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Venous Thromboembolism (VTE) In Pregnancy and the Puerperium: Risk assessment, Diagnosis and Management.

Introduction and Aim

Pregnancy is a risk factor for developing a deep vein thrombosis (DVT) or pulmonary embolism (PE), which are types of venous thromboembolism (VTE). As VTE is the leading direct cause of maternal mortality in the UK, risk assessment and prophylactic treatment are a crucial aspect of high standard antenatal care. Clinical diagnosis of VTE is unreliable, therefore clear pathways for the investigation and management of acute VTE are presented here.

Objectives

- This guideline provides pathways for risk reduction, investigation and management of VTE in pregnancy and the puerperium.

Executive Summary

Guidance	Comment	Link
VTE Risk Assessment: Antenatal	Form to be completed at booking and every subsequent antenatal admission.	3.2.1.1
VTE Risk Assessment: Postnatal	Form to be completed after delivery, before transfer from delivery suite or midwifery led unit. To be completed at any subsequent postnatal readmission.	3.2.2.1
Acute Deep Venous Thrombosis (DVT)	Pathway for the investigation and management.	4.4
Acute Superficial Venous Thrombophlebitis (SVT)	Pathway for the investigation and management.	5
Acute Pulmonary Embolism (PE)	Pathway for the investigation and management.	6.4
CTPA vs V/Q scan	Counselling women in pregnancy and puerperium	6.3.1
Life Threatening PE	Referral pathways and management.	8
Anticoagulation: Treatment with Enoxaparin	Prescribing advice, dosage and monitoring.	7.2
Management of Enoxaparin during labour.	Including guidance on the use of spinal anaesthetic and epidural catheters.	9
Referral to Obstetric Haematology Clinic	Pathway for referral	7.1

Scope

This procedure applies to all of our staff in all locations including those with honorary contracts.

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Equality Health Impact Assessment	An Equality Health Impact Assessment (EHIA) has been completed. The Equality Impact Assessment completed for the policy found here to be no impact.
Documents to read alongside this Procedure	Royal College of Obstetricians and Gynaecologists, Greentop Guidelines: Venous Thromboembolism in Pregnancy
Approved by	Maternity Professional Forum Quality and Safety, Directorate of Obstetrics and Gynaecology

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2 Introduction

- Pregnancy is a risk factor for developing a deep vein thrombosis (DVT) or pulmonary embolism (PE), which are types of venous thromboembolism (VTE).
- The signs and symptoms of VTE such as tachycardia, swollen legs and shortness of breath, overlap with physiological changes in pregnancy and it is often difficult to distinguish between the two.
- Clinical diagnosis of VTE is unreliable. Less than half of women with clinically suspected VTE have the diagnosis confirmed when objective testing is employed.
- VTE is the leading, direct cause of maternal death in the UK, the recent MBRRACE-UK report demonstrated an increase in mortality (MBRRACE-UK: Saving Lives Improving Mothers' Care report for 2019) to 1.5 per 100,000 maternities (from 1 per 100,000 maternities in previous report).
- Prompt diagnosis and treatment is essential to reduce these unnecessary maternal deaths. Equally, accurate exclusion of VTE is important to reduce the unnecessary exposure to therapeutic anticoagulation and to accurately inform the management of future pregnancy.
- VTE can occur at any time during pregnancy but the puerperium (first six weeks after giving birth) is the time of highest risk.

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3 Preventing Venous Thromboembolism (VTE) in Pregnancy

3.1 Risk Factors for the Development of VTE in pregnancy and the puerperium

All women should be assessed for the risk of VTE during and after pregnancy at their midwifery booking appointment and referred for obstetric-led antenatal care if risk factors are present. Medical staff should assess all women receiving obstetric led antenatal care at their first hospital clinic visit. Risk factors can change during pregnancy and **every contact should be seen as an opportunity to reassess risk**, including events which may have occurred in family members since the last assessment.

Indications for thromboprohylaxis vary – a small number of women should have outpatient, ambulatory thromboprophylaxis with LMWH. Any woman admitted to hospital should be assessed for the current risk of VTE, determined by the reason for admission and individual risk factors.

In general, offer thromboprophylaxis with **LMWH alone.** Consider combined LMWH and mechanical thromboprophylaxis for women who gave birth or had a miscarriage or termination of pregnancy in the past 6 weeks and who are likely to be immobilised or have significantly reduced mobility relative to their normal or anticipated mobility for three or more days after surgery, including caesarean section.

Where pharmacological thromboprophylaxis is deemed unsafe or combined mechanical and pharmacological prophylaxis is indicated then intermittent pneumatic compression (IPC) devices are recommended.

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3.2 Risk Assessment

3.2.1 Risk Assessment at Booking and on Antenatal Admission

The first column of the risk assessment is to be completed at first contact with obstetric services (gynaecology have a simplified version) and filed in the handheld maternity record (or hospital record if midwifery booking not yet completed).

Any admission in the antenatal period, including assessments in accident and emergency (A&E) or obstetric assessment unit (OAU) should prompt a review of risk factors for VTE, even if the woman is not admitted onto the ward. A new risk assessment form should be done for each admission. The ‘Booking Assessment’ column should be filled again, to confirm pre-existing VTE risk factors. The clinician should then complete the ‘antenatal admission’ column to identify transient risk factors associated with the admission. A fresh copy of the risk assessment should be completed and filed in the woman’s handheld maternity record for any presentation to acute services or antenatal admission. It is not necessary to complete a fresh form at routine antenatal clinic/midwifery appointments, but is good practice to review the VTE risk factors to ensure there have been no changes in the woman’s risk factors.

Unless contraindicated <u>all</u> pregnant women who are non-ambulant and admitted to hospital and have **1 or more risk factors** for venous thromboembolism should receive thromboprophylaxis with enoxaparin.

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3.2.1.1 Antenatal Risk Assessment for VTE

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GIG CYMRU NHS WALES | Bwrdd Iechyd Prifysgol Caerdydd a'r Fro | Cardiff and Vale University Health Board

Patient Addressograph

Reducing the risk of Venous Thromboembolism (VTE) during Pregnancy

Antenatal Admission

Do not prescribe Enoxaparin to women who are admitted in active labour.
Women should discontinue their thromboprophylaxis at the first sign of labour.

Prescribe pharmacological thromboprophylaxis for all pregnant women who are non-ambulant and admitted to hospital and have **≥1 risk factor** for venous thromboembolism (see below) and no contraindication.

If there are contraindications to pharmacological TP, intermittent pneumatic compression (IPC) devices should be used. **Anti embolic stockings are not recommended**.

At Booking

All women should be risk assessed for VTE at their midwifery booking appointment and referred for obstetric led antenatal care if risk factors are present.
Medical staff should assess all women receiving obstetric led antenatal care at their first hospital clinic visit.

