Worcestershire Acute Hospitals NHS Trust

Management of Ectopic Pregnancy and Pregnancy of Unknown Location

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Key Admendements

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29th December 2023	Document extended for another 6 months whilst under review.	Alex Blackwell
12th Jan 2024	Updated process flow included	Gynaecology Governance Meeting

Management of Ectopic Pregnancy and Pregnancy of Unknown Location

Introduction

Ectopic pregnancy is defined as any pregnancy occurring outside of the uterine cavity. It affects approximately 11,000 women per year in the United Kingdom and is life threatening if left untreated. The commonest site of ectopic pregnancy is the Fallopian tube (98%) although cases of ectopic pregnancy affecting the ovary, cervix, tubal intersitium and previous Caesarean Section scar have also been reported.
This guideline is intended to cover all women presenting with abdominal pain and a positive urine pregnancy test whom have not yet had the location of their pregnancy confirmed. It is designed for use by both ED and gynaecology staff.

Initial Assessment

- All women presenting to A&E with abdominal pain and positive pregnancy test should be managed as an ectopic pregnancy until proven otherwise.

- The history should explore predisposing conditions as listed below although it should be noted that 37% of cases will have no risk factors:
    - Previous ectopic pregnancy
    - Tubal disease/ history of pelvic inflammatory disease
    - Previous tubal surgery
    - Assisted conception
    - Smoking
    - IUCD use
    - Previous pelvic or abdominal surgery
- Symptoms of pain and vaginal bleeding should be carefully evaluated
- The presentation of ectopic pregnancy can be atypical with a variety of symptoms.
- The key examination findings include:
    - Vital signs
    - Presence of guarding
    - Presence of adnexal tenderness

Referral Pathways

Patients may be referred to Emergency Gynaecology Assessment Unit (EGAU) . Referrals are accepted from:

- General Practitioners countywide
- Antenatal clinic (ANC)
- Ultrasound services (USS)
- Accident and Emergency Department from both sites

Investigations

- All women in whom ectopic pregnancy is suspected should have IV access undertaken by the initially reviewing specialty and blood sent for FBC, G&S and beta HCG.
- There is no known serum HCG threshold for ectopic pregnancy and diagnosis is based on clinical symptoms and suspicion can be raised if there is suboptimal rise in HCG levels in early pregnancy.
- Trans-vaginal ultrasound can confirm majority of intrauterine gestations when beta HCG is greater than 1000 and should be obtained in all patients in whom ectopic pregnancy is suspected as a matter of urgency

Management Options for Ectopic Pregnancy

All women with an ectopic pregnancy must be given oral and written information about:
• the treatment options and what to expect during and after treatment
• how they can contact a healthcare professional for advice after treatment if needed, and who this will be
• where and when to get help in an emergency.

Women who have had an ectopic pregnancy should be informed that they can self-refer to an early pregnancy assessment service in future pregnancies if they have any early concerns.

Surgical Management of Ectopic Pregnancy

Surgical management of ectopic pregnancy is indicated as first line in the following situations:

- A haemodynamically unstable patient
- An ectopic pregnancy with significant pain
- The presence of an adnexal mass 35mm or larger
- Beta HCG levels >5000
- The presence of a fetal heart
- Patients who are unwilling or unable to return for post methotrexate follow up

Choice of access

- Laparoscopic management of ectopic pregnancy by a trained laparoscopic surgeon is the preferred management in the absence of contraindications. Advantages include shorter recovery, reduced hospital stay and less likelihood of intra-abdominal adhesions.
- Laparotomy can be considered in the following situations:
  - A haemodynamically unstable patient
  - If operator skills will enable more rapid hemostasis with laparoscopic management this should be used instead
  - Significant medical condition limiting the duration or extent of pneumo-peritoneum
  - Theatre staff/ surgeon unfamiliar with equipment
  - Presence of extensive intra-abdominal or pelvic adhesions

