NHS
University Hospitals Sussex
NHS Foundation Trust
St Richards, Worthing & Southlands Hospitals

Management and diagnosis of an Ectopic Pregnancy and /or Pregnancy of Unknown Location (PUL) Guideline	
Summary statement: How does the document support patient care?	By providing evidence based guidance for staff in the management of ectopic pregnancy and Pregnancy of Unknown Location (PUL)
Staff/stakeholders involved in development:	Leads for Maternity Risk Management (Obstetric and Midwifery), Labour Ward Leads (Obstetric and Midwifery), Joint Obstetric Guidelines Group, Consultant leads for Early Pregnancy & Gynaecology Emergency, Gynaecology Matron, Superintendent Sonographer
Division:	Women and Children's
Department:	Gynaecology
Responsible Person:	Chief of Service
Author:	Obstetrics and Gynaecology Consultant and Registrar, Gynaecology QI&I Matron, Gynaecology Matron
For use by:	Gynaecology, Obstetric, A & E, Nursing and Midwifery staff, Sonographers and General Practitioners (GP)
Purpose:	To provide clear evidence-based guidance on the management of ectopic pregnancy and PUL
This document supports:	NICE guideline NG126; Ectopic pregnancy and miscarriage: diagnosis and initial management, April 2019, updated November 2021 RCOG Diagnosis and management of Ectopic Pregnancy - Green-top Guideline No. 21, November 2016
Key related documents:	**UH Sussex (SRH&WH) Gynaecology Guidelines**: Miscarriage and early pregnancy loss management
Approved by:	Joint Obstetric and Gynaecology Guidelines Group MGC (13TH December 2022)
Approval date:	16th October 2022 Date uploaded: 04th January 2023
Ratified by Board of Directors/ Committee of the Board of Directors	Not Applicable – Divisional Ratification only required
Ratification Date:	Not Applicable – Divisional Ratification only required
Expiry Date:	June 2023
Review date:	December 2022
If you require this document in another format such as Braille, large print, audio or another language please contact the Trusts Communications Team	
Reference Number:	CG12018

Version	Date	Author	Status	Comment
1.0	Feb 2012	Consultant Obstetrician	Archived	New Trust guideline
2.0	November 2013	Consultant Obstetrician	Archived	Guideline updated
3.0	June 2019	Gynaecology Matron Consultant leads for Early Pregnancy & Gynaecology Emergency and Specialist Registrar Dr A Stienen-Durand	Archived *(Not taken through JOGG & uploaded to Staffnet)*	Guideline updated
4.0	October 2022	J. Birrell, Gynaecology Matron Consultant leads for Early Pregnancy & Gynaecology Emergency and Specialist	LIVE	3 year review

The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician.
If in doubt contact a senior colleague or expert.

Contents

Ectopic Pregnancy and Pregnancy of Unknown Location (PUL) Guideline

1.0 Aim

The aim is to provide clear guidance for all staff caring for pregnant women and people with early pregnancy complications.

2.0 Scope

This guideline applies to:

- Gynaecology medical and nursing staff
- Obstetricians
- Junior doctors
- A & E doctors and nurses
- General Practitioners (GPs)
- Midwives
- Sonographers

3.0 Responsibilities

This guidance is for staff employed at University Hospitals Sussex within at Richards' and Worthing Hospitals. The guidance is flexible and should be tailored to the individual circumstances of the patient.

Obstetricians and Gynaecologists, Gynaecology Nurses, Junior Doctors, A & E Staff, GPs, Midwives and Sonographers to:

- Access, read, understand and follow this guidance.
- Use their professional judgement in application of this guideline.
- Document the reason and/or justify, with clear documentation of alternative plans and discussions that have taken place if the guidance is not being followed.

Clinical Managers are to ensure:

- The guideline is reviewed as required in line with Trust, National RCOG and NICE recommendations'
- The guideline is accessible to all relevant staff'

4.0 Abbreviations used within this guideline

SRH St Richards Hospital	**WH** Worthing Hospital
EPAC Early Pregnancy Assessment Clinic	**GDU** Gynae Day Unit
PUL Pregnancy of Unknown Location	**TVS** Transvaginal Scan
FBC Full blood count	**G&S** Group & Save
U&Es Urea & Electrolytes	**BHCG** Beta-Human Chorionic Gonadotropin
LFT Liver Function Test	**NSAIDs** Non Steroidal Anti Inflammatory Drugs
IV Intravenous	**O&G** Obstetrics and Gynaecology
BP Blood pressure	**hCG** Human Chorionic Gonadotropin
PV Per vaginal	

5.0 Introduction

Ectopic pregnancy has an adverse effect on the quality of life of many women. The incidence of ectopic pregnancy is approximately 11 per 1000 pregnancies (RCOG, 2016, NICE, 2019) and the maternal (and birthing parent) mortality rate is 0.2 per 1000 (HSIB, 2018). Improvement in diagnosis and management of early pregnancy loss is therefore of vital importance, in order to reduce the incidence of the associated psychological morbidity and avoid the unnecessary death of women with ectopic pregnancies (NICE, 2019).

The fallopian tube is the most common site accounting for nearly 95% of ectopic pregnancies. Other possible sites of an ectopic pregnancy are interstitial (2-4%), ovarian (3%), cornual (<1%), cervical (<1%), caesarean section scar or abdominal (rare) (Lin, Bhatt & Dogra, 2008). An abdominal ectopic pregnancy may be primary or secondary resulting from a tubal miscarriage.

6.0 Risk factors

Risk factors for ectopic pregnancy are present only in 25% - 50% of patients with an ectopic pregnancy. They include a history of:

- Previous pelvic inflammatory disease
- Previous pelvic surgery
- Previous ectopic pregnancy
- Subfertility
- In vitro fertilisation
- Intrauterine contraceptive device
- Failure of emergency contraception (Levonelle)
- Smoking
- Maternal or birthing parent age more than 40 years

7.0 Signs and symptoms

GPs and midwives should refer pregnant women and people who are haemodynamically unstable, or in whom there is significant concern about the degree of pain or bleeding, directly to A & E.

Between 6-16% of pregnant women and people who attend A&E with vaginal bleeding or abdominal pain in the first trimester of pregnancy will have an ectopic pregnancy (HSIB, 2018). Be aware that atypical presentation for ectopic pregnancy is common.