Indications to consider antenatal thromboprophylaxis (tick if present)

Previous DVT/PE Refer to haematology clinic		Antiphospholipid syndrome Refer to haematology clinic	
Significant medical illness (SLE**,Myeloproliferative disorder**, Sickle cell disorder **, active inflammatory bowel disease, active cancer, nephrotic syndrome **Refer to haematology clinic		Antithrombin deficiency with no personal history of VTE Refer to haematology clinic	
Severe ovarian hyperstimulation syndrome (duration of treatment with enoxaparin) must be individualised)		BMI ≥45kg/m^2 Ref. to anaesthetic clinic by 32/40 if booking BMI≥45	

Assessed by:

Date / Signature

Thromboprophylaxis where the only risk factor is BMI ≥45kg/m^2

Women who have a BMI ≥45kg/m^2 will be referred to consultant led obstetric care and will be seen at 16 weeks gestation.
They will also require an anaesthetic clinic at 32-34 weeks for assessment. The anaesthetist will identify potential anaesthetic risks especially relating to general anaesthesia. They will discuss the risk of a major thrombotic event versus not receiving an epidural or spinal anaesthetic should thromboprophylaxis continue to delivery.

Weight based dosing of enoxaparin thromboprophylaxis only if Creatinine Clearance is >30mL/min	Out patient regimen	In patient regimen*
Weight ≤50kg	20mg **Once** daily	20mg **Once** daily
Weight 51-100kg	40mg **Once** daily	40mg **Once** daily
Weight 101-150kg	60mg **Once** daily	40mg **Twice** daily
Weight >150kg	80mg **Once** daily	60mg **Twice** daily

Indications for thromboprophylaxis whilst antenatal inpatient (tick if present)

Hyperemesis/Dehydration		Medical co-morbidities	
Infection/sepsis (if COVID-19, see below)*		Age >35 years	
Pre-eclampsia in current pregnancy (except when delivery is planned in the next 12h)		Significant varicose veins	
Admission for surgical procedure (e.g. appendicectomy)		Multiple pregnancy	
First degree relative with history of VTE		Obesity (BMI greater than 30kg/m²)	
Immobility		ART/IVF (current pregnancy)	

Before prescribing Enoxaparin, confirm that there are no contraindications (see below).
*** If admitted with COVID-19, refer to CAV UHB Guideline: Reducing the Risk of VTE in Adult Patients with COVID-19**

Are there contraindications to Enoxaparin? (tick if present)

Spinal/epidural within the past 6h or due in the next 12h		Thrombocytopenia: platelet count < 75 x 10^9/L	
Do not remove epidural catheter within 12 hours of Enoxaparin thromboprophylaxis administration.		Known bleeding disorder	
Active bleeding or at risk of bleeding		Severe renal impairment: If CrCl < 30ml/min or evidence of acute renal failure, use subcutaneous unfractionated heparin 5000u bd	
Currently receiving therapeutic anticoagulation		Severe liver disease	
Past history of heparin-induced thrombocytopenia (discuss with haematologist)		Disseminated intravascular coagulopathy (DIC)	

If Enoxaparin thromboprophylaxis is indicated and not contraindicated confirm:

Patients Weight at booking: .....Kg

Enoxaparin Thromboprophylaxis dose*: .....mg

Assessed by:

Date / Signature

3.2.2 Risk Assessment in the Postnatal period.

Encourage early mobilisation, hydration and awareness of symptoms of VTE in all women.

Complete the first postnatal risk assessment before the woman leaves delivery suite or the midwifery led unit. This should be reviewed following any significant events in the postpartum period (e.g. return to theatre) and prior to discharge from the postnatal ward.

A new postnatal risk assessment must be completed if a woman is re-admitted to hospital at any time in the postpartum period, and filed in the hospital records.

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3.2.2.1 Postnatal Risk Assessment for VTE

Starts on next page.

Reducing the risk of Venous Thromboembolism (VTE) after Pregnancy

Encourage early mobilisation, hydration and awareness of symptoms of VTE in all women

Patient Addressograph

Indications for thromboprophylaxis in the postnatal period (tick if present)			
PPH ≥1500ml		Mid-cavity or rotational forceps delivery	
Red blood cell transfusion or transfusion of coagulation factors		Sepsis/ COVID-19 positive	
Caesarean section (elective or emergency)		BMI >40kg/m^2	
Still-birth in current pregnancy		Immobility	

Commence Enoxaparin 6 hours following delivery, provided there are no concerns about bleeding.
Delay Enoxaparin administration for 6 hours following removal of epidural catheter or completion of spinal anaesthesia.
(In COVID-19 positive in-patients, see CAV UHB Guideline: Reducing the Risk of VTE in Adult Patients with COVID-19)

Review antenatal risk factors. Women receiving Enoxaparin thromboprophylaxis **antenatally** should continue treatment for **6 weeks postpartum.**

Women who have had COVID-19 while an inpatient should be prescribed a minimum of 14 days of standard (not 'enhanced') outpatient dose thromboprophylaxis on discharge.

Women requiring **postnatal** Enoxaparin thromboprophylaxis should continue for minimum of **10 days postpartum, a longer duration may be appropriate for some women.**

Mechanical Thromboprophylaxis

Where pharmacological thromboprophylaxis is deemed unsafe, intermittent pneumatic compression (IPC) devices are recommended (ensure no contraindication).

Combined IPC & enoxaparin thromboprophylaxis can be considered in very high risk cases, these include women who have:
- Significantly reduced mobility relative to their normal (anticipated to last >3days) post C-section, return to theatre or hysterectomy
- Consider in Level 2 HDU cases (e.g. severe pre-eclampsia, massive obstetric haemorrhage)

Decision regarding providing combined IPC & enoxaparin thromboprophylaxis should be following MDT discussion between Obstetrics, Anaesthetics and Haematology, and documented in the maternal notes.

Anti-embolic stockings are not recommended.

Weight based dosing of enoxaparin thromboprophylaxis only applicable if Creatinine Clearance is >30mL/min	Out patient regimen	In patient regimen
Weight ≤50kg	20mg **Once** daily	20mg **Once** daily
Weight >51-100kg	40mg **Once** daily	40mg **Once** daily
Weight 101-150kg	60mg **Once** daily	40mg **Twice** daily
Weight >150kg	80mg **Once** daily	60mg **Twice** daily

If Enoxaparin thromboprophylaxis is indicated and not contraindicated confirm:

Patients Weight at booking: .....Kg

Enoxaparin Thromboprophylaxis dose: .....mg

Duration post-delivery: 6 weeks/10 days/ other……

Assessed by:

Date / Signature

Title: 'Reducing the risk of VTE during pregnancy/after pregnancy' ***Authors***: *H Roberts, R. Halabi*
Version 1.0 18-JUN-2020 ***Ratified by***: *MPF on 24-JUN-2020*

3.3 Contraindications to anticoagulation with Enoxaparin

Consider contraindications to enoxaparin (thromboprophylaxis or therapeutic dose). Women with an identified contraindication to enoxaparin but the need for therapeutic enoxaparin should be discussed urgently with Haematology.

