Nottingham University Hospitals NHS Trust

Guideline Number & Full Title:	1096 - Guideline for the Management of Acute Thromboembolism in Pregnancy and the Puerperium
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Division & Specialty:	Family Health (Obstetrics)
Version:	8
Ratified by:	Haemostasis and thrombosis governance
Consultation:	"Discussed/circulate and ratified by Haemostasis and thrombosis governance Maternity governance Medicine governance"
Scope *(Target audience, state if Trust wide):*	Doctors, midwives, nurses in acute medical and obstetric admissions areas
Review date *(when this version goes out of date):*	October 2028
Explicit definition of patient group to which it applies *(e.g. inclusion and exclusion criteria, diagnosis):*	Women with suspected or confirmed thromboembolism who are currently or recently pregnant
Changes from previous version *(not applicable if this is a new guideline, enter below if extensive):*	Document describes the new VTE diagnostic pathway via AMRA and new VTE follow up referral pathway on careflow Amended 23.12.24 to remove preference for VQ over CTPA pending discussion with radiology
NICE guidance reference:	NG158
Summary of evidence base this guideline has been created from: (other than NICE)	RCOG 37b, NICE NG158, British Thoracic Society Guidelines for the management of PE
This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.	

Introduction

Venous thrombo-embolic events (VTE) occur in approximately 1 -2 per 1000 women during pregnancy and the postnatal period. VTE can occur at any stage in pregnancy but the postnatal period is the time of highest risk.

VTE remains one of the main direct causes of maternal death in the UK, occurring in 1.6 (0.10 – 1.24) per 100,000 maternities in 2019 – 2021. Sequential reports on Confidential Enquiries into Maternal Deaths have highlighted failures in obtaining objective diagnoses and employing adequate treatment as contributory problems (MMBRACE 2023).

This guideline outlines the investigation and management of VTE in pregnancy. It is based on clinical evidence where available however much data is extrapolated from the non-pregnant, male population; this should be borne in mind.

Reference should be made to other clinical guidelines available at NUH

- Guideline on the management of pulmonary embolism (PE Pathway) https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=992367a7649c000fd759275a91dcb548

- Pulmonary emboli; guidelines for imaging

  https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=9abf7bca7093b371780af103656b24a7

- Guideline for the management of ultrasound proven superficial vein thrombosis (superficial thrombophlebitis) of the lower limb https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=ba1ae377ccb53d94fd95966f79afaa5a

- Epidural anaesthesia for operative interventions in obstetrics https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=6193eb31956e4a675a812cf7e908e39e

- Thromboprophylaxis in pregnancy https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=a2987e4e7a3c86b884705e51bba0bf18

This guideline applies to women up to six weeks postnatal and over-rides the medical guideline for the management of DVT/PE, as pregnancy and the puerperium are times of exceptional risk

Guideline

1. Presentation with suspected DVT/PE (Flowchart 1 and 2)

Clinical diagnosis of VTE is unreliable. Recent local data (NUH) shows that approximately 1% of women with clinically suspected VTE in pregnancy have the diagnosis confirmed when objective testing is employed. This is similar to the reported literature. Symptoms include;

Deep Vein Thrombosis

- Leg pain (or discomfort)
- Swelling – usually unilateral– especially the left leg
- Lower abdominal, back or groin pain may be a feature of an iliofemoral DVT

Pulmonary Embolus

- Pleuritic chest pain
- Breathlessness
- Haemoptysis
- Tachycardia
- Collapse
- Faintness
- Raised JVP
- Symptoms and signs associated with DVT

- Initial approach to women who contact the maternity advice line (MAL) with suspected DVT/PE is described in the SOP (see appendix 1)
- Any woman with signs and symptoms suggestive of DVT or PE should have objective testing as soon as possible and commenced on treatment dose low-molecular-weight heparin (LMWH) until the diagnosis is excluded
- The LMWH used at NUH is Enoxaparin (brand names Clexane, Inhixa, Arovi) however the term LMWH will be used throughout this guideline to recognise that some women take alternative preparations
- Treatment with LMWH should be started immediately on suspicion of VTE, unless there is a contraindication including (but not limited to)
    - Active bleeding
    - Imminent labour
    - renal failure

  If treatment is contraindicated, discuss immediately with a consultant obstetrician
- Patients who are more than 36 weeks gestation require admission and should be discussed with consultant obstetrician and haematologist

2. Diagnostic testing

Women presenting with symptoms and/or signs suggestive of VTE should have objective testing performed as soon as possible. If DVT remains untreated, 15–24% of these patients will develop PE. PE during pregnancy may be fatal in almost 15% of patients.