7.1 Common symptoms

- Abdominal or pelvic pain
- Amenorrhoea, missed period or irregular bleeding
- Vaginal bleeding of more than three days duration

7.2 More common signs

- Abdominal tenderness, guarding and rigidity.
- Pelvic tenderness.
- Adnexal tenderness.
- Cervical motion tenderness.
- Pallor.
- Abdominal distension.
- Enlarged uterus.
- Tachycardia (heart rate greater than 100 beats per minute).
- Hypotension (blood pressure lower than 100/60 mmHg).
- Shock or collapse.
- Orthostatic hypotension.

7.3 Other reported symptoms – causes for concern

- Diarrhoea on more than three occasions in the previous 24 hours.
- Dizziness, fainting or syncope.
- Shoulder tip pain.
- Urinary symptoms (difficulty or unable to pass urine).
- Passage of tissue.
- Rectal pressure or pain on defaecation.

8.0 Initial assessment

(see Appendix 1)

All women and people of reproductive age should have a pregnancy test. The symptoms and signs of ectopic pregnancy can resemble common symptoms and signs of other conditions such as gastrointestinal conditions or urinary tract infection.

If clinically stable refer to the Early Pregnancy Assessment Clinic (EPAC) or Gynaecology Day Unit. Out-of-hours or if EPAC/GDU is unavailable contact the on call Gynaecology Registrar for further assessment of women and people with a positive pregnancy test and the following on examination:

- Pain and abdominal tenderness or
- Pelvic tenderness or
- Cervical motion tenderness

to exclude the possibility of ectopic pregnancy even in the absence of risk factors. The majority of women and people with an ectopic pregnancy will have no known risk factors.

9.0 Diagnosis of ectopic pregnancy

9.1 Ultrasound diagnosis of intrauterine, PUL and ectopic pregnancies

All pregnancies have a natural history of evolution; hence the ultrasound findings depend on the developmental stage at the time of examination. Before making a diagnosis take into account, patient history, intrauterine and adnexal findings, the patient's clinical presentation and serum HCG levels.

9.2 Ultrasound diagnosis of intrauterine pregnancy (Jurkovic, Valentin & Vyas, 2009)

- A gestation sac seen within the endometrium that is spherical, regular and eccentrically situated towards the fundus can be visualised from 4+3-4+6/40.
- A yolk sac within the chorionic cavity should be visible in all pregnancies from 5-5+6/40 when the mean gestational sac diameter is >12mm.
- The embryonic pole should be visible from 5+6/40.

9.3 Ultrasound Diagnosis of PUL and Ectopic Pregnancy

Ultrasound features suggestive of PUL and ectopic pregnancy can be a combination of intrauterine and adnexal findings. The fallopian tube is the most common site accounting for nearly 95% of ectopic pregnancies. Other possible sites of an ectopic pregnancy are interstitial (2-4%), ovarian (3%), cornual (<1%), cervical (<1%), caesarean section scar or abdominal (rare) (Lin, Bhatt & Dogra, 2008). An abdominal ectopic pregnancy may be primary or secondary resulting from a tubal miscarriage.

Further in-depth detail can be found in Appendix 2.

When carrying out transvaginal ultrasound scan in early pregnancy, it is important to look for the following signs which are indications of the possibility, high probability or existence of a tubal ectopic pregnancy.

9.3.1 Intrauterine and adnexal appearance for a PUL or ectopic pregnancy:

- An empty uterus or
- A variable degree of thickening of the endometrium or
- A collection of fluid within the uterine cavity (sometimes described as a 'pseudo-sac' and found in 20% of all ectopic pregnancies. This collection of fluid must be differentiated from an early intrauterine sac, which is identified by the presence of an eccentrically located hypoechoic structure with a double decidual sign (gestational sac surrounded by 2 concentric rings) in the endometrium.
- An adnexal mass, moving separate to the ovary (sometimes called the 'sliding sign'), comprising a gestation sac containing a yolk sac **or**
- An adnexal mass, moving separately to the ovary, comprising a gestational sac and fetal pole (with or without a fetal heartbeat) (NICE 2019).
- An adnexal mass, moving separately to the ovary (sometimes called the 'sliding sign'), with an empty gestational sac (sometimes described as a 'tubal ring' or a 'bagel sign' and will be present in around 20-40% of cases **or**
- A complex, inhomogeneous adnexal mass, moving separate to the ovary and uterus and is the most common finding in around 50-60% of cases.
- An extrauterine gestational sac moving separately to the uterus with a yolk sac +/- an embryo with or without cardiac activity in 15-20% of cases.
- Echogenic fluid in the Pouch of Douglas, signifying blood leaking from the fimbrial end of the fallopian tube or tubal rupture, in 28-56% of cases.
- The corpus luteum may be present on the ipsilateral side in 85% of cases.

It is important to:

- Ensure the use of colour Doppler when assessing an ectopic pregnancy.
- Report the location and enter the size in three dimensions.
- Report and measure on any free fluid.

9.3.2 Interstitial ectopic pregnancy

- Implantation of the conceptus in the interstitial portion of the fallopian tube which is surrounded by the muscular wall of the uterus.
- An empty uterine cavity and a gestational sac seen adjacent to the lateral aspect of the uterine cavity surrounded by a thin myometrial layer.

- The interstitial line sign refers to the proximal part of the interstitial tube which joins the lateral aspect of the uterine cavity and the ectopic gestational sac.
- Three dimensional ultrasound can also be helpful to differentiate between intrauterine and interstitial pregnancies.

9.3.3 Cervical ectopic pregnancy

- Implantation of the conceptus within the cervix, **below*** the level of the internal os.
- Intracervical localisation of an ectopic gestational sac or trophoblastic mass is the cornerstone for the diagnosis of cervical pregnancy.
- The finding of a gestational sac which contains an embryo with visible heart activity within the cervical canal gives a definitive diagnosis of cervical pregnancy.

9.3.4 Caesarean scar ectopic pregnancy

- Ultrasound diagnosis is based on the visualisation of the gestational sac, which is located **at*** the level of the internal os, and penetrating the anterior uterine wall approaching the bladder.
- The use of Doppler helps to confirm that the implantation has occurred within the myometrial defect.
- The diagnosis of caesarean pregnancy is most accurate in the early first trimester and becomes more difficult as the pregnancy progresses.

9.3.5 Ovarian ectopic pregnancy

- Implantation of the conceptus on the surface or inside the ovary.
- Most case reports include the description of a cystic structure surrounded by an echogenic ring and healthy ovarian tissue.

9.3.6 Abdominal ectopic pregnancy

- Differentiating an abdominal pregnancy from a tubal ectopic pregnancy might be difficult in early pregnancy.
- An empty uterus and the presence of a gestational sac or a mass separate from the uterus, adnexae and ovaries should raise the degree of suspicion of an early abdominal pregnancy.
- In later pregnancy an abdominal pregnancy is characterised by an empty uterus, abnormal fetal lie, oligohydramnios and poor placental definition.