Salpingectomy vs. Salpingostomy

- Salpingectomy is the recommended modality of treatment unless other risk factors for infertility are present. We encourage seeking second opinion if there is a diagnostic doubt on the diagnosis of ectopic pregnancy before the removal of the fallopian tube.
- Uterine instrumentation is discouraged unless the possibility of the intrauterine pregnancy has been ruled out with certainty. i.e. heterotopic pregnancy and false diagnosis of ectopic due to tubal disease for other reasons.
- Salpingotomy can be considered if the patient wishes to conceive again and the following criteria are met:
    - Presence of one fallopian tube only
    - Unhealthy appearance of the contralateral tube
- Patients should be fully counselled in the case of salpingotomy:
    - Serum HCG follow up will be required weekly until non pregnant level reached.
    - Up to 1 in 5 women may need further treatment, for example for persistent trophoblastic disease. This treatment may include methotrexate and/or a salpingectomy.
    - There is an increased risk of repeat ectopic pregnancy after salpingostomy (15-20%)
    - The chance of a subsequent intrauterine pregnancy is about 60%.

Post-Operative Follow-Up

- Patients undergoing surgery for ectopic pregnancy should be debriefed afterwards receiving oral and written information
- All Rhesus negative patients requiring surgery for ectopic pregnancy should receive Anti-D 250iu (see Anti-D Guideline)
- Patients should be advised to undertake urine pregnancy testing 3 weeks after their salpingectomy and make contact with gynaecology services if positive.
- During future pregnancies patients should be advised to make contact with early pregnancy services at an early stage if they have any concerns and to arrange an early scan due to the increased risk of repeat ectopic
- Salpingotomy patients should be aware of the arrangements for follow up:
    - Beta HCG check seven days post op
        - Anticipate a drop of >50%
        - If the decrease in beta HCG levels is sub optimal this should be repeated after 48hrs
    - Subsequent weekly beta HCG until levels negative
    - Methotrexate should be considered in the presence of gestational trophoblastic disease

Medical Management of Ectopic Pregnancy

Medical management of ectopic is advantageous to both patients and clinicians in terms of its cost effectiveness and avoidance of surgery and general anaesthesia. Success rates are as high as 90% and it is also useful in the management of persistent trophoblastic disease following salpingotomy.

Women who choose methotrexate must be advised that their chance of needing further intervention is increased and they may need to be urgently admitted if their condition deteriorates.

Methotrexate treatment must not be prescribed without consultant involvement.

- **Methotrexate is suitable as a first line treatment for selected patients with ectopic pregnancy:**
    - Stable patient with no evidence of tubal rupture or significant pain
    - No intrauterine pregnancy
    - Confirmed or suspected diagnosis of ectopic pregnancy by ultrasound/ beta HCG alone (without laparoscopy)
        - Ectopic <35mm in size
        - No fetal cardiac activity
        - Beta HCG <1500IU
    - No contraindications to methotrexate
    - Normal FBC/hepatic/renal function
    - Reliable/compliant patient with 24hr easy access to gynaecology services
- **Medical management of ectopic pregnancy is contraindicated in the following**:
    - Methotrexate allergy
    - Breast feeding
    - Renal/hepatic disease
    - Anaemia/ leucopoenia/ thrombocytopenia
    - Immune suppression
    - Beta HCG >5000
    - Ruptured fallopian tube
    - Ultrasonic evidence of significant free fluid suggesting intra-abdominal bleed

- Offer the choice of either methotrexate or surgical management to patients with HCG levels >1500 but <5000 with no other contraindications to medical management.

Pre-Medical Management: Role of RN

- Complete basic nursing documentation
- Obtain baseline observations: heart rate, blood pressure, temperature, respiratory rate, urinalysis and weight
- Apply identification wristbands containing as a minimum patient name, date of birth and hospital number. This includes red allergy bands where appropriate.
- Explain the procedure to the best of their knowledge and answer any preliminary questions the patient may have
- Discuss support available and give information leaflets were appropriate
    - These can be obtained from the RCOG website

Pre-Medical Management: Role of Doctor

On arrival on the unit the patient will be seen by the on-call Gynaecology SHO/Registrar who will:

- Review referral notes/ investigation results and complete a basic medical clerking
- History should include specifically asking about history of liver dysfunction
- Bloods should be taken (if not available) for FBC/U&E/LFT/G&S/Beta-HCG
- **Ultrasound findings and investigation results should be discussed with the on call consultant before a final decision for medical management is made.**
- The patient should be fully counselled before the procedure, given written information and obtain informed written consent.