If a diagnosis of VTE is excluded, review and consideration of alternative causes of symptoms must be undertaken

2.1. Blood tests

- Blood should be sent at presentation for FBC, clotting screen, Urea and electrolytes (U&E) and liver function tests (LFTs)
- D-dimers are raised in normal pregnancy and cannot reliably exclude VTE; testing should not be performed
- Thrombophilia testing should not be performed in the acute setting as it has no impact on the immediate management of acute VTE

2.2. Imaging for DVT

- Compression duplex ultrasound (USS) should be undertaken where there is clinical suspicion of DVT or when there are signs and symptoms of DVT in women with suspected PE
- If ultrasound is negative and there is a low level of clinical suspicion treatment dose LMWH can be stopped.
- If ultrasound is negative and a high level of clinical suspicion exists, continue treatment dose LMWH and seek advice
  - Discuss first with radiology regarding further imaging
  - Refer to obstetric haematology team for advice (contact haematology ST on call phone via switchboard)

2.3. Imaging for PE

- Additional guidance is available in the NUH PE Pathway here https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=992367a7649c000fd759275a91dcb548
- All women should have an electrocardiogram (ECG) and a chest X-ray (CXR) performed at presentation
- Women who also have symptoms and signs of DVT should have compression duplex USS performed as the initial investigation
- If USS confirms the presence of DVT, no further investigation is necessary and treatment for VTE should continue.
- Women *without symptoms and signs of DVT* should have a ventilation/perfusion (V/Q) lung scan or a computerised tomography pulmonary angiogram (CTPA)
  - If the CxR is abnormal CTPA should be performed in preference to a V/Q scan
- Where V/Q scan or CTPA is normal but the clinical suspicion of PE remains.
  - Anticoagulant treatment should be continued until PE is definitively excluded
  - Discuss with radiology regarding further imaging
  - Refer to obstetric haematology team for advice (contact haematology ST on call phone via switchboard)

- Women should be counselled about imaging for PE in pregnancy and provided with a written information leaflet (available on badgernet)

3. Management of high risk PE in pregnancy

The on-call medical team and obstetric consultant should be contacted immediately.

Investigation and treatment of suspected acute PE in pregnancy, including massive PE is detailed in the NUH PE guidelines https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=992367a7649c000fd759275a91dcb548

- Collapsed, shocked patients must be assessed by a team of experienced clinicians, including the on- call consultant obstetrician and anaesthetist, who should decide the most appropriate treatment on an individual basis
- Maternal resuscitation should commence following the principles of ABC and if cardiac arrest occurs, cardiopulmonary resuscitation should be performed with the woman in a left lateral tilt.
- A perimortem caesarean section should be performed by 5 minutes if resuscitation is unsuccessful and the pregnancy is more than 20 weeks.

- An urgent portable echocardiogram or CTPA within 1 hour of presentation should be arranged (if stable enough); if high risk PE is confirmed or, in extreme circumstances prior to confirmation, immediate thrombolysis should be considered.
- IV UFH is the preferred treatment in high risk PE because of its rapid effect and extensive experience of its use in this situation.
- In high risk life-threatening PE with haemodynamic compromise thrombolytic therapy should be considered as anticoagulant therapy alone will not reduce the obstruction in the circulation
    - This should be with alteplase in pregnancy with dosing as per the NUH PE pathway (using current weight)

  Pregnancy is NOT a contraindication for Thrombolysis

- After thrombolytic therapy has been given, an infusion of IV UFH can be given
    - The loading dose should be given as per this policy
    - The starting rate is 1ml/hour (NOT based on weight) and then the rate is adjusted as per APTT after 4-6 hours
- IV UFH should be dosed and monitored following the NUH heparin prescription chart
- APTT monitoring of IV UFH can be problematic in late pregnancy due to increased fibrinogen and factor VIII. These influence the APTT and may lead to unnecessarily high doses of heparin being used with subsequent haemorrhagic problems.
    - Anti Xa monitoring may be required for some women and will be guided by discussions with haematology
    - With UFH a lower level of anti-Xa is considered therapeutic (target range 0.35–0.7 u/ml or 0.5–1.0 u/ml for patients with life-threatening PE)
- Patients who are managed according to the non-high-risk PE protocol and have received LMWH who subsequently deteriorate and need thrombolysis should be managed in accordance with the NUH PE pathway.