All pregnant women and people with an ectopic pregnancy should receive oral and written information about the treatment options and what to expect during and after treatment, how and who they can contact for advice after treatment if needed as well as where and when to get help

in an emergency. Inform women and people who have had an ectopic pregnancy that they can self-refer to the EPAC for an early scan in all future pregnancies.

(Jurkovic, Valentin & Vyas, 2009)

10.0 Management of ectopic pregnancy

(see Appendix 3)

10.1 Expectant management

Not all ectopic pregnancies progress and pose a risk to the mother or birthing parent. Spontaneous resolution of tubal ectopic pregnancies is well documented.

10.1.1 Selection criteria for expectant management

- Patient is clinically stable and pain free with no signs of rupture or intraperitoneal bleeding and
- A tubal ectopic pregnancy of **less than 35mm** is visualised on transvaginal ultrasound scan with **no heartbeat** and
- Serum hCG level ≤1000IU/L. Expectant management is a documented Consultant decision if the two previous criteria are satisfied but the serum hCG level ≥1000 but ≤1500IU/L.
- The patient is able to return for follow up and review.

The Consultant on-call must be involved in the decision-making. The patient must be well motivated to accept that the rate of ectopic pregnancy resolution, risk of tubal rupture, need for additional treatment and future fertility outcomes are likely to be the same with either expectant or medical management.

Studies have reported success rates of between 80-90% for spontaneous resolution of an ectopic pregnancy when the initial hCG level is <1000 IU/L. The risk of tubal rupture in a patient with an ectopic pregnancy exists until the hCG level has fallen to <20 IU/L.

10.1.2 Follow-up

Repeat serum hCG levels on day 2, day 4 and day 7 after the original test.

- If serum hCG levels drop by 15% or more from the previous value on day 2, day 4 and day 7 then repeat weekly until a negative result (less than 20IU/L) is obtained or
- If serum hCG levels do not fall by 15%, stay the same or rise from the previous value review the patient's clinical condition and seek Consultant advice. If at any stage the patient develops pain then surgery needs to be considered whereas if the patient remains asymptomatic then medical management should be offered.

The patient should be provided with written contact details of the Gynaecology department and counselled that if they develop significant lower abdominal pain, heavy bleeding or vasovagal symptoms they should contact the department or call 999 depending on the severity of their symptoms.

10.2 Medical management

Methotrexate is a folic acid-antagonist (anti-metabolite) that prevents the growth of rapidly dividing cells by interfering with DNA synthesis. It is most commonly given as a single intra-muscular dose of 50 mg/m^2. Methotrexate should only be offered on a first visit when there is a definitive diagnosis of an ectopic pregnancy and a viable intrauterine pregnancy has been excluded following Consultant discussion. Offer surgery where treatment with methotrexate is not acceptable to the patient.

10.2.1 Selection criteria for medical management

- Patient is clinically stable with no significant pain **and**
- Unruptured tubal ectopic pregnancy with an adnexal mass of less than 35mm with no visible heart beat **and**
- No echogenic free fluid on TVS **and**
- No intrauterine pregnancy on transvaginal ultrasound scan **and**
- A serum hCG (day 0) <1500IU/L **and**
- Normal FBC, U&E's and LFT's **and**
- Are able to return for follow up and are remaining within the UK.

10.2.2 Medical or surgical management

Women and people with a BhCG of >1500 IU/L and <5000 IU/L offer the choice of medical or surgical management.

- Patient is clinically stable with no significant pain **and**
- Unruptured tubal ectopic pregnancy with an adnexal mass of less than 35mm with no visible heart beat **and**
- No echogenic free fluid on TVS **and**
- No intrauterine pregnancy on transvaginal ultrasound scan **and**
- Normal FBC, U&E's and LFT's **and**
- Are able to return for follow up and are remaining within the UK/

Or in cases of:

- A persistent trophoblast after salpingotomy.
- Selective cases of Pregnancy of Unknown Location (check the PUL flow chart).

10.2.3 Exclusion criteria

- An ectopic pregnancy and significant pain.
- Any evidence of intraperitoneal haemorrhage i.e. haemoperitoneum (echogenic fluid- not anechoic) on transvaginal ultrasound scan.
- An ectopic pregnancy with serum HCG (day 0) ≥5000 IU/L.
- An ectopic pregnancy with an adnexal mass >35mm.
- The presence of fetal cardiac activity in an ectopic pregnancy.
- Heterotopic pregnancy (simultaneous intrauterine and extrauterine pregnancy).
- Any hepatic dysfunction, thrombocytopenia (platelet count <100,000), blood dyscrasia (WCC <2000 cells/cm^3).
- Difficulty or unwillingness of patient to undertake prolonged follow-up (average 35 days).
- Women or people on concurrent corticosteroid therapy.
- Patients who are due to travel abroad and are not available to monitor FU bloods.

10.2.4 Medical management treatment protocol

The administration of Methotrexate for the medical management of an ectopic pregnancy would only occur following discussion with a Consultant. Methotrexate must not be administered on a single BhCG result**.** Medical management may be considered in cases of persistent PUL and static or persistent low BhCGs.

Discuss options for management (expectant/medical/surgical) based on patient eligibility and exclusion criteria. Patient selection is important for their safety and treatment success.

The dose is calculated on the body surface area (50 mgs/ m^2) and this is calculated using the Dubois calculator omnicalculator.com/health/bsa

All patients must:

- Have their height and weight taken within clinic to support the accurate calculation of the dosage required.
- FBC, G&S, BHCG, U&E'S, LFT'S taken and checked prior to treatment.
- Be counselled and the medical management treatment protocol explained in detail.
- Agree to be compliant with the regime and follow up bloods as this can continue for several weeks.
- Remain within the UK during the follow up regime with access to emergency services.
- Understand the importance of refraining from intercourse and alcohol until bloods have returned to normal.
- Aspirin and NSAID's should not be taken.
- Provided with the Ectopic Trust and Miscarriage Association information leaflet specific to medical management of an ectopic pregnancy.

- Be able to provide informed consent.
- Be informed of the follow up schedule for further bloods.
- Be informed of the side effects associated with Methotrexate.

Refer to the Standard Operating Procedure for the Administration of Intra Muscular Methotrexate for the management of Ectopic Pregnancy and Persistent Trophoblastic Disease (Appendix 4).

The person prescribing the Methotrexate is responsible for:

- Documenting the calculation for dose of Methotrexate on a drug chart.
- Sending the drug chart or electronic prescription to Pharmacy (24 hours' notice is required to dispense the Methotrexate).

