return to work with little difference in operating time compared to diagnostic laparoscopy followed by laparotomy.

Criteria for laparoscopic salpingotomy

This procedure should be considered when all of the following criteria are met:

- Future fertility is desired.
- Patient is haemodynamically stable.
- Tubal pregnancy confirmed by diagnostic laparoscopy.
- No fetal heartbeat seen on ultrasound.
- Diameter of tubal pregnancy less than 4cm.
- Good haemostasis maintained during the procedure.
- Good access to tube (no dense bowel adhesions or peritoneal adhesions).
- Tube (especially the fimbrial end) should be normal.
- Serum β -hCG levels should be less than 5000 IU/l.
- Concurrent pathology requiring laparotomy is not present.

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Surgical Treatment of Ectopic Pregnancy, continued

Criteria for laparoscopic salpingectomy

This procedure should be considered in the following groups:

- Haemodynamically stable patients.

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- Future fertility is not desired.
- Fallopian tube is significantly damaged, particularly the fimbrial end.
- Fetal heart activity is seen on the scan.
- Previous tubal surgery (microsurgery/salpingotomy) on the side of the ectopic pregnancy unless the patient specifically requests tubal preservation.
- Ruptured ectopic pregnancy.
- Diameter of ectopic pregnancy is greater than 5cm.
- Persistent bleeding from the ectopic site at salpingotomy or if the patient has to be taken back to theatre following salpingotomy.
- Patients who are unwilling or unable to return for follow-up.

There is little to be gained in terms of future fertility from saving a diseased tube if the other tube appears normal. Salpingectomy will be the most commonly performed laparoscopic procedure:

- 5 to 15% of patients having a laparoscopic salpingotomy will have persistent trophoblastic tissue, they may require methotrexate or further surgical management. Therefore weekly β -hCG measurement is essential¹⁴.
- Patients who have conservative tubal surgery have a 12 - 15% risk of an ectopic pregnancy in subsequent pregnancies¹².

Blood Transfusion

Transfusion is usually intra-operative and sometimes postoperatively. Patient should always be counselled about the possibility of transfusion.

Other Issues

Risk of Future Ectopic Pregnancy

Depends on:

- Number of previous ectopic pregnancies.
- State of remaining tube.
- Type of treatment to present ectopic pregnancy.

First ectopic with remaining tube normal, 6-12% chance of another ectopic.

First ectopic with remaining tube abnormal, 28-50% chance of another ectopic.

More than 1 ectopic pregnancy, 26-40% chance of another ectopic¹².

Management Guidelines for Ruptured Ectopic Pregnancy

Developed by: Deputy Clinical Director
Authorised by: Clinical Director O&G

Classification: NMP200/SSG/006
Date Issued: Reviewed May 2012

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If a referring doctor calls to admit a patient with a diagnosis of suspected ruptured ectopic pregnancy, the following advice should be given:

- **If the patient is haemodynamically stable**

- Secure good intravenous access with a large bore needle and infuse I.V. fluids.
- Arrange transfer by ambulance to the Women's Assessment Unit (WAU).
- Collect blood for full blood count, group and cross-match and β -hCG.
- Initial counselling for possible surgical management.
- Arrangements to be made by NWH:
 - Advise Duty Manager and GAU of possible ruptured ectopic admission.
 - Anaesthetic and theatre staff to be informed.
 - Registrar/specialist assessment to decide on further investigations and surgical intervention, which may be laparoscopy or laparotomy.

- **If ruptured ectopic and the patient is unstable**

- Trendelenberg position.
- Two large bore needles for I.V. access and colloid infusion if available or crystalloids.
- Oxygen to be administered.
- Immediate ambulance transfer to WAU with the GP accompanying patient.
- Collect blood for FBC and cross-match.

Arrangements to be made by NWH:

- Specialist on call to be informed and to attend to manage patient with Registrar. Registrar to notify Duty Manager.
- Patient should be directed to Theatre from ED/WAU.
- Anaesthetic and O.T. staff available for resuscitation and stabilisation of patient for immediate laparotomy.
- Uncross-matched blood may be used in rare circumstances only.

Checklist for Discharge of Women with Ectopic Pregnancy

Process

Follow the steps below when discharging a patient who has had an ectopic pregnancy diagnosis:

- Discuss the surgical procedure and findings within the rest of the pelvis in detail e.g. adhesions, ovaries, and condition of fallopian tubes. Discuss follow up:
 - **Salpingectomy:** Either by laparoscopy or laparotomy do not require follow up with serial β - β -hCG unless specifically requested.
 - **Salpingotomy:** Either by laparoscopy or laparotomy requires follow up with serial β -hCG measurement because 5-10% of these patients may require further treatment. This is generally done through GAU.
 - **Medical Management:** Ensure follow up blood tests are arranged (refer protocol page).

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Checklist for Discharge of Women with Ectopic Pregnancy, Continued

- Full blood count if :
 - blood was transfused
 - blood loss was greater than 500mls
 - requested by surgeon
 - clinically indicated
 - Iron replacement if necessary.

Rhesus Status

Currently, it is recommended that rhesus negative women are given Anti-D1

- Check blood group and Rhesus status:
Anti-D given within 72 hours if indicated
- Future Fertility Desires: Patients are generally advised to delay another pregnancy until recovered both physically and emotionally from this pregnancy. The chance of another ectopic pregnancy should be explained. Patients are advised to have a pregnancy test on missing her menses and if pregnant a trans-vaginal ultrasound scan should be arranged to locate the pregnancy. Patients with bilateral tubal disease or salpingectomy should be referred to discuss IVF if future fertility is desired.

Contraception

The IUCD is used with caution for women with treatment.

The progestogen only pill are contra-indicated for women with a history of ectopic pregnancy.

It is important to rule out ectopic pregnancy early in all future pregnancies.

N.B : Unless specifically requested most of these patients are followed by their GP or EPAU and a copy of the histology should be available within 2 – 4 weeks.

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Associated Documents

The table below indicates other documents associated with this policy:

Board Policy

- Informed Consent

Board Clinical Practice

- Blood components & Blood Administration

Patient Information

- Ectopic Pregnancy
- Methotrexate in Ectopic Pregnancy

Other

- Medsafe - Methotrexate
-

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