Contraindications to anticoagulation with Enoxaparin.
Spinal/epidural within the past 6 hours or due in the next 12 hours.
Do not remove epidural catheter within 12 hours of Enoxaparin thromboprophylaxis administration.
Active bleeding or at risk of bleeding.
Currently receiving therapeutic anticoagulation.
Thrombocytopenia: platelet count <75 x 10^9
Known bleeding disorder that has not been fully replaced with factor (discuss with haematology).
Severe renal impairment. If **Creatinine clearance** is 15-30ml/min, use with caution. If there is evidence of acute renal failure use subcutaneous unfractionated heparin 5000 units BD.
Severe liver disease.
Past history of heparin induced thrombocytopenia (discuss with haematologist).
Disseminated intravascular coagulopathy (DIC)

Table 1 Contraindications to anticoagulation with Enoxaparin

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3.4 Mechanical Thromboprophylaxis

- Where pharmacological thromboprophylaxis is deemed unsafe, intermittent pneumatic compression (IPC) devices are recommended (ensure no contraindication).
- Combined IPC & enoxaparin thromboprophylaxis can be considered in very high-risk cases, these include women who have:
    - Significantly reduced mobility relative to their normal (anticipated to last >3days) post C-section, return to theatre or hysterectomy
    - Consider in Level 2 HDU cases (e.g. severe pre-eclampsia, massive obstetric haemorrhage)

Decision regarding providing combined IPC & enoxaparin thromboprophylaxis should befollowing MDT discussion between Obstetrics, Anaesthetics and Haematology, and documented in the maternal notes.

Anti-embolic stockings are not recommended.

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4 Deep Venous Thromboembolism (DVT) in Pregnancy: Investigation and Management

4.1 Signs and Symptoms of DVT

If a woman phones with unilateral leg pain or swelling suspect a DVT and arrange urgent clinical review via the emergency department.
Out of hours, provided there are no contraindications, and the circulation to the leg is not compromised, administer 1mg/kg Clexane bd and arrange review in the DVT clinic the next working day (referrals can be made electronically through e-Advice and communications: https://caveadcomm.cymru.nhs.uk/)

Early signs and symptoms of DVT may be subtle and may overlap with "normal" pregnancy symptoms. Consider the possibility of DVT in the presence of any one of the symptoms listed below, especially if the woman has a personal or family history of VTE or has been identified as needing thromboprophylaxis either during or following pregnancy

Consider DVT in a woman who has:

- Leg pain or discomfort, especially on the left side.
- Unilateral leg/calf swelling:
    - Measure the calves using a tape measure at a distance of 10 cm below the tibial tuberosity. A difference of >3 cm is significant (Wells PS, Anderson DR, Bormanis J et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. **Lancet**. 1997 Dec 20-27;350(9094):1795–1798).
- Increased temperature of the limb in the absence of infection.
- Unilateral leg oedema.
- Newly prominent superficial veins.
- Pain along the distribution of the deep veins (posterior calf compression, compression of the popliteal fossa, and compression along the inner anterior thigh from the groin to the adductor canal).
- The commonest site for DVT in pregnancy is iliofemoral, this may present with **pelvic/lower abdominal pain.**

  NB Thrombosis in the Inferior Vena Cava (IVC) may cause **bilatera**l leg swelling

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4.2 Differential Diagnosis of DVT

- Cellulitis.
- Large or ruptured Baker's cyst.
- Calf muscle or Achilles' tendon tear.
- Calf muscle haematoma – consider if history of trauma or woman using an anticoagulant
- Pelvic/thigh mass/tumour compressing venous outflow from the leg.

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4.3 Limb threatening DVT

Where a DVT threatens leg viability through venous gangrene, the leg should be elevated, anticoagulation given, and consideration given to surgical embolectomy or thrombolytic therapy. In this situation, advice should be sought **urgently** from the vascular surgical on

call team (Vascular SpR on call bleep 5208).

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4.4 DVT: Investigation and Management

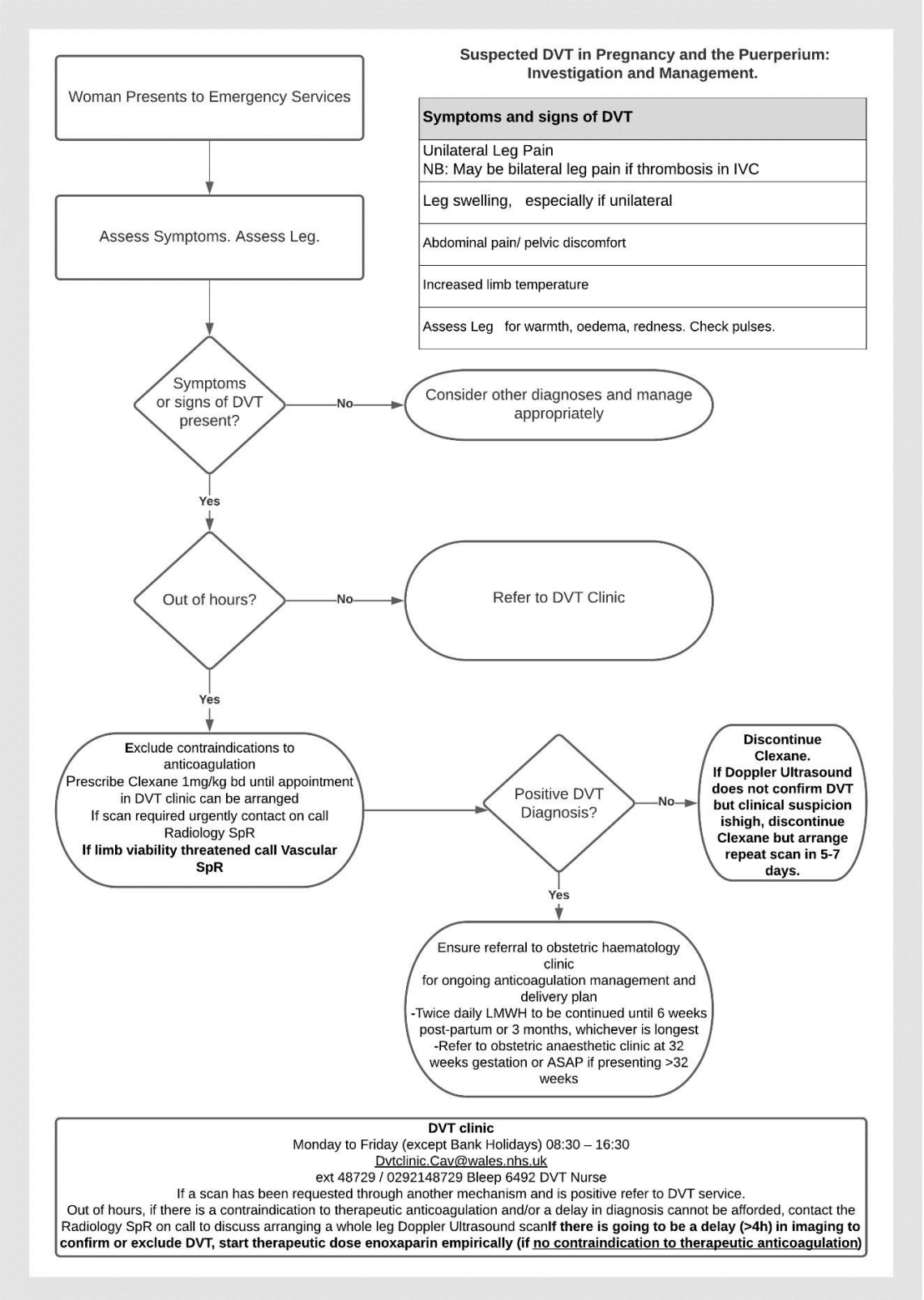

Figure 1DVT: Investigation and Management

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5 Superficial Vein Thrombophlebitis (SVT): Investigation and Management

Women may present with SVT in pregnancy. Treatment will prevent progression to DVT.