- After recovery of from the acute episode, women should be switched to Enoxaparin 1mg/kg BD; timing is individualised and should involve discussion with obstetric haematology
- Women should be cared for in an adult intensive care or medical high dependency area with daily consultant obstetric review
- A repeat ECHO should be performed before discharge from hospital
- Subsequent management and follow up is as described for DVT and non high risk PE below

4. Management of DVT and non-high risk PE

Patients who are more than 36 weeks gestation require admission and should be discussed with consultant obstetrician and haematologist

4.1. Treatment with LMWH

- Women with confirmed DVT and PE require treatment with LMWH
- Dosing of enoxaparin in pregnancy is described in appendix 2.
- LMWH should be given in doses titrated against the woman's current weight
  - LMWH dose should be rounded to the nearest syringe size
  - Do not instruct patients to squirt dose out of the syringe
- Women should be shown how to self inject LMWH and given an information leaflet on Enoxaparin During Pregnancy. This can be found on Badgernet.
- Vitamin K antagonists, such as warfarin should not be used to treat antenatal VTE unless specifically directed by an obstetric haematologist
- Direct oral anticoagulants (DOAC) should not be used in pregnancy

4.2. Monitoring of LMWH

Monitoring is not required for most patients

- Routine measurement of peak anti-Xa activity is not recommended except in women who have
  - Antithrombin deficiency (these women should be managed in the obstetric haematology clinic)
  - Renal impairment (creat clearance <30 ml/min) should be discuss with the ward pharmacist
  - As described previously, it may be required for some women being treated with IV UFH
- Routine platelet count monitoring is not recommended for women taking LMWH
- Obstetric patients who are postoperative and receiving UFH should have platelet count monitoring performed every 2–3 days from days 4 to 14 or until heparin is stopped. This is due to the risk of heparin induced thrombocytopenia (HIT) associated with UFH.

4.3. Dosing and Duration of anticoagulation

- Treatment with therapeutic doses of subcutaneous LMWH should be given throughout pregnancy and for at least 6 weeks postnatally to a minimum of 3 months treatment
- For most women, Enoxaparin will be continued at a dose of 1mg/kg BD however it may be possible to reduce this to a 1.5mg/kg once daily dose if the VTE occurred early in pregnancy and if sufficient anticoagulation has been given; this will be decided in the obstetric haematology clinic.
- Absolute treatment duration will be decided in the obstetric haematology clinic

4.4. Referral for ongoing management

- All women must be referred to the VTE outcome meeting (via careflow) and the obstetric haematology service ObstetricHaematologyService@nuh.nhs.uk
- All women must be seen in the obstetric anaesthetic clinic as they will be treated with therapeutic anticoagulation peri delivery

4.5. IVC filters

Temporary IVC filters may be considered for women with proximal (iliac vein) DVT who are anticipated to deliver within 2 weeks of diagnosis.
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

The admitting team should contact
- The on call interventional radiology ‘Consultant of the Day’ (COD) phone to discuss this
- The obstetric haematology team for advice (contact haematology ST on call phone via switchboard)

5. Management of labour and delivery

Timing or delivery will be individualised depending on the timing of thrombosis and the thrombotic risk of the woman.

All women who are diagnosed with a DVT or PE in pregnancy will be seen in the obstetric haematology clinic and by the obstetric anaesthetic team. An individualised delivery plan will be written; this will be uploaded to Badgernet, Notis and Careflow

General principles for management of women taking therapeutic enoxaparin during pregnancy and approaching delivery

- Women should be advised if they think they are in labour to stop LMWH and call MAL
- Where delivery is planned, either by elective caesarean section or induction of labour, LMWH treatment should be discontinued 24 hours prior to planned delivery
- Check FBC, clotting screen and group and save on admission and ensure IV access
- Inform the obstetric anaesthetist when the patient is admitted. See section 6 for more information on regional anaesthesia.