Patient Counselling

As a minimum, patients should be aware of the following:

- Methotrexate is a folic acid antagonist which interferes with DNA synthesis
- It is usually given as a single or divided intramuscular based on patient body weight and surface area
- Side effects include
  - Nausea, vomiting, gastritis, diarrhea
  - Bone marrow suppression, conjunctivitis and stomatitis
  - Abdominal pain:
    - 75% of patients will experience this
    - MAY be a sign of tubal rupture in 7% and if pain becomes severe patients should be aware to contact the unit
  - Reversible alopecia
  - Teratogenicity if conception within 3/12 of dose
  - Photosensitivity
    - Advise avoiding bright sunlight
- Stringent follow up will be needed (detailed below) and this may require another dose of methotrexate in 15% of patients

Methotrexate Dosing

- Methotrexate dosage should be calculated by the prescribing doctor on the patient's actual body weight or body surface area.
- Methotrexate should only be prescribed by registrars; staff grades or Consultants.
- Dosing for methotrexate is as follows:
  - ***A ONCE ONLY PRESCRIPTION***
  - ***1Mg/kg by IM injection as a single or divided dose***
  - ***50mg/m^2 by IM injection as a single or divided dose***
- Folinic acid rescue is not needed

Once the prescription has been completed, nursing staff should forward the chart to Pharmacy to prepare and dispense the medication. Pharmacy should be telephoned to fast-track the prescription in hours; during the normal working day (Monday to Friday) contact pharmacy aseptic suite (WRH 39217/Alex 42136) or out of hours contact the on-call pharmacist via switchboard. Out of hours the on call pharmacist should be contacted via switchboard.

Administration of Methotrexate in Medical Management of Ectopic Pregnancy

- Dose should be calculated and prescribed as detailed above
- The drug will be dispensed readily prepared in syringes from which it can be directly administered by appropriately trained nursing staff or medical staff following the guidance in WAHT NUR-064
- A maximum of 2ml injection can be given at any one site
- The administering clinician needs to sign the appropriate documentation
- The waste and all accompanying contaminated protective equipment should be disposed of in line with Trust policy for safe handling and administration of cytotoxic drugs (WAHT NUR-064) and Policy for cytotoxic spillage (WAHT-PHA-002)

Immediate Post Methotrexate Care

- Baseline observations should be recorded by nursing staff (pulse, BP, temperature)
- The patient should be observed for 2 hours following methotrexate administration for pain or excessive vaginal loss

- Anti D is not required for women who have solely medical management of ectopic or have PUL
- Patients may be discharged when the above criteria are met with the following:
    - Patient information leaflets
    - Ward / EGAU contact information
    - Dates and times of follow up appointments
    - Simple analgesia: avoid non-steroidal drugs

Post Methotrexate Follow Up

- Blood to be taken for serum beta HCG levels/FBC/ U&E/LFT at day 4 and day 7
- Consider a second dose (after consultant input) if beta HCG levels have not fallen by >15% between day 4 and day 7
- If beta HCG levels are falling appropriately at day 7 the patient can be monitored with weekly beta-HCG levels. If HCG levels subsequently plateau or rise the patient must be reviewed by doctors through EGAU to consider further treatment.
- Patients should be advised not to conceive for 3 months after methotrexate owing to risk of teratogenicity
- Patients should be advised that they are able to self-refer for an early reassurance scan in subsequent pregnancies in view of the increased risk of future ectopic.

Expectant Management of Ectopic Pregnancy

Patients can be advised that based on the limited available evidence, there seems to be no difference following expectant or medical management in:

- Rate of ectopic pregnancies ending naturally
- Risk of tubal rupture
- Need for additional treatment

The time taken for ectopic pregnancies to resolve and future fertility outcomes are likely to be the same with either expectant or medical management.

Patients must be advised that there may be a need for them to be admitted urgently if their health deteriorates.