The person administering the Methotrexate is responsible for:

- Ensuring they are not pregnant, or trying to become pregnant or breastfeeding.
- Should wear Personal Protective Equipment (PPE) of an apron and gloves.
- Injecting the Methotrexate into the gluteal muscle.
- Disposing of the sharps in accordance with the SOP and Trust policy.

Arrange follow-up by EPAC, provide written contact details of the Gynaecology department and counsel the patient that if she develops significant lower abdominal pain, heavy bleeding or vasovagal symptoms she should contact the department or call 999 depending on the severity of her symptoms.

10.2.5 Medical Management Single – Dose Regime

Day 0	Serum hCG, FBC, U&Es, LFTs, G&S	Prescription request to Pharmacy
Day 1	Serum hCG	Intramuscular Methotrexate 50 mg/m^2
Day 4	Serum hCG	
Day 7	Serum hCG, FBC, U&E's, LFTs	If serum hCG decreases <15% between days 4-7 reassess the patient, consider repeating transvaginal ultrasound scan and/or repeating second dose of Methotrexate If serum hCG decreases >15% between days 4-7 repeat serum hCG weekly until <15 IU/L

10.2.5.1 Information for the clinician

- Up to 75% of patients may complain of pain on days 3-7 and this is thought to be due to tubal miscarriage. The risk of tubal rupture is 7% and this risk remains while there is a persistently elevated serum hCG.
- In up to 86% of patients' serum hCG levels may initially rise between days 1 – 4.
- 14% of medically treated women will require more than one dose of Methotrexate. A second dose may be administered on day 7 if serum hCG levels fail to fall by more than 15% between days 4-7.
- Mean time to resolution is 35 days.
- Folinic acid rescue is not required for the single dose regime.
- During treatment patients should avoid:
    - Alcohol and vitamins containing folate.
    - Intercourse to reduce the risk of rupture.
- Avoid vaginal examination. Transvaginal ultrasound scan may be undertaken if clinically indicated.
- Ovarian cysts, that undergo spontaneous resolution, may be found following treatment.
- It is recommended that women and people treated with Methotrexate wait at least 3 months from a negative urine pregnancy test before trying to conceive again.
- Once the serum hCG has returned to normal patients that would like to try for a pregnancy after their 3 month period should start taking folic acid 400 mcg unless the patients BMI is >35 when 5 mgs of folic acid is required.

10.2.5.2 Patients need to be aware

- to make contact or attend ED if unwell or symptomatic
- the risk of sun sensitivity
- developing mouth ulcers/soreness
- minimal hair loss
- the review process can go on for 4-8 weeks
- using contraception and not becoming pregnant in the next 3 months due to the risk of fetal abnormality
- increased risk of ectopic pregnancy in future pregnancies and that an early scan at 6-7 weeks gestation is recommended to ensure that the pregnancy is intrauterine

10.3 Surgical management of ectopic pregnancy by laparoscopy

When surgical treatment is indicated for pregnant women and people with an ectopic pregnancy, it should be performed laparoscopically whenever possible, taking into account the condition of the patient and the complexity of the surgical procedure. Surgeons providing care to women and people with ectopic pregnancy should be competent to perform laparoscopic surgery. Evidence suggests that there is no difference in terms of health benefits between laparoscopy and laparotomy including subsequent successful pregnancy.

10.3.1 Advantages of laparoscopic surgery

- Shorter hospital stay (1 days).
- Significantly less intraoperative blood loss.
- Less adhesion formation.
- Lower analgesic requirements.
- Quicker post operative recovery time.

10.3.2 Disadvantages

- Increased risk of bowel/vascular injury.

10.4 Management by laparotomy

Management in the presence of haemodynamic instability should be by the most expedient method.

Experienced operators may be able to manage women and people with even a large haemoperitoneum safely by laparoscopic method but the surgical procedure that prevents further blood loss most quickly should be used.

10.5 Safety

10.5.1 Salpingectomy v salpingotomy

- There is no significant difference in the subsequent intrauterine pregnancy rate following salpingotomy or salpingectomy (61% v 56%).
- The recurrent ectopic pregnancy rate is higher following salpingotomy (8%) than after salpingectomy (5%).
- Following salpingotomy persistent trophoblast was noted in 7% of patients hence there is a need to monitor serum hCG post salpingotomy.
- Following salpingectomy <1% of patients have persistent trophoblast however all women and people should take a urine pregnancy test 3 weeks post operatively and contact EPAC if it is positive.

In the presence of a healthy contralateral tube there is no clear evidence that salpingotomy should be performed in preference to salpingectomy. Laparoscopic salpingotomy should be considered as the primary treatment when managing tubal pregnancy in the presence of contralateral tubal disease and the desire for future fertility. Pre-operatively, treatment should be discussed with the patient with the option of conserving or removing the tube.

10.6 Follow-up regime after salpingotomy

While trophoblast remains in the tube it has a capacity to rupture. Between 4-11% of patients having a salpingotomy may need further surgical or medical treatment.

- Follow-up with weekly serum hCG until the level is <20 IU/L.
- If hCG level rises or plateaus consider further treatment with Methotrexate.
- Surgical management if serum hCG level >4000 IU/L.

Outcome after conservative surgery in women and people with one tube:

- Subsequent intrauterine pregnancy rate is 75%

Conservative surgery is only appropriate if the patient is aware of the risk involved. Salpingectomy followed by In vitro fertilisation may be alternative treatment in such cases.

The patient should be provided with written contact details of the Gynaecology department and counselled that if they develop significant lower abdominal pain, heavy bleeding or vasovagal symptoms, they should contact the department or call 999 depending on the severity of their symptoms.

10.7 Recommendations arising from the 33rd RCOG Study Group

At laparoscopy for ectopic pregnancy, precise documentation of the state of the pelvis, with particular emphasis on the affected and contralateral tube and ovaries, should be undertaken to determine prognosis of future fertility.

The definitive procedure undertaken at surgery (removal of the ectopic by salpingotomy; unilateral salpingectomy; bilateral salpingectomy) should be determined by the reproductive aspirations of the patient, her reproductive history, the state of the pelvis and the availability of assisted conception services.

Fimbrial evacuation (milking) of ectopic pregnancy from the fallopian tube should not be as it predisposes to persistence of tubal pregnancy.

11.0 Management of Ruptured Ectopic with Collapse

(see Appendix 5)

- Assess and support A, B, C.
- Get help; contact O&G Registrar, O&G Consultant on-call and CEPOD Anaesthetist.
- Site two intravenous lines (at least 16G), commence IV fluids (crystalloid), give facial oxygen and insert indwelling catheter.
- Send blood for FBC, clotting screen and cross-match at least 4 units of blood.
- Arrange theatre admission for laparotomy or laparoscopy.