- Monitor carefully for excessive bleeding.
- Hydration and use of graduated compression stockings are recommended throughout labour.
- If a recent injection of therapeutic enoxaparin has been given, women should be advised to avoid pool birth. Labouring in the pool and getting out to deliver may be possible in some circumstances.
- For caesarean birth
  - Wound drains should be considered at caesarean section and skin incision should be closed with interrupted sutures to allow drainage of any haematoma
  - Meticulous haemostasis is important and peritoneal closure should be considered, as it aids earlier recognition of intra-abdominal bleeding
  - Consider pressure dressings

6. Regional anaesthetics

Women who are prescribed therapeutic anticoagulation must be referred to the obstetric anaesthetist antenatally (or during admission if admitted due to VTE in late pregnancy)

Guidelines for obstetric regional anaesthesia/analgesia should be consulted https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=6193eb31956e4a675a812cf7e908e39e

General principals;

- Regional analgesic techniques should not be undertaken until at least 24 hours after the last dose of therapeutic LMWH
- LMWH should not be given for 4 hours after the use of spinal anaesthesia or epidural catheter removal
- Epidural catheter should not be removed within 12 hours of the most recent injection.

7. Postnatal management

7.1. Immediate postnatal management

- Active management of 3rd stage of labour is advised
- Any perineal tear/ trauma should be repaired as soon as possible with close attention to haemostasis
- If tranexamic acid is clinically indicated, this can be used as it is not considered to be prothrombotic
- Women should be monitored for postpartum haemorrhage throughout admission
- Check FBC on day + 1 delivery
- Anticoagulation should only be recommenced postnatally when haemostasis is secure; this decision should be made by a Doctor
  - Individualised birth plans should be followed for anticoagulation management

7.2. Postpartum anticoagulation

- Women should be offered a choice of LMWH or oral anticoagulant for postnatal therapy
- Women should be advised that heparin and warfarin can be taken safely whilst breast feeding
    - Postpartum warfarin (if used) should be avoided until at least the fifth day and for longer in women at increased risk of postpartum haemorrhage; specific advice will be given in the individualised delivery plan
- Many women choose to stay just on LMWH during the puerperium, due to the difficulties in stabilising warfarin doses and the need for frequent blood tests.
- There is little evidence for direct oral anticoagulants (DOAC) in breastfeeding. It is thought that Rivaroxaban levels in breast milk are considerably below dose required for anticoagulation in the neonate (Lactmed) and this would be the preferred DOAC,
    - If used we advise switching only after initial lochia has settled due to the risk of increasing PV losses
- Treatment dose anticoagulation therapy should be given for at least 6 weeks postnatally and until at least 3 months of treatment has been given in total
    - The risks of thrombosis must be reviewed before stopping anticoagulation
    - Absolute duration will be decided in the obstetric haematology clinic

7.3. Discharge advice

- Women should be referred to the obstetric haematology clinic for a postnatal appointment 2-3 weeks postnatally
    - This appointment should be made by contacting the ANC administration tea, and details given to the women before she is discharged from hospital
    - The obstetric haematology clinics run at both QMC and City; please ensure referral is sent to the site of antenatal management
- 4 weeks or anticoagulation treatment must be provided in the TTO medication
- Women should be advised to monitor postnatal blood loss and to contact MAL if they have any concerns about heavy or abnormal bleeding

7.4. Diagnosis of DVT or PE in the postnatal period (up to 6 weeks postnatally)

- Women who are diagnosed with DVT and PE in the postnatal period should follow the same guidance as described above.
- Women should be offered a choice of LMWH or oral anticoagulant for postnatal therapy as described in section 7.2
- It should however be noted that the therapeutic dose of enoxaparin in the non pregnant population is 1.5mg/kg once daily
- Women should be referred to the obstetric haematology team for follow up by referral to the VTE follow up pathway on careflow

8. Management of miscarriage or termination of pregnancy for women who have a recent diagnosis of VTE

8.1. Miscarriage and termination of pregnancy <15 weeks gestation

- Women with recent DVT or PE requesting termination of pregnancy should be discussed with the obstetric haematology team for advice**.**
    - We recognise the local service provision for planned termination is an external provider (British Pregnancy Advisory Service, BPAS) and this can lead to challenges in management of women with complicated medical history
    - All women for whom advice has been sought will have an individualised anticoagulation management plan will be made and uploaded to careflow/badgernet/notis
    - Their management will follow the principals described below.