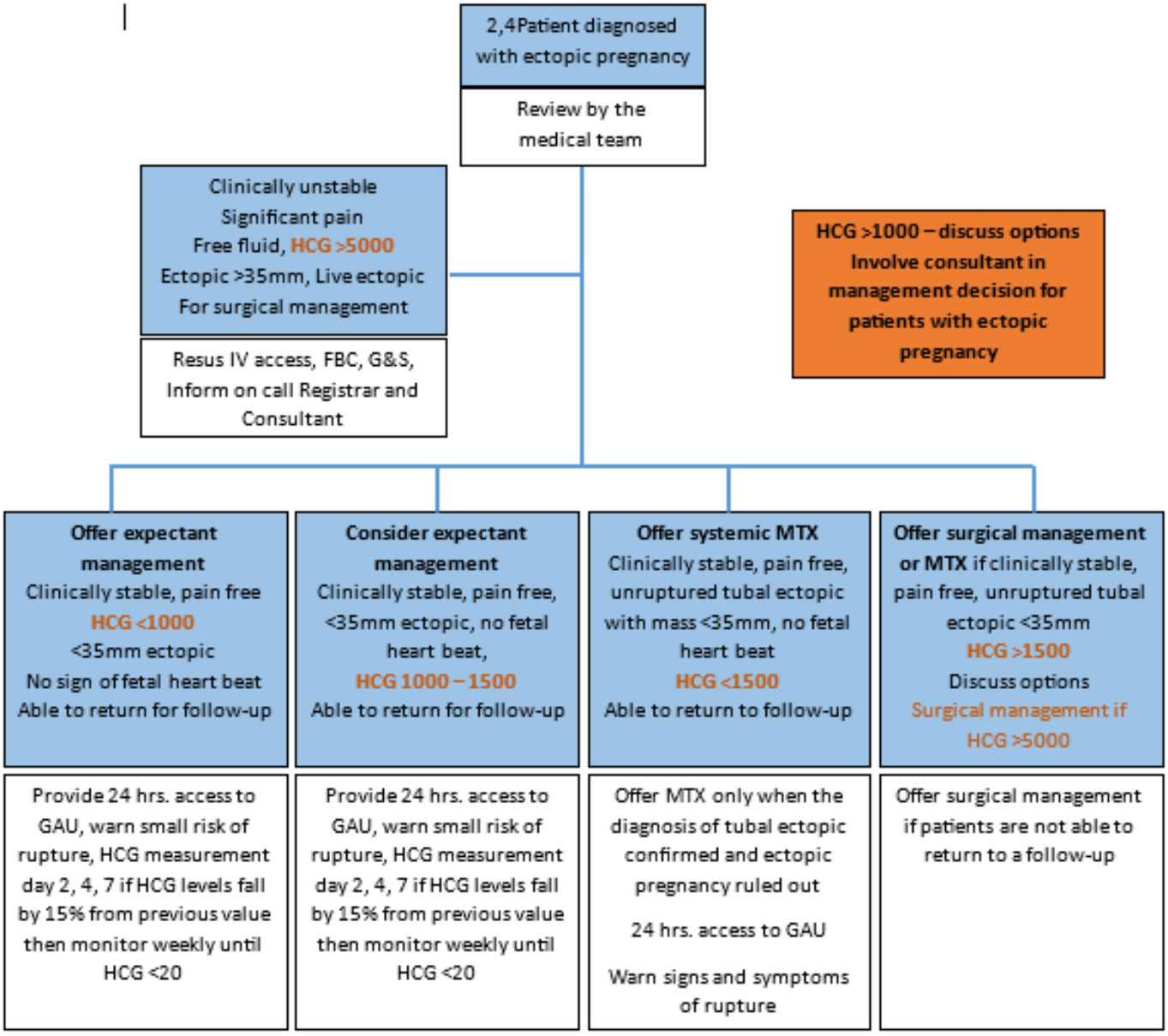
Expectant management can be offered as an option to patients who:

- Are pain free/clinically stable
- Are able to return for follow up
- Have an ectopic pregnancy measuring <35mm with no fetal heartbeat on TV USS
- Have HCG levels ≤1000 (can consider expectant management as an option with HCG levels 1000 – 1500)

For patients opting for expectant management:

- Repeat HCG days 2,4 and 7 after original test
    - If HCG drops by ≥15% on days 2,4 and 7, then repeat weekly until HCG < 20
    - If HCG falls by < 15%, stays the same or rises from the previous value, the patient must have a medical review and their management plan must be discussed with consultant on call

Consultant on call should be involved in decision making when managing patients with ectopic pregnancy. Clear follow-up plan and documentation should be done in notes. Patient information leaflets and contact details for GAU should be provided in case of deterioration of symptoms.