Figure on Next Page.

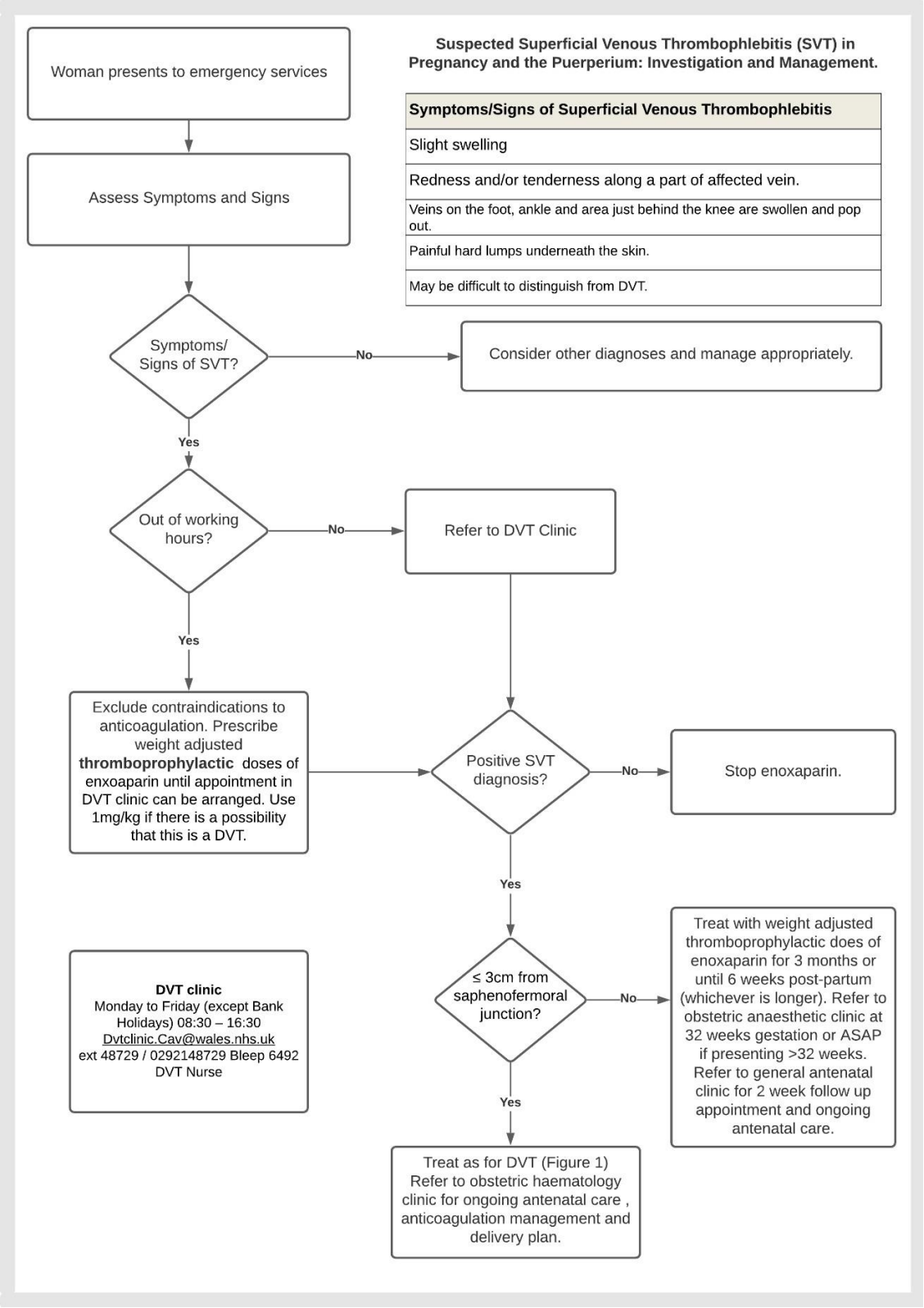

Figure 2 Investigation and Management of Superficial Venous Thrombophlebitis

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6 Pulmonary Embolism (PE) in Pregnancy: Investigations and Management

All women who report acute onset of breathlessness and/or pleuritic chest pain and/or haemoptysis should be reviewed by a physician with experience in managing pulmonary embolism. Women who contact the obstetric unit with symptoms of PE should be directed to the Emergency Department.

A woman who is 17⁺ weeks' gestation should be discussed with the obstetric team prior to discharge (Senior Reg bleep 6900).

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6.1 Signs and Symptoms of PE

The symptoms of PE may be subtle and overlap with normal changes that occur during pregnancy due progesterone, vasodilation and the gravid uterus.

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6.1.1 Symptoms of PE

Breathlessness – at rest or on exertion. Might be quite sudden in onset
Pleuritic chest pain – pain on inspiration or coughing
Haemoptysis
Collapse

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6.1.2 Clinical Assessment

- Full history considering the differential diagnoses (see Section 6.2) and looking for risk factors for VTE other than pregnancy (see Section 3.1).
- Full set of observations should be charted on a **Maternity Early Warning Score** chart, to take into account the normal ranges of pregnancy.
- Respiratory system examination, looking for signs of consolidation, pleural rub, absent air entry.
- Assess the lower limbs for clinical evidence of DVT (see Section 4.1). If present, follow pathway for the investigation and management of DVT.
- Oxygen saturation in air.
- **Do not use** the Pulmonary Embolism Severity Index (PESI) as a risk stratification tool as it is not validated in pregnancy ((Konstantinides & et al, 2019) (Royal College of Obstetricians and Gynaecologists, 2015)
- Check for past medical history of asthma, chronic lung disease or cardiac disease, any history of contrast allergy, history of or current renal impairment.

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6.1.2.1 Normal ranges in pregnancy

Observation	Range
Respiratory rate	11-20 breaths/min
Heart rate	50-100 beats/min
Systolic blood pressure	100-150 mmHg

Table 2 Maternity Early Warning Score: Normal Ranges of Observations in Pregnant Women

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6.2 Differential Diagnosis of PE

Respiratory causes	Cardiac causes	Other causes
Pneumonia	Pericarditis	Costochondritis
Bronchitis	Myocardial infarction	Panic disorder
Acute exacerbation of asthma	Acute exacerbation of congestive cardiac failure	Physiological breathlessness of pregnancy – increased sensitivity to PaCO2
Pneumothorax	Angina	Anaemia
Acute exacerbation of COPD	Cardiac tamponade	
Pulmonary hypertension		

Table 3 Differential Diagnosis of Pulmonary Embolism

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6.3 Investigation of suspected PE

All women require a CXR.