- All women with recent VTE who require management of early miscarriage or request elective termination of pregnancy referred to NUH should be managed by a named Consultant Obstetrician/Gynaecologist and Consultant Haematologist

- Women who are treated with anticoagulation and present with first trimester miscarriage and bleeding require urgent assessment and should be admitted to A23
    - No further anticoagulation should be given until the patient has been seen and assessed
    - The Gynecology 'hot week' consultant should be notified immediately
    - Haematology should be contacted for advice (Haematology ST on call phone)
    - Management should be a joint approach with discussion between obstetrics/gynaecology and haematology and will depend on the gestation of pregnancy and assessment of pregnancy status

- Women with recent VTE should be offered surgical management rather than expectant or medical management unless a significant contraindication exists; in this case the risks and benefits of each approach should be discussed at consultant level and the safest approach adopted on an individual patient basis
- The risks and benefits of each approach should be clearly discussed with the patient and she should be involved in the decision making process.
- Women must be counselled that as anticoagulation has to be stopped to allow management of the pregnancy, there is a small risk of recurrent thrombosis. Although we try and ameliorate this risk as much as possible with an anticoagulation plan, recurrence does rarely still occur and can be life threatening

- All women undergoing management of miscarriage or elective termination referred to NUH should have a formal written plan for anticoagulation made and this should be available on her Notis and badgernet record.
- If complications arise during the procedure which means that the anticoagulation plan cannot be followed, the patient should be discussed again with the named consultant Obstetrician/Gynaecologist and consultant Haematologist.
- The risk of recurrent VTE when anticoagulation is stopped is highest within the first 4 weeks after an acute event. Therefore, consideration should be given to delaying the

procedure if this is clinically appropriate; this is only likely to be possible for elective termination of pregnancy

- Women with recent VTE who have a miscarriage or request termination of pregnancy should be considered as high risk. Therefore, for elective procedures these should be performed within normal working hours.
- If a woman presents with miscarriage out of hours, she should be discussed with the senior gynaecology/obstetric team and the on call haematologist. In both cases the consultant gynaecologist/obstetrician and consultant haematologist should be informed of the patient and be involved in the management plan. In the event that the surgical plan has been changed (eg theatre cancellation) then the consultant gynaecologist/obstetrician and consultant haematologist should be re contacted.

8.2. Miscarriage >15 weeks gestation

- Women who present with later pregnancy loss should be managed on an individual basis, depending on gestation.
- An joint management plan between obstetrics/gynaecology and haematology will be required

8.3. Follow up after miscarriage or termination

- Women should be referred to the obstetric haematology team for follow up by emailing ObstetricHaematologyService@nuh.nhs.uk and also referral to the VTE follow up pathway on careflow (if not already done)
  - Women who have undergone termination or pregnancy loss are seen in the thrombosis clinic not the obstetric clinic setting
- 4 weeks of anticoagulation treatment must be provided in the eTTO medication
- Women should be advised to monitor vaginal blood loss and to contact MAL if they have any concerns about heavy or abnormal bleeding
- Women should be discharged initially on enoxaparin 1.5mg/kg once daily, pending review in the thrombosis clinic
- Treatment dose anticoagulation therapy should be given for at least 6 weeks post miscarriage/termination and until at least 3 months of treatment has been given in total
  - The risks of thrombosis must be reviewed before stopping anticoagulation
  - Absolute duration will be decided in the obstetric haematology clinic

9. Clinical conundrums

- Women who have bleeding risk or contraindication to anticoagulation
  This represents a difficult clinical situation and management should involve discussion at consultant level between obstetric and haematology. Options for women considered to be at high risk of haemorrhage include

- IV UFH until the risk factors for haemorrhage have resolved form women in whom anticoagulation is considered essential
- IVC filter if an absolute contraindication to anticoagulation exists

- Women who require aspirin and therapeutic LMWH
  Aspirin can be continued at the same time as treatment dose LMWH. Women should be advised that they may bruise more with LMWH injections and to phone MAL if they have any concerns about bleeding

  - Allergy to Enoxaparin
    Enoxaparin is the first line LMWH used at NUH. Women with a known allergy or who develop an allergy to enoxaparin should be offered an alternative LMWH such as Dalteparin (Fragmin). In the unlikely event of allergy to both Enoxaparin and Dalteparin, Tinzaparin can be used. Pharmacy advice can be sought as needed.