Pregnancy of Unknown Location: Management Guideline

Introduction

Pregnancy of Unknown Location (PUL) is important as it often presents a clinical conundrum where it can be both hazardous to miss an ectopic pregnancy but also to over-treat (and consequently harm) a potentially viable intrauterine pregnancy (IUP).

In the presence of early intrauterine sac which is eccentrically placed with decidual sign should be interpreted as early intrauterine pregnancy. Clinical correlation to be made to avoid intervention and in the absence of any obvious clinical concern.

Rates should ideally be <15%. They are determined partly by the quality of scanning, where improved detection of ectopic pregnancy using ultrasound as a single diagnostic test (i.e. in specialised units) can

result in fewer women being classified with a PUL. They are also influenced by the gestational age at which ultrasound is commenced as at earlier gestations more scans will be non-diagnostic. Errors in ultrasound will also become more common when the HCG is <1500mIU/ml.

Most PULs are not aggressive and represent either failing intrauterine or ectopic pregnancies which are never visualized using transvaginal scans (TVS) (failing PULs) or intrauterine pregnancies too early to visualize using TVS. Variations of PUL can arise due to the very early gestation and difficulties in determining the true site of the pregnancy on ultrasound.

Outcome after initial PUL classification:

1) IUP (30-47%)
2) Failed PUL (appropriate fall in HCG levels)
3) Ectopic pregnancy (6-20%)
4) Persistent PUL (plateauing HCG levels) may represent small ectopic not visualised or small retained trophoblast in the endometrial cavity or in rare cases an HCG-secreting tumour

Management of PUL

- Regardless of serum HCG levels, give women with a pregnancy of unknown location (PUL) written information about what to do if they experience any new or worsening symptoms, including details about how to access emergency care 24 hours a day.
- Advise women to return if there are new symptoms or if existing symptoms worsen
- In a woman with a pregnancy of unknown location, place more importance on clinical symptoms than on serum HCG results, and review the woman's condition if any of her symptoms change, regardless of previous results and assessments.

Use of the M6 model in the management of PUL

The M6 risk model can be used by clinicians to characterize pregnancies of unknown location. The model was based on women with a PUL who had a serum hCG level on presentation >25 IU/L. M6 predicts the probability that the PUL is a failed pregnancy, an intra-uterine pregnancy (IUP), or an ectopic pregnancy (including persisting PUL).

To apply the M6 model we need to following tests

1 Initial HCG

2 Initial serum progesterone

3 48Hr HCG

The progesterone level cannot be used if the patient is on progesterone.

M6 was developed by clinicians and statisticians. The model has been externally validated on 2899 PUL recruited between 2015 and 2017 at 8 teaching and district general hospitals in the UK.

M6 is part of a two-step triage protocol to identify patients at high risk of ectopic pregnancy.

Step One

The first step triages patients after the first visit using initial progesterone: if the level is ≤2 nmol/L the patient is classified as low risk and discharged can do a pregnancy test in 4 weeks.