Both V/Q (pregnancy protocol) scans and CTPA are acceptable modes of imaging in pregnancy. They both have advantages and disadvantages:

The modality used for diagnosis of PE in pregnancy depends on the availability of each (V/Q scans are only available during normal working hours and may not be available each day), the choice of the woman and **thorough discussion with radiology (specific issues including any CXR abnormalities, past medical history of significant asthma, chronic lung or cardiac disease, history of contrast allergy and impaired renal function will affect decision of imaging modality).**

- The pregnant woman should be involved in the decision to undergo CTPA or V/Q scan and given patient information (RCOG 2015 '*Diagnosis and treatment of venous thrombosis in pregnancy and after birth*') in order to help her make an informed decision.
- Women with suspected PE should be advised that, compared with CTPA, V/Q scanning may carry a slight increased risk of childhood cancer but is associated with a lower risk of maternal breast cancer. They should be advised that in both cases, the risk is very small and that the risks of undiagnosed PE are much higher.
- The ventilation component of the V/Q lung scan is often be omitted during pregnancy, thereby minimising the radiation dose for the fetus (which is in any event small and not associated with a substantial increased risk of complications such as childhood cancer), especially if the X-ray is normal. In addition half dose perfusion agents are routinely used in Cardiff & Vale..
- Inform medical physics that the woman is pregnant in order to provide correct radioisotope and perfusion scan protocol. This is different to the usual VQ perfusion scan protocol and has been designed to result in the lowest radiation possible.
- After a V/Q scan, a lactating mother should be advised to express and discard her milk for 7 hours to avoid giving her child milk contaminated with radio isotope. If women have a CTPA there are no issues with breastfeeding immediately- please ensure this is discussed with all postpartum women.

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6.3.1 CTPA vs V/Q scan: advantages and disadvantages

Advantages of CTPA	Advantages of VQ scan
Better sensitivity and specificity	Lower radiation dose to the maternal breasts (CTPA increases the lifetime risk of developing breast cancer from a background risk of 1/200 to 1/176 in women who had a CTPA in pregnancy) - an increase of a factor of 1.0003 - 1.0007 [ESC 2019]
Lower radiation dose to the fetus (increased risk of childhood cancer of approximately 1:170,000 for CTPA vs 1:34,000 for V/Q scan) [RCOG 2015]	May identify small peripheral PE not visualised on CTPA
Can identify other pathology, such as pneumonia, pulmonary oedema, aortic dissection	High negative predictive value

Table 4 CTPA vs V/Q scan: Advantages vs Disadvantages

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6.3.2 Further investigations if PE is suspected/ diagnosed

- ECG – to assess for right heart strain.
- Arterial blood gases.
- Troponin
- Consider ECHO if evidence of right heart strain on CTPA or in scenario of haemodynamic collapse
- When the PE is diagnosed by V/Q scan, request an ECHO where there are abnormal clinical parameters of sats/BP/heart rate, thought to be caused by the PE.

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6.4 Suspected Pulmonary Embolus (PE): Investigation and Management.

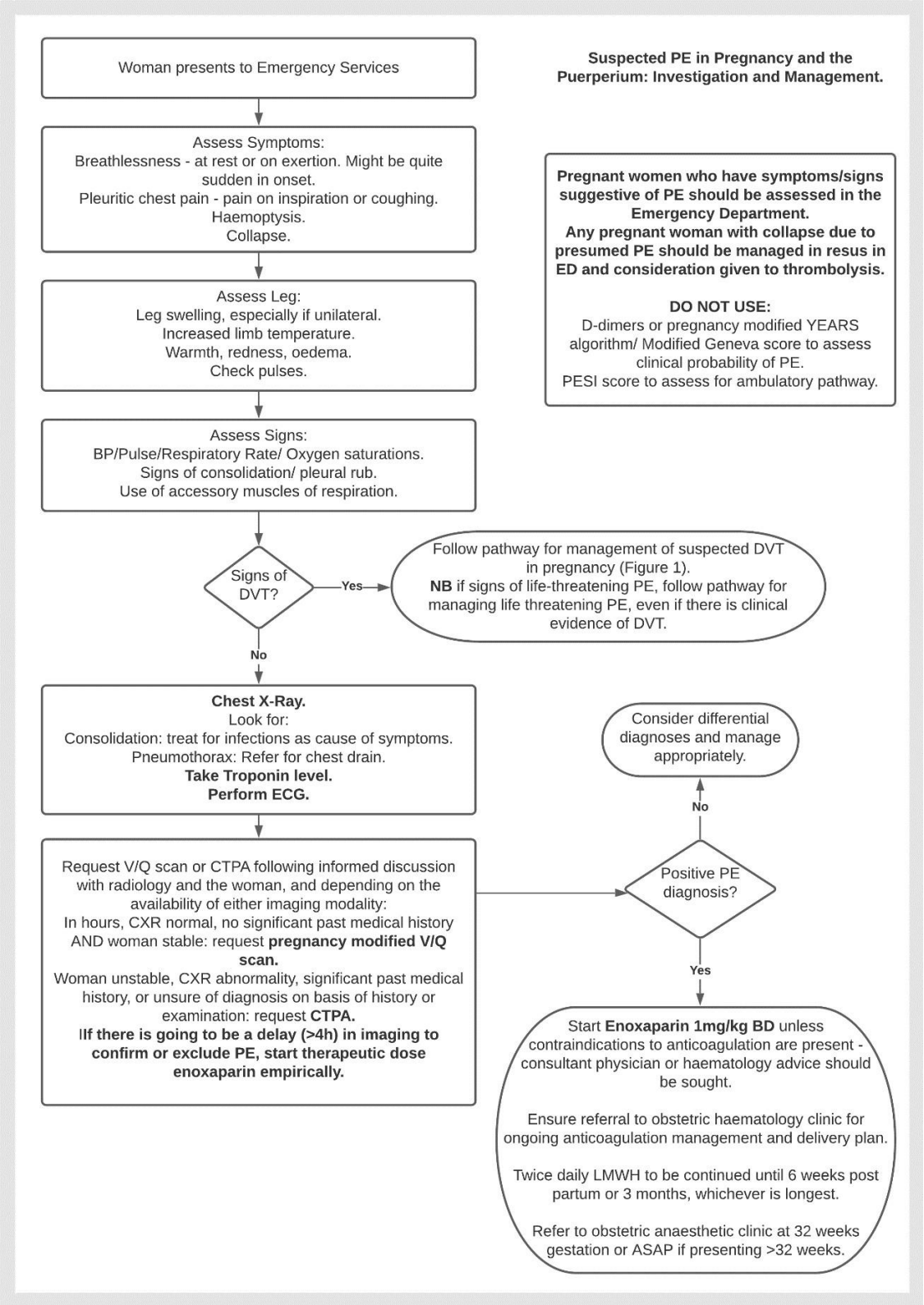

Figure 3 PE: Investigation and Management

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7 Management of Venous Thromboembolism (VTE) – PE and DVT

All pregnant and postpartum women presenting with suspected or confirmed PE should be reviewed by a consultant in emergency medicine prior to discharge. If no consultant is available, then a senior clinician should perform the review – (ST4 or above). The on-call senior O&G SpR on 6900 should be informed.

