

Ectopic pregnancy

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Definition

- > Ectopic pregnancy (EP) is a pregnancy outside the uterus, usually in the fallopian tube, but may also occur in the abdomen, ovary or cervix

Introduction

- > Ectopic pregnancy occurs when the fertilised zygote fails to reach the uterus, implanting elsewhere, usually in the ampullary portion of the fallopian tube
- > The incidence is around 1 in 100 pregnancies but increases to 1 in 30 pregnancies in high-risk populations (Mascarenhas in Luesley and Baker 2004)
- > Ectopic pregnancy is the most common cause of maternal mortality in the first trimester. Early diagnosis is critical to prevent serious morbidity and allow use of more conservative treatment options that may help preserve fertility (American Academy of Family Physicians 2000)
- > Treatment options may be:
 - > Pharmacological (Intramuscular methotrexate)
 - > Surgical (Laparoscopy with salpingectomy / salpingostomy)
- > Ruptured ectopic pregnancy requires immediate surgical intervention (Thorstensen 2000)

Risk factors

- > Any condition that affects the patency and function of the fallopian tube increases the risk of ectopic pregnancy. Many women with an ectopic pregnancy have no risk factors
- > Women at highest risk for ectopic pregnancy should be evaluated to rule out ectopic pregnancy as soon as the pregnancy is reported

Risk factors:

- > Previous tubal surgery
- > Previous ectopic pregnancy
- > Previous pelvic infection (PID)
- > In vitro fertilisation
- > Documented tubal pathology
- > Cigarette smoking

Signs and symptoms

- > Ectopic pregnancy is initially asymptomatic and is easily missed as symptoms masquerade as a normal pregnancy. Ectopic pregnancy remains an important cause of maternal mortality
- > Normal symptoms of pregnancy present e.g. amenorrhoea, positive pregnancy test followed by:
 - > Pain (generally lower abdominal and unilateral)
 - > Vaginal bleeding following a short period of amenorrhoea
 - > Bleeding may be gradual or catastrophic (usually irregular, often prolonged, light and brownish, rarely profuse)
 - > Tender adnexal mass (may not be clinically apparent)

Signs of ruptured ectopic

- > Signs of haemoperitoneum and shock including a distended silent, 'doughy' abdomen, shoulder pain, bulging cul-de-sac into the posterior fornix of the vagina and hypotension

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Diagnosis

- > Serum β -hCG
- > Transvaginal ultrasound examination
- > Correlation of serum β -hCG levels with ultrasound findings provides the most diagnostic significance
 - > In ectopic pregnancy, serial β -hCG usually shows a failure to double in 48 hours or a static or slow increase or decrease
 - > The failure to double in 48 hours predicts pregnancy failure but does not distinguish between an intrauterine spontaneous miscarriage and an ectopic pregnancy
 - > If the β -hCG is around 1,500 IU/L a gestational sac should be visible on transvaginal ultrasound
 - > If the intrauterine gestational sac is not visible by the time the β -hCG is at or above this threshold, the pregnancy has a high likelihood of being ectopic, indicating the need for a laparoscopy
 - > Combined intrauterine and extrauterine pregnancy is rare following spontaneous conception but is relatively common in pregnancy resulting from in-vitro fertilisation (IVF). Accordingly, the finding of an intrauterine gestation on ultrasound almost always excludes the presence of an ectopic pregnancy unless IVF has been performed
- > Laparoscopy can confirm the diagnosis and treat the ectopic pregnancy at the same time

Management

- > There is no place for expectant management in ectopic pregnancy
- > Treatment options include:
 - > Medical management with methotrexate
 - > Surgical management (usually laparoscopy)
- > Women who present with suspected ectopic pregnancy (amenorrhoea, pain, vaginal bleeding) should have:
 - > A urine pregnancy test
 - > Baseline temperature, pulse, blood pressure
 - > Check and document abdominal pain, amount of bleeding
 - > Take blood for quantitative β -hCG, group and save, complete blood picture
- > If haemodynamically unstable, refer to gynaecology registrar / consultant for emergency dilatation and curettage / laparoscopy / laparotomy as required
- > If haemodynamically stable, organise pelvic ultrasound (by an experienced registrar or consultant or in ultrasound department)
- > If the diagnosis is unclear, the medical officer should arrange for the woman to return to the hospital for a repeat β -hCG after 48 hours (discuss with consultant on call first).
- > It is the registrar's responsibility to decide whether the woman should be managed at home or in hospital over the next 48 hours.
- > The woman should receive clear instructions about indications for readmission if symptoms worsen. Inform general practitioner if possible.
- > If β -hCG is < 1,500 IU/L, the woman should commence serial follow up β -hCG at 48 hour intervals. Ectopic pregnancy is suspected when there is a static or slow increase or decrease in the β -hCG level.
- > If β -hCG is > 1,500 IU/L, arrange laparoscopy (salpingectomy / salpingostomy with or without methotrexate as required). A small number of women will require a repeat β -hCG or Pipelle biopsy. A negative result at laparoscopy requires β -hCG follow up.