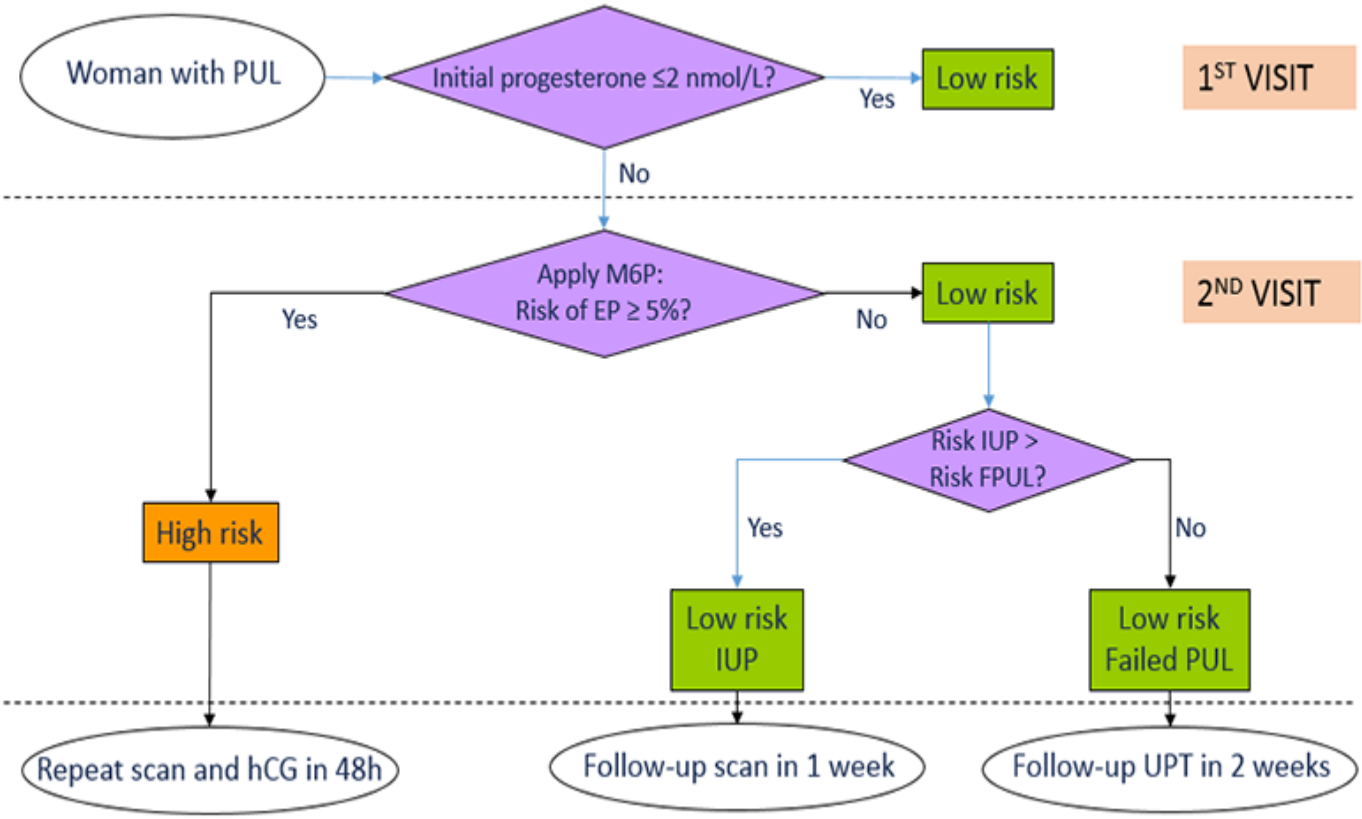
Step two

If the level is >2 nmol/L the patient is scheduled to come back after around 48 hours to have a second hCG measurement (second step). Then M6 is applied, and if the predicted risk of being EP is at least 5% the patient is classified as high risk. If the risk of being EP is <5% then the patient is classified as low risk.

- If the predicted risk of being EP is at least 5% the patient is classified as high risk. The advice is for a repeat hCG and transvaginal ultrasound in a further 48 hours;
- If the risk of being EP is less than 5% the patient is classified as 'low risk – failed pregnancy (FPUL)' or as 'low risk – intrauterine pregnancy (IUP)' depending on which predicted risk is highest:
  - If the risk is low – IUP, the advice is for a repeat transvaginal ultrasound in one week;
  - If the risk is low – FPUL, the advice is for a urine pregnancy test in two weeks.

Please note - this guide on management advice is based on using the M6 model to triage women with PUL in the recent clinical implementation study. Although this is a guide for management, final management decision should take into account senior clinical review and current patient status.

Figure 1. Two-step triage protocol, including suggested management.



Flowchart of two-step protocol for managing pregnancies of unknown location (PUL). EP, ectopic pregnancy; FPUL, failed PUL; hCG, human chorionic gonadotropin; IUP, intrauterine pregnancy; UPT, urine pregnancy test; US, ultrasound examination.

Please look at the M6 model on

https://homes.esat.kuleuven.be/~sistawww/biomed/earlypregnancycare/m6/index.html

Please click and paste this link on the search engine
Click on the Excel sheet options which is editable to input your patient data.

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