- All women with diagnosed VTE should be referred to the next available Obstetric Haematology Clinic. These run every Tuesday afternoon.
  If a woman develops a DVT/PE at or beyond 34 weeks' gestation, please contact the Haemostasis & Thrombosis registrar on bleep 5886 09:00 – 17:00 Monday to Friday or the Haematology registrar on call via Switchboard for out of hours for advice with regard to the need for an IVC filter. Alternatively contact the consultant on call for haemostasis via switchboard.

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7.1 Referral to Obstetric Haematology Clinic

Contact the on-call Obstetric Senior Registrar (bleep 6900, or via delivery suite x42686). The obstetric SR will liaise with antenatal clinic in working hours to generate an appointment for the woman. An appointment letter will be sent to the woman at her home address.

Please ensure hospital records have an up-to-date address and contact telephone number for the woman. If she has not received an appointment letter within 7 days, advise her to contact the antenatal clinic (numbers are in her maternity record).

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7.2 Anticoagulation: Low Molecular Weight Heparin (LMWH)

7.2.1 Prescribing advice

- Mandatory blood tests to perform prior to starting heparin therapy (either LMWH or UFH):
  - Full blood count (FBC) and coagulation screen.
  - Renal function tests (U&E's) and liver function tests (LFT's).
- **Thrombophilia testing should not be performed**.

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7.2.2 Therapeutic Low Molecular Weight Heparin (LMWH)

In the majority of women the dose of LMWH can be calculated using the eGFR, which is supplied with urea + electrolytes + Creatinine. The eGFR may be affected by acute illness and if the eGFR is significantly reduced then the prescriber should ensure the calculated creatinine clearance is >30mL/min Creatinine Clearance Calculator

Cockroft-Gault Formula for Estimating Creatinine Clearance (CrCl)

$$\text{CrCl (mL/min)} = \frac{\text{N x (140 - age) x weight (Kg)}}{\text{Serum Creatinine (µmol/L)}}$$

N = x 1.04 if female; x 1.23 if male

Figure 4 Cockroft-Gault Formula for Estimating Creatinine Clearance.

- Ensure that there are no contraindications to therapeutic anticoagulation

Prescribe **1mg/kg of Enoxaparin twice daily, round to the nearest measurable dose vial see suggestion below: Early pregnancy weight**	**Initial* dose of Enoxaparin**
<50kg	40mg twice daily
50-69kg	60mg twice daily
70-89kg	80mg twice daily
>90kg	100mg twice daily

Table 5 Therapeutic Dose Enoxaparin

- Women should be taught how to self-inject wherever possible. It is important to rotate the injection sites. Pregnant women may collect their enoxaparin and attend Antenatal Day Assessment Unit the next day (Mon – Friday 9-5) to see a midwife to be taught how to self-inject. Sat/Sun – attend Obstetric Assessment Unit.
- Please contact day assessment unit (DAU) on ext.42207 or out of hours the obstetric assessment unit (OAU) on ext. 42635 to inform them the woman will be attending the following day.
- Women should be provided with a yellow sharps bin to allow safe disposal of the needles.

Twice daily Enoxaparin is preferred. If the woman is struggling with this and more than 6 weeks' anticoagulation has been given, then 1.5mg/kg Enoxaparin once daily can be considered for the remainder of the treatment. This should only be done through the obstetric haematology clinic

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7.2.3 Monitoring therapeutic LMWH/Enoxaparin

- Prolonged monitoring of Enoxaparin is not required and should only be done on the advice of haematology
- All women diagnosed with VTE in pregnancy should be referred to the next available Obstetric Haematology Clinic for ongoing care.

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7.2.4 Risks of Enoxaparin/ LMWH

- As contrasted with unfractionated heparin, long-term use of LMWHs is associated with a lower risk of osteoporosis and bone fractures.
- Occasionally, women may develop haemorrhage, hyperkalaemia or an allergic rash.
- Heparin- induced thrombocytopenia (HIT) is extremely rare in pregnancy and with LMWH.
- Care should be taken with women with long term diabetes, chronic renal failure and metabolic disorders.

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7.3 Anticoagulation: Therapeutic intravenous unfractionated heparin (UFH)

- UFH may be indicated to bridge the delivery of a very high-risk woman – e.g. mechanical heart valve – this will be planned through the antenatal clinic team.

Please use the Trust protocol prescription to start UFH and for dose adjustment: available from pharmacy.

- Use patient's early pregnancy weight to dose.
- APTT ratio must be checked at least daily.
- Platelet count should be checked at least every other day.
- Suspect heparin induced thrombocytopenia (HIT) if there is a significant fall in platelet count. A fall of 50% is considered significant even if the platelet count remains in the normal range. Please consider HIT particularly if the fall in platelet count is in addition to new venous or arterial thrombotic events. If you suspect HIT, please contact the Haemostasis & Thrombosis registrar on bleep 5886 09:00 – 17:00 Monday to Friday or the Haematology registrar on call via Switchboard out of hours for advice.
- In late pregnancy it may be difficult to prolong the APTT with unfractionated heparin due to increased levels of factor VIII and fibrinogen and monitoring with an anti-Xa assay is required (target range 0.3-0.7iu/ml). If you are struggling to achieve a therapeutic anti-Xa level, please contact the Haemostasis & Thrombosis registrar on bleep 5886 09:00 – 17:00 Monday to Friday or the Haematology registrar on call via Switchboard out of hours for advice.

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7.4 Inferior Vena Cava (IVC) filters

- A temporary IVC filter may be required in women with recurrent PE despite satisfactory anticoagulation or in situations where anticoagulation is contra-indicated.
- It is also important to consider a filter if a large, proximal clot is diagnosed close to delivery or if there is a recurrent clot.
- If you think your patient may require an IVC filter please contact the Haemostasis & Thrombosis registrar on bleep 5886 09:00 – 17:00 Monday to Friday or the Haematology registrar on call via Switchboard out of hours for advice. The decision to place an IVC filter will require the involvement of the Haematologists, Obstetricians and Interventional Radiologists.
- It should be remembered that IVC filters have their own risks, and liaison with a senior radiologist, haematologist and obstetrician is needed with clear counselling of these risks to the woman.

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8 Life threatening Pulmonary Embolism (PE)

8.1 Risk stratification in confirmed PE

- Once a diagnosis of PE has been confirmed all women should be assessed looking for features that are associated with an increased risk of PE related mortality (severity assessment).
- Do not use the Pulmonary Embolism Severity Index (PESI) as a risk stratification tool as it is NOT validated in pregnancy (Konstantinides & et al, 2019) (Royal College of Obstetricians and Gynaecologists, 2015).
- PE can be categorised as low, intermediate or high risk based on the presence of haemodynamic instability and the presence or absence of right ventricular (RV) dysfunction and cardiac biomarkers (Troponin). The presence or absence of RV dysfunction should be reported on every CTPA. If a VQ scan has been the imaging modality then an echocardiogram will be required (urgent echocardiograms can be arranged via the cardiology SpR on call – bleep 5770).
- In cases of suspected high risk/ massive PE the on-call medical and cardiology SpR's (to perform echo) will assess the with a view to thrombolysis.
- The presence of life-threatening (high risk) PE is defined by haemodynamic compromise (Table 6) and is an indication for consideration of thrombolysis. The risks/benefits of thrombolysis will need to be made on an individual basis with MDT decision including on-call obstetric consultant. Complications of thrombolysis during pregnancy include the risk of major bleeding (risk highest in those thrombolysed in the post-partum period) and the risk of pregnancy loss (approx.12%). Thrombolytic agents do not cross the placenta. Alternative catheter-based treatments are now available at UHW for the treatment of hemodynamically significant PE, but their consideration should not delay the administration of systemic thrombolysis in patients who are deemed safe to have it and who meet the criteria. In patients with a contraindication to lysis, an emergency review should be requested via the on-call cardiology registrar bleep 5770.