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Medical management

- > Medical management using methotrexate is appropriate in properly selected women with unruptured ectopic pregnancies
- > For guidelines on the safe handling of cytotoxic drugs and related waste link to <http://www.osh.dol.govt.nz/order/catalogue/37.shtml>

Eligibility criteria for methotrexate treatment

- > Stable vital signs and healthy
- > Absent signs of peritonism

Vaginal ultrasound scan

- > absent intrauterine pregnancy
- > adnexal mass < 4 cm
- > absence of large amount of fluid in pouch of Douglas (>1 cm pool relative contraindication)
- > Absence of fetal heart in ectopic

Serum β -hCG

- > Preferably two values with suboptimal elevation (plus ultrasound evidence)
- > Level > 4,000 IU/L is a relative contraindication

Social considerations

- > Women must be reliable and compliant
- > Adult company available for at least the first 3 – 5 days after injection
- > Clearly aware of advantages and disadvantages

Exclusion criteria

- > Active bleeding
- > Significant haemoperitoneum on basis of vital signs / haematocrit / physical examination / ultrasonography
- > Fetal cardiac activity
- > Hepatic / renal disease e.g. renal insufficiency
- > Significant pelvic pain

Medical treatment regimen

If the registrar considers the woman suitable for methotrexate treatment, they should confirm this treatment option with the consultant-on-call

Day 1:

- > Baseline pulse, blood pressure, height, weight
- > Take blood for complete blood picture, urea and electrolytes, liver function tests, quantitative β -hCG
- > If results are normal, an accredited midwife / medical officer may administer single dose of intramuscular methotrexate 50 milligrams per square metre using the Body Surface Area (BSA) equation below

Body Surface Area (BSA) Equation

Methotrexate dose

$$\sqrt{[\text{Height (cm)} \times \text{Weight (kg)}] / 3600}$$

- > The BSA equation is: Take the square root of (height in cm x weight divided by 3600) and then multiply by 50 mg methotrexate (Kemp and McDowell 2002)
- > For example:
 - > Height = 165 cm, Weight = 65 kg

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- > $165 \times 65 = 10,725$
- > Divide this by 3600 = 2.979
- > Then take the square root = 1.726 and multiply by 50
- > = 86 mg of methotrexate

- > NB: In obese women the BSA equation may result in a dose that is too high, due to the increased adipose to body weight distribution. Dose adjustment may be necessary. The maximum dose is capped at 100 mg
- > Women may discharge home after administration of the injection

Day 4:

- > Take blood for quantitative β -hCG levels (expect a slight rise)

Day 7:

- > Take blood for complete blood picture, urea and electrolytes, liver function tests and quantitative β -hCG (β -hCG level should be lower)

Weekly:

- > Take blood for quantitative β -hCG levels until negative (< 5 IU/L)

Further follow up is not routinely required (unless previous infertility or the woman is concerned)

Counselling:

- > Explain to the woman why she needs to be compliant to tests and hospital attendances
- > Explain there is a failure of treatment (3 – 4 % rupture) and can occur at any time although rare after 2 weeks
- > Average time for β -hCG to reach a level < 5 IU/L is 4 weeks

Methotrexate side effects:

- > Side effects are minimal with single dose
 - > Impaired liver function is the most common side effect
- > Other side effects include:
 - > Stomatitis
 - > Gastritis and enteritis
 - > Bone marrow suppression

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Education:

- > The woman should avoid direct sunlight (photosensitivity), sexual intercourse
- > Do not use non steroidal anti-inflammatory agents, penicillin, alcohol, vitamins containing folic acid for 48 hours
- > Transient pelvic pain frequently occurs between 3 – 7 days after injection
- > Colicky abdominal pain first 2 – 3 days after injection is common and women should avoid gas producing food such as leeks and cabbage
- > Avoid pregnancy for three months
- > A second dose of methotrexate may be required for a small number of women (if no decline of β -hCG after 7 days)
- > 80 % of women will have patent tubes and > 60 % will have normal pregnancies in the future
- > Approximately 10 % of women will have recurrent ectopic pregnancies
- > If concerned, the woman should return to the hospital – check pulse, blood pressure, complete blood picture and ultrasound scan to exclude rupture

Methotrexate

- > A folic acid antagonist, methotrexate acts on rapidly proliferating trophoblasts leading to lysis of cells.
- > A single dose of 50 mg / m² (body surface area equation) significantly blunts the β -hCG increment over the following 7 days
- > It appears that methotrexate directly impairs trophoblastic production of β -hCG with a secondary decrement of corpus luteum progesterone secretion

Surgical management

- > Surgical management is the standard treatment option
- > Standard management is laparoscopic salpingectomy if the other tube is normal
- > Future fertility rates are similar whether a salpingotomy or salpingectomy is performed
- > Any products (e.g. fallopian tube) removed should be sent to Histopathology
- > Salpingostomy (conservation of the tube) is advocated only if the other tube is lost or unhealthy
- > When salpingectomy is performed β -hCG follow up may be required
- > If salpingostomy is performed, the woman should be advised that β -hCG follow up is required weekly until the level is < 5 IU/L. If the β -hCG level is not decreasing at a satisfactory rate, referral to registrar or consultant is indicated.
- > Ensure that appropriate information and pregnancy loss information is given to the woman before discharge. Refer to social work as indicated

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Version control and change history

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