- Continue fluid resuscitation and ensure intensive monitoring of haemodynamic state whilst awaiting transfer to theatre. Do not wait for BP and pulse to normalise prior to transfer.
- Salpingectomy and wash out abdomen.
- Assess bloods and consider Critical Care care after discussion with anaesthetist.
- Record operative as per RCOG recommendations findings including the state of the remaining tube.
- A Datix form should be completed following all ruptured ectopics.

12.0 Anti-D rhesus prophylaxis

Offer anti-D rhesus prophylaxis at a dose of 1500IU to all rhesus negative women and people who have a surgical procedure to manage an ectopic pregnancy or a miscarriage.

Do not offer anti-D rhesus prophylaxis to women and people who:

- Receive solely expectant or medical management for an ectopic pregnancy or miscarriage or
- Have a threatened miscarriage or
- Have a complete miscarriage or
- Have a pregnancy of unknown location.

Do not use a Kleihauer test for quantifying feto–maternal haemorrhage.

13.0 Pregnancy of Unknown Location (PUL)

(see Appendix 6)

The term ‘pregnancy of unknown location’ (PUL) is used whenever there is no sign of either intra or extrauterine pregnancy or retained products of conception on transvaginal ultrasound, despite a positive pregnancy test. A pregnancy site will not be visualised in 8–25% of early pregnancy scans.

The sonographer’s experience and resolution of the ultrasound machine, the patient’s body habitus and the chair or couch used to perform the scan influences the prevalence of PUL. Be aware that women and people with a PUL could have an ectopic pregnancy until the location is determined.

In a patient with a PUL, place more importance on clinical symptoms than on serum hCG results, and review the patient's condition if any of their symptoms change, regardless of previous results and assessments.

With a positive pregnancy test, there could be three reasons for a scan to be classified as PUL:

- A very early intrauterine pregnancy *or*
- A complete miscarriage *or*
- An early ectopic pregnancy

At subsequent follow-up visits the diagnosis may become clear. However, if symptoms and signs of pregnancy are resolving (including serum hCG levels), this can be classified as a 'resolving PUL'

14.0 Serum hCG

Do not use serum hCG measurements to determine the location of the pregnancy. Use serum hCG measurements only for assessing trophoblastic proliferation to help to determine subsequent management in conjunction with the patients clinical history.

Take one serum hCG measurement and if it is:

- Less than 1000, clinically well repeat in 48 hours to determine subsequent management of a PUL.
- Greater than 1000IU/L with no clinical history of miscarriage arrange a rescan for a second opinion preferably by a Consultant (specialising early pregnancy and emergency gynaecology) within 48-72 hours if clinically stable, otherwise review as an emergency.
- Greater than 1000 with a clinical history of of heavy PV bleeding, clots and possibly passing products of conception repeat BhCG in 48 hours.

For a patient with an increase in serum hCG concentration greater than 63% after 48 hours:

- Inform the patient that it is likely to be a developing intrauterine pregnancy although the possibility of an ectopic pregnancy cannot be excluded
- Offer a transvaginal ultrasound scan to determine the location of the pregnancy 7 to 14 days later
- If a viable intrauterine pregnancy is confirmed, offer routine antenatal care. If a viable intrauterine pregnancy is not confirmed, refer for immediate clinical review by a senior Gynaecologist.

For a patient with a decrease in serum hCG concentration greater than 50% after 48 hours:

- Inform them that the pregnancy is unlikely to continue but that this is not confirmed and provide them with oral and written information about where they can access support and counselling services.
- Ask them to take a urine pregnancy test 3 weeks after the second serum hCG test, and explain that:

- If the test is negative, no further action is necessary.
- If the test is positive, they should return to EPAC for clinical review within 24 hours.

For a patient with a change in serum hCG concentration between a 50% decline and 63% rise inclusive repeat a third serum hCG after 48 hours:

- If there is a decrease in serum hcg concentration of greater than 50% irrespective of serum progesterone inform them that the pregnancy is unlikely to continue but that this is not confirmed. Ask the patient to take a urine pregnancy test in 3 weeks.
  - If the test is negative, no further action is necessary.
  - If the test is positive, the patient should be contacted by EPAC for telephone review within 24 hours and invited to return if clinically indicated .
- Repeat serum hcg in 7 days and weekly until serum hcg is less than 20IU/L

Regardless of serum hCG the patient should be provided with written contact details of the Gynaecology department and counselled that if they develop any new or worsening symptoms such as significant lower abdominal pain, heavy bleeding or vasovagal symptoms, they should contact the department or call 999 depending on the severity of their symptoms.

Regardless of serum hCG levels, give women and people with a 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 and people to return if there are new symptoms or if existing symptoms worsen.

Serum hCG should always be measured even if the diagnosis of an ectopic pregnancy is clear on scan findings as its level is used as a predictor for the success of expectant, medical or surgical management of the ectopic pregnancy.

15.0 Serum progesterone

A serum progesterone level below 20nmol/l has been shown to have a positive predictive value greater than 95% of predicting pregnancy failure. Levels below 20nmol/l are likely to indicate a failing pregnancy and above 20nmol/l are associated with a viable pregnancy irrespective of its location.

Whilst a single serum progesterone measurement has a good discriminative capacity to distinguish between pregnancy failure and a viable IUP, a single measurement cannot discriminate between ectopic pregnancy and non-ectopic pregnancy. In summary serum progesterone level is good at predicting viability, but not the location of pregnancy.

16.0 Patient follow up after an ectopic pregnancy and PUL

When patients who have had an ectopic pregnancy or a PUL had registered their pregnancy with maternity services the healthcare provider should inform the maternity department of the pregnancy outcome prior to discharging the patient. Patients should also be provided with information on support networks including the Ectopic Pregnancy Trust and the Miscarriage Association (see details on the following page). Patients who have had an ectopic pregnancy should be advised to contact the EPAC with any subsequent positive pregnancy test in order to book an early scan.

17.0 Audit

The process for audit and monitoring of this guideline are contained within the Gynaecology Audit Document.