Cardiac Arrest	**Obstructive shock**	**Persistent Hypotension**
Need for cardiopulmonary resuscitation	Systolic BP <90mmHg **OR**	Systolic BP <90mm Hg **OR**
	Vasopressors required to achieve a BP >90mmHg despite adequate filling status **AND**	Systolic BP drop >40mmHg, lasting longer than 15mins and not caused by new-onset arrhythmia, hypovolaemia of sepsis
	End organ hypoperfusion (altered mental status; cold, clammy skin; oliguria; increased serum lactate	

Table 6 Recognition of haemodynamic instability associated with high risk PE

- The presence of minor RV dysfunction on CTPA or echo is a relatively common finding however increasing RV dilatation is associated with worse prognosis. If RV dysfunction is identified on CTPA (or echo) then a serum cardiac troponin should be requested.
- The presence of RV dysfunction AND an elevated troponin is considered an

'intermediate-high' risk PE and women should be closely monitored, consideration may be given to the use of catheter directed thrombolysis

- If only the RV or only the troponin (i.e. not both) is abnormal, patients are deemed 'intermediate-low risk'. These women would usually be monitored in hospital for at least 24h.
- If there are no signs of either RV dysfunction or troponin elevation, then the PE is considered low risk. There are no studies of ambulatory treatment in pregnancy.

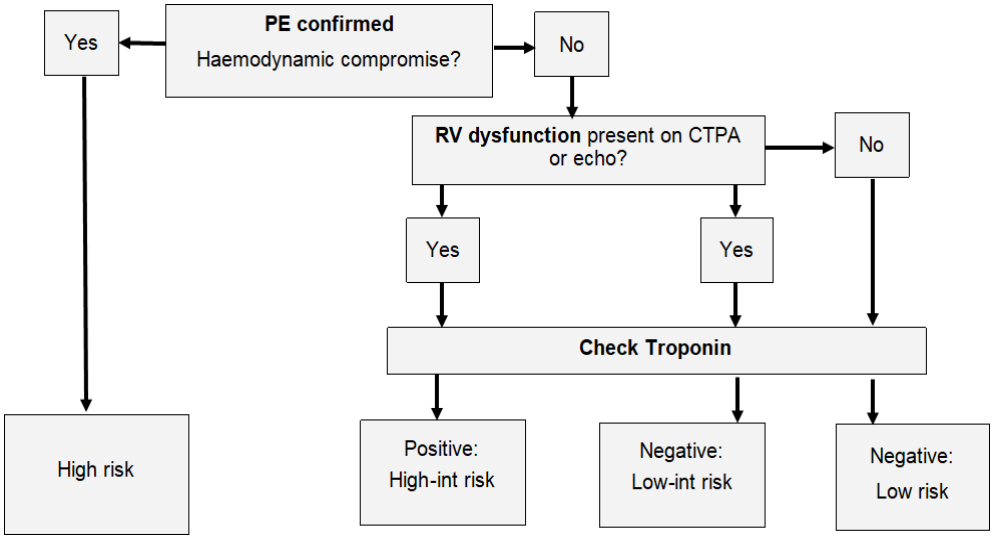

Figure 5 Risk stratification of PE.

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8.2 Catheter directed therapies – low dose thrombolysis and/or aspiration thrombectomy.

- Please ensure all patients considered for CDT are discussed with on-call consultant obstetrician with an MDT plan for monitoring, admission ward & obstetric review.
- Catheter-directed treatments for large volume pulmonary embolism are now available at UHW for the treatment of pregnant and post-partum patients via the cardiology team. There are currently two technologies available with more to come in early 2021. All utilise the femoral vein to access the pulmonary arteries.
- The first is aspiration thrombectomy with the Penumbra device. This has the advantage of offering treatment for large volume central pulmonary embolism without the need for thrombolytics.
- The second technology is Ekos catheter-directed thrombolysis, which can offload right ventricular strain with as little as 8mg of alteplase, as opposed to the 100mg systemic dose used in normal bodyweight adults.
- Both devices require ionising radiation to guide treatment, though the entire treatment can be done under low dose fluoroscopy, so pregnant mothers can have lead shielding of their abdomens and sustain a relatively low dose for an interventional procedure. Nevertheless, ionising radiation does carry risk to the foetus, though the dose will typically be lower than that of a CTPA
- There are two categories of patients who may require this treatment:
    - Those with signs of RV strain (on a CTPA or an echocardiogram) but a preserved systolic blood pressure of over 90mmHg (so-called 'intermediate-risk', aka 'sub-massive' PE patients)
    - Those in shock, with a systolic BP less than 90mmHg, should be first considered for systemic IV thrombolysis (so-called 'high-risk', aka 'massive' PE). If the

patient has a very high bleeding risk, catheter treatments could be considered on a compassionate emergency basis, but such patients would clearly require immediate discussion given the high risk of imminent death.

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8.2.1 Who are the best candidates for CDT in the intermediate-high risk (sub-massive) PE group?

- In a post hoc analysis of the PEITHO study of systemic thrombolysis for sub-massive PE in adults (all patients had a starting SBP>90mmHg and RV strain), the following presenting clinical parameters were most likely to be associated with subsequent decompensation or death on a heparin-based strategy:
  - Patients with a relatively low BP (90-110 systolic)
  - Patients with a raised respiratory rate (>20 despite oxygen supplementation)
  - Patients with a history of congestive cardiac failure
- If patients had two of more of the above three criteria, the chances of death or haemodynamic collapse at 7 days were 20% when anticoagulation was used as the treatment strategy and so consideration of CDT in those patients may be reasonable.
- Patients with sustained tachycardia (>100 bpm) are also considered a fourth criteria, although may not be so clearly defined in a pregnant woman.
  However, if two of those four criteria are present in a patient with large volume PE, consideration should be given to a discussion with the cardiology team (via the cardiology registrar on bleep 5770) so that an echocardiogram can be obtained, and the CT can be reviewed for suitability for catheter-directed treatments. This should be discussed and confirmed with the senior obstetric team.

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8.2.2 What are the risks of CDT?