  - Superficial thrombophlebitis
    Women who are diagnosed with superficial thrombophlebitis should be managed in line with the NUH guidance (see flowchart 2). Women should be referred to the VTE MDT and obstetric haematology service in the same way as women with DVT/PE. Guidelines for the management of superficial thrombophlebitis are available https://nuhp.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=ba1ae377ccb53d94fd95966f79afaa5a

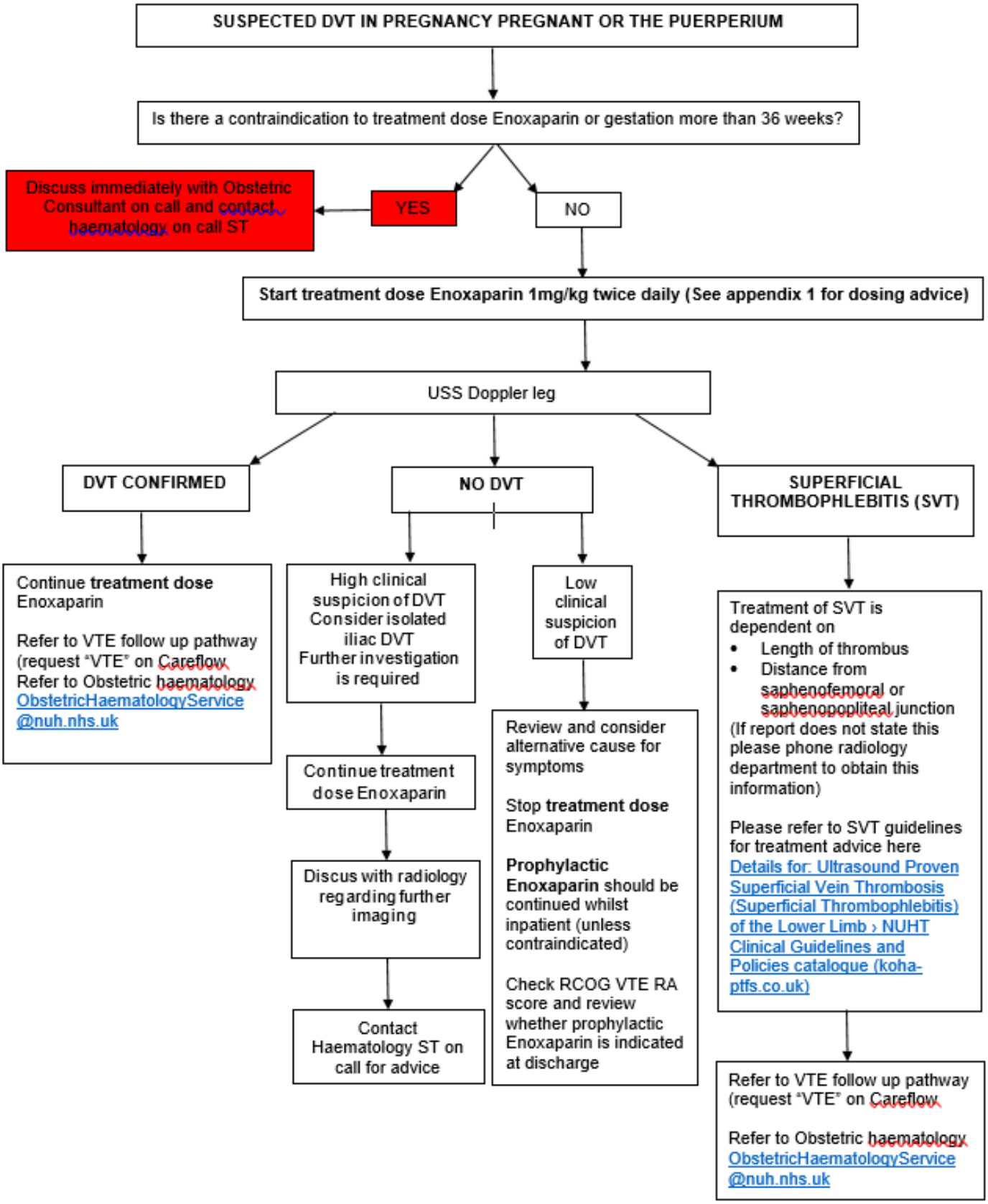
  - Negative imaging but ongoing clinical suspicion of VTE
    If clinical suspicion of DVT/PE persists despite negative initial imaging, treatment dose anticoagulation should be continued and advice sought on further imaging.

  - Women who decline imaging for PE
    All women who require imaging for PE should be provided with a written information leaflet. Counselling should initially