References

Association of Early Pregnancy Units Guidelines, 2007 (Archived)

Healthcare Safety Investigation Branch (HSIB) Interim Bulletin: The Diagnosis of Ectopic Pregnancy, 2018

Jurkovic, Valentin & Vyas, 2009. Gynaecological ultrasound in clinical practice: Ultrasound imaging in the management of gynaecological conditions.
Royal College of Obstetrics and Gynaecology. LONDON

Kirk, E. & Bourne, T. 2008. Predicting Outcomes in Pregnancies of Unknown Location. Women's Health, 4 (5) pp. 491-499

Linn E., Bhatt, S. & Dogra, V. 2008. Diagnostic Clues to Ectopic Pregnancy RadioGraphics 28 (6) pp.1661-1671t

NICE Clinical Guideline CG154 Dec 2012; Ectopic pregnancy and miscarriage: diagnosis and initial management.

NICE guideline NG126, April 2019; Ectopic pregnancy and miscarriage: diagnosis and initial management. Updated November 2019

33rd RCOG Study Group. Recommendations arising from the33rd RCOG Study Group: Problems in Early Pregnancy–Advances in Diagnosis and Management. In: Grudzinskas JG, O'Brien PM, editors. Problems in Early Pregnancy: Advances in Diagnosis andManagement. London: RCOG Press; 1997. p. 327–31and cited in RCOG/AEPU Greentop Guideline No 21. Nov 2016; Diagnosis and management of Ectopic Pregnancy

RCOG Green-top Guideline No.21, Diagnosis and Management of Ectopic Pregnancy, November 2016, British Journal of Obstetrics and Gynaecology

Sagili, H. & Mohamed, K. 2008. Pregnancy of Unknown Location: an Evidence-Based Approach to
Management. The Obstetrician & Gynaecologist, 10 pp.224–230

Support Networks

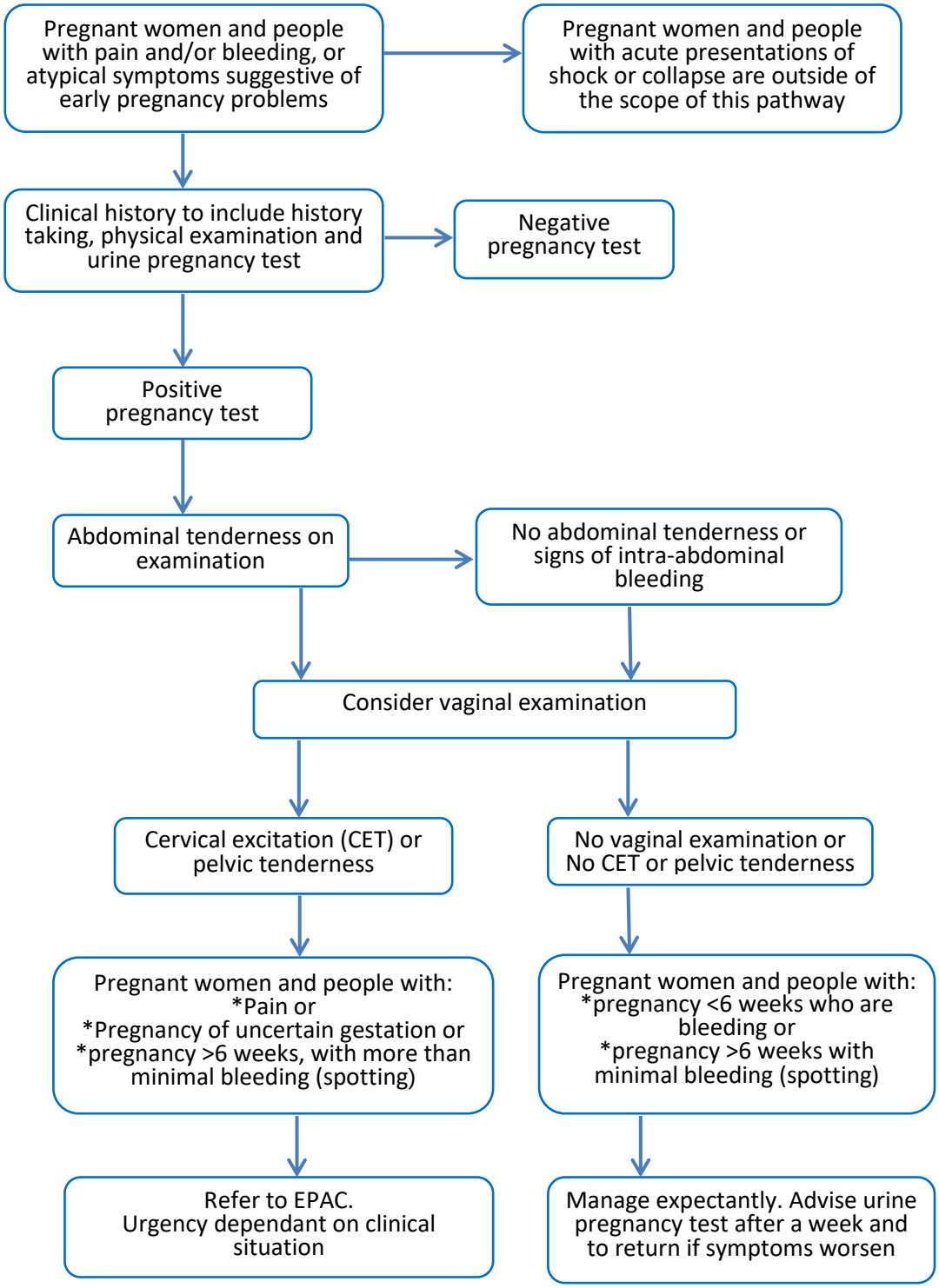
The Ectopic Pregnancy Trust
(www.ectopic.org.uk)

'Supporting people who have experienced an early pregnancy complication and the healthcare professionals who care for them'

The Miscarriage Association
(www.miscarriageassociation.org.uk)

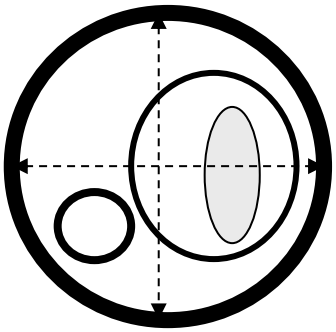
'Founded in 1982 by a group of people who had experienced miscarriage and we continue to offer support and information to anyone affected by the loss of a baby in pregnancy, to raise awareness and promote good practice in medical care.'