- The risks and estimated frequency of risk (in percentages) are detailed below:
  - Femoral venous access in anticoagulated patients:
    - Bruising: 10%
    - Bleeding requiring transfusion or surgery: 1-2%
  - Thrombolytic agents (where used) – whilst lower doses are used in CDT, the risk of the following remain:
    - Intracranial bleeding (stroke) <1%
    - Internal bleeding requiring blood transfusions: <5%
    - Damage to blood vessels from equipment, requiring major surgery: <1%
    - Damage to the heart or lungs from equipment, requiring major surgery: <1%
    - Need for conversion of strategy to full-dose systemic thrombolysis due to deterioration of patient's clinical condition: <3%
    - Damage to the foetus of a pregnant mother – published data unavailable

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8.2.3 I have a patient who may benefit from CDT. What do I do?

- Discuss with senior obstetrician (on-call consultant), bleep the cardiology registrar on 5770 and ask to speak to a member of the cardiology medical team regarding the possibility of CDT.
- If your patient is shock and has an absolute contraindication to systemic thrombolysis, ring the cardiology registrar and ensure they understand that the patient is in shock and needs emergency management.

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8.3 Surgical Embolectomy and ECMO

- In situations of life-threatening PE there is some evidence for both surgical embolectomy and extra corporeal membrane oxygenation (ECMO), though such indications typically require very early intervention. If UHW becomes an ECMO centre, then VA ECMO may have a role in patients with haemodynamic collapse.

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9 Management of Enoxaparin during labour

9.1 General Principles

General principles for management of women taking therapeutic enoxaparin during pregnancy include:

- Omit enoxaparin and contact the hospital at the first signs of spontaneous labour.
- Planned omission of enoxaparin if labour is to be induced or for elective caesarean section (as advised by the Obstetric Haematology Clinic Plan available in Letters section on CAV Portal).
- Check FBC, clotting screen and group and save on admission and ensure intravenous access.
- Inform the obstetric anaesthetist when the woman is admitted.
- Monitor carefully for excessive bleeding.
- Hydration should be maintained throughout labour.
- Active management of 3rd stage of labour. Consider prophylactic syntocinon infusion 40 units over 4 hours.
- Any perineal tear/ trauma should be repaired as soon as possible with close attention to haemostasis.
- Monitor carefully for postpartum haemorrhage.
- Anticoagulation should only be recommenced postnatally when haemostasis is secure; this decision should be made by a doctor (O&G registrar or consultant).
- If the patient has had a Caesarean section (C-section) there is a risk of wound haematoma. If it is a planned C-section then please follow the plan from the Obstetric Haematology Clinic review (available on CAV Portal in Letters section). If it is an emergency C-section please contact the Haemostasis & Thrombosis registrar on bleep 5886 09:00 – 17:00 Monday to Friday or the Haematology registrar on call via Switchboard out of hours for advice.

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9.2 Epidural and Spinal Anaesthesia

- Spinal/epidural anaesthesia - should be avoided for at least 24h from the last dose of therapeutic Enoxaparin.
- Spinal/epidural anaesthesia should be avoided for at least 12h from the last dose of prophylactic Enoxaparin
- Enoxaparin should not be given for at least 6h after the epidural catheter has been removed.
- All women on therapeutic anticoagulation and those on prophylaxis with complicating circumstances should be reviewed in the combined Obstetric Haematology Antenatal Clinic.
- All women on either therapeutic or prophylactic anticoagulation should be booked to see the obstetric anaesthetist at 32 weeks gestation.
- Always inform the on-call consultant anaesthetist when a pregnant woman on anticoagulation therapy is admitted in labour or with antenatal complications likely to result in imminent delivery.
- Full anticoagulation is a contraindication to spinal or epidural anaesthesia.
- There is a risk of spinal haematoma when an epidural is inserted or removed. Early diagnosis improves outcome. To minimise the risk, the following guideline should be followed:

Patient Group	Action
Intravenous unfractionated heparin	Stop infusion for 2 hours Check APTT ratio If APTT normal proceed to epidural insertion

"Low risk"/ "intermediate risk" prophylactic LMWH (20-40mg OD)	Ensure a delay of 12 hours from the last dose before inserting or removing an epidural.
Therapeutic dose LMWH (above 40mg BD)	Ensure a delay of 24 hours from the last dose before inserting or removing an epidural.

Table 7 Guidelines for reducing risk of spinal haematoma in women on prophylactic or therapeutic anticoagulation who require an epidural.

- Heparin, including enoxaparin, should not be given for at least 6 hours following the removal of an epidural catheter.
- These times are a guide and a risk benefit ratio assessment regarding regional or general anaesthesia should be made for each individual patient dependent on the specific clinical circumstances.

NB: Renal impairment:
LMWH (such as enoxaparin) is cleared more slowly and the above recommended times may not be sufficient. Discuss with haematologist and perform an urgent anti-Xa level prior to insertion or removal of an epidural.

- If an epidural must be removed before these times have elapsed or falls out accidentally then documented regular assessment of changes in either motor or sensory function is recommended to ensure that a spinal haematoma is detected early. In addition, it is noted that deep-seated back pain may be a symptom of a spinal haematoma.

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10 Management of miscarriage, termination of pregnancy, ectopic pregnancy and pregnancy of unknown location (PUL) for women who have a recent diagnosis of venous thrombosis.

The management of miscarriage or planned termination (medical or surgical) will depend on the clinical situation and gestation as well as the time since the diagnosis of the acute VTE. The management will involve a senior O&G consultant, Haematology consultant and the patient.
These women should be considered as high risk. Therefore, for elective procedures these should be performed within normal working hours.

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11 Discharge

- Anticoagulant therapy should be continued for 6 weeks post-partum, or until at least 6 months of therapy for PE or 3 months of therapy for DVT has been completed, whichever is longer.
- Warfarin may be commenced on the 2nd post-partum day. Continue LMWH until the INR is greater than 2.0 on two consecutive days and to a minimum of 5 days (whichever is longest). Commence 5mg warfarin daily and titrate the dose according to the INR.
- **Breast feeding:**
  Warfarin and heparin are safe to give whilst a woman is breastfeeding. Direct oral anticoagulants (DOACs) including Apixaban, Rivaroxaban, Edoxaban and Dabigitran are not safe whilst a woman is breast feeding.
- **Bottle feeding:**
  Apixaban is the recommended anticoagulant for a woman who is no longer breast feeding **since it causes less problems with menorrhagia.**
- A woman who has been diagnosed with a PE should be referred to the Respiratory team for outpatient follow-up to assess for long term respiratory complications such as pulmonary hypertension. This would normally be done at the time of PE diagnosis. However, it should be done prior to discharge from maternity services, at the latest.
- It may be appropriate to investigate some women further for causes other than pregnancy that may have contributed towards VTE development (such as antiphospholipid syndrome). Such patients will be identified at the joint obstetric-haematology clinic and follow up investigations arranged following delivery.
- **Women should be advised regarding contraception and told to avoid oestrogen containing contraceptives. Progesterone only contraception is acceptable.**
- Women should be counselled regarding the need to cover all future pregnancies with thromboprophylaxis.

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12 Auditable Standards

1. All women to have an antenatal VTE risk assessment completed and filed in their maternity notes at booking: 100%
2. All antenatal admissions to have an antenatal VTE risk assessment completed and filed in their maternity notes: 100%
3. All women to have a postnatal VTE risk assessment completed and filed in the maternity notes after delivery, regardless of site of delivery: 100%

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