Appendix 1: Early Pregnancy Assessment Clinic Initial Clinical Assessment

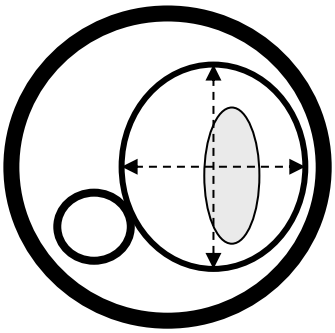


Appendix 2: Early Pregnancy ultrasound diagnosis

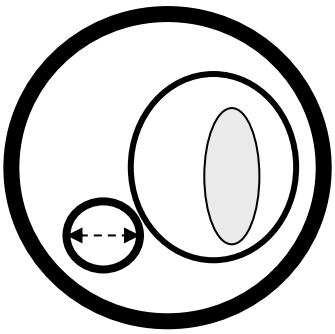
Gestational (chorionic) sac
Measurements should be performed from the inner edges of trophoblast in three planes. The diameters measured correspond to those of the chorionic cavity. The maximum and mean diameters should be recorded. The volume may also be calculated using formula for ellipsoid V= A x B x C x 0.523. *(Robinson HP. Gestational sac volumes as determined by sonar in the first trimester of pregnancy. Br J Obstet Gynecology, 1975; 82:100)*



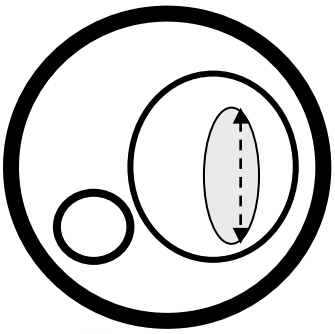
Amniotic sac - The three perpendicular diameters should be measured and the mean diameter calculated. As the amnion is very thin the measurements should be taken from the centre of the membrane. (*Horrow M. Enlarged amniotic cavity: new sonographic sign of early embryonic death. Am J Roentgen 1992; 158:359*)



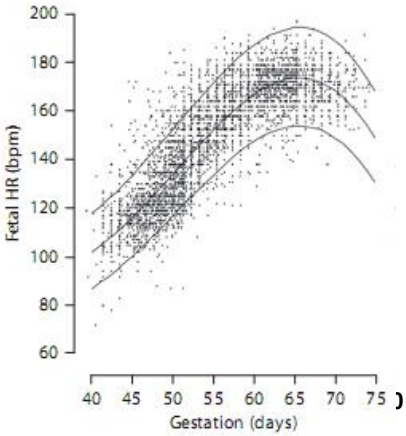
Measure three perpendicular diameters from the centre of the yolk sac wall. *(Jauniaux E et al. Development of the secondary human yolk sac: Correlation of sonographic and anatomic features. Human Reproduction 1991; 6:1160)*



In early pregnancy this is the greatest length of the embryo, as the crown and rump cannot be distinguished. From seven weeks onwards the measurement should be taken from a saggital section of the embryo, with care taken not to include the yolk sac. (*Robinson HP et al. A critical evaluation of sonar crown-rump length measurement. Br J Obstet Gynecology,1975; 82:702)*



Embryonic cardiac activity is usually evident as soon as the embryo itself can be visualised. In the first trimester the heart rate should be measured using M-mode only.

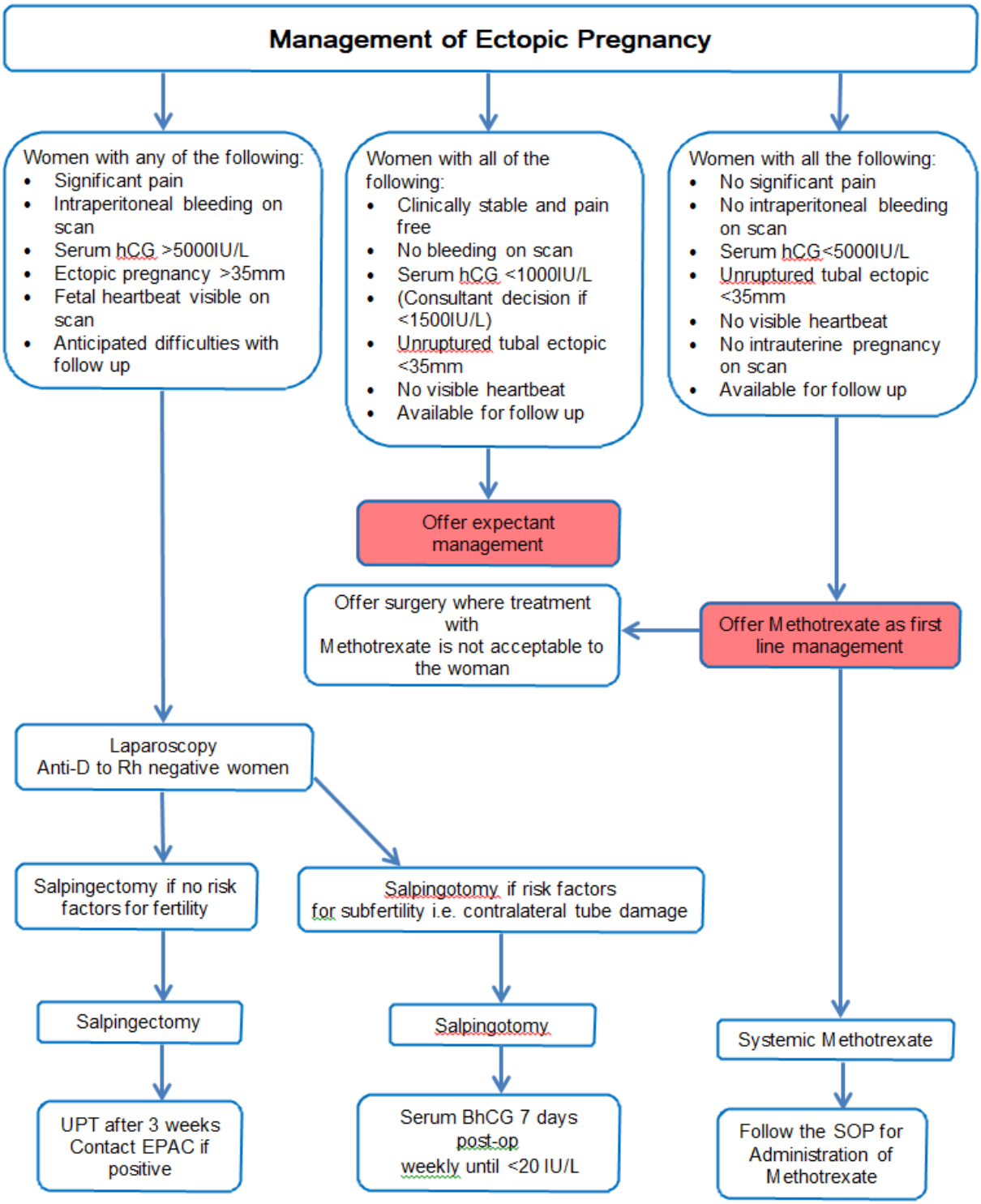


Landmarks for diagnosis

(Jurkovic D et al. Ultrasound features of normal early pregnancy development. Current Opinion in Obstetrics and Gynaecology, 1995;7:493)

4^{+3} to 5^{+0}	A small gestation sac (2-5 mm) is seen within the endometrium. The sac is spherical, regular in outline and eccentrically situated towards the fundus. It is implanted just below the surface of the endometrium (midline echo) and is surrounded by echogenic trophoblast. In symptomatic patients the scan should be repeated in a week when yolk sac should be visible.
5^{+1} to 5^{+5}	Yolk sac becomes visible within the chorionic cavity. This should be seen in all pregnancies with a mean gestational sac diameter of > 12 mm. If it is not, the diagnosis of blighted ovum is almost certain and the scan should be repeated a week later to confirm this.
5^{+6} to 6^{+0}	The embryonic pole is visible and it measures 2-4 mm in length. Heart action is also detectable. An embryo is usually visible with a mean gestational sac diameter of > 18 mm. If this is not the case then the pregnancy is likely to be abnormal and another scan should be organised a week later.
6^{+1} to 6^{+6}	The embryo changes from being a straight line at the top of the yolk sac to being kidney bean shaped, with the yolk sac separated from the embryo by the vitelline duct. The crown-rump length measures 4 to 10 mm. If the heart rate is not detectable the diagnosis of missed miscarriage is almost certain.
7^{+0} to 7^{+6}	The crown-rump length measures 11 to16 mm. The rhombencephalon becomes distinguishable as a diamond shaped cavity, enabling distinction of cephalad and caudal. The spine is seen as double echogenic parallel lines. The amniotic membrane becomes visible defining the amniotic cavity from the chorionic cavity. The umbilical cord can also be seen.
8^{+0} to 8^{+6}	Crown-rump length 17-23 mm. Forebrain, midbrain, hindbrain and skull are distinguishable. Limb buds are also visible. Midgut hernia is present. The amniotic cavity expands and the umbilical cord and vitteline duct lengthens.
9^{+0} to 10^{+0}	Crown-rump length 23-32 mm. The limbs lengthen and hands and feet are seen. Embryonic heart rate peaks at 170-180 bpm.

Appendix 3: Management of ectopic pregnancy

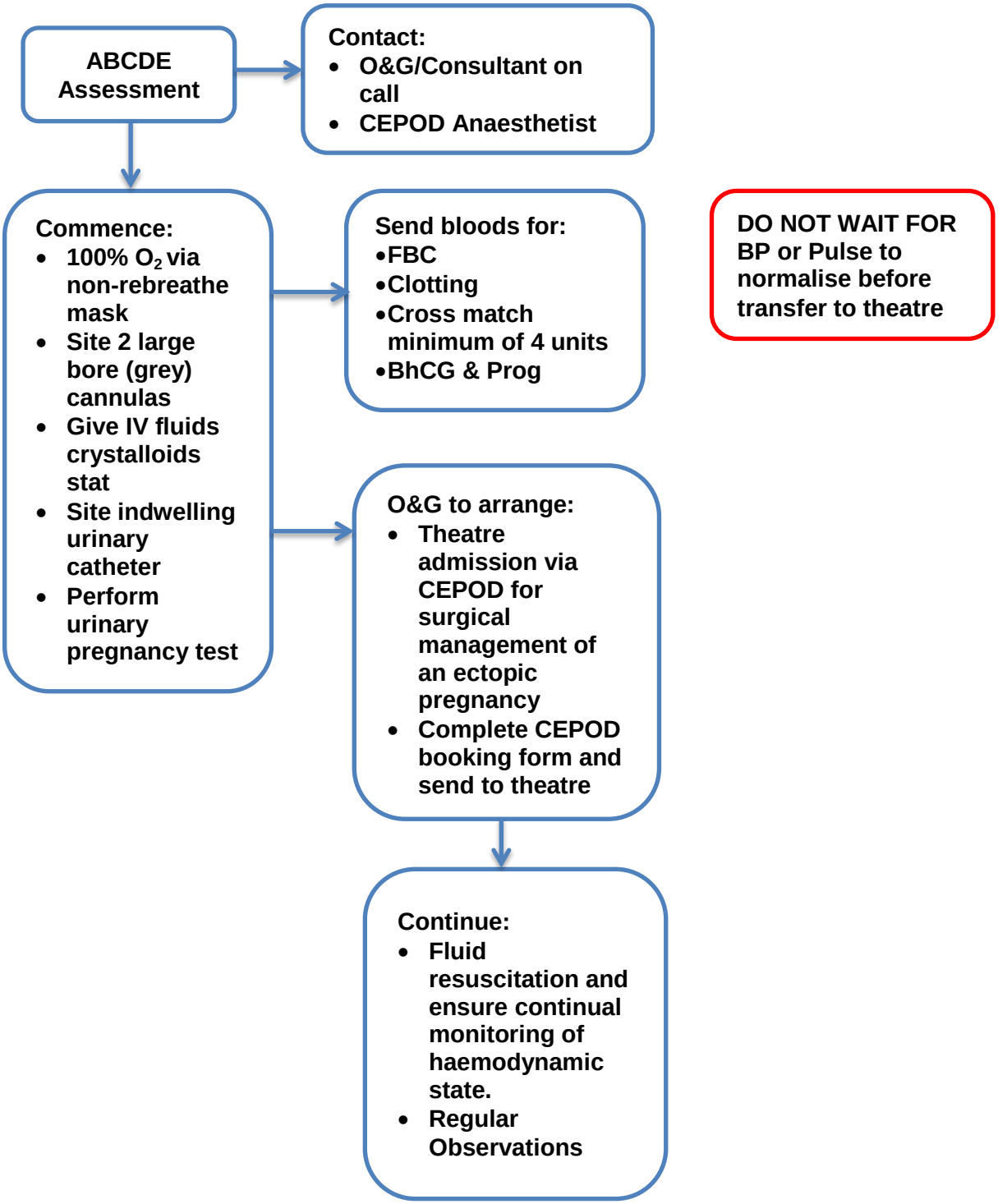


Appendix 4: Standard Operating Procedure for the administration of intramuscular Methotrexate for the management of ectopic pregnancy and persistent trophoblastic disease

Please click on link for SOP & competency document:

http://nww.westernsussexhospitals.nhs.uk/assets/im-methotrexate-sop-and-competency-document-v1-0-oct-2022.pdf

Appendix 5: Management of a ruptured ectopic with collapse in A&E



Appendix 6: Flowchart for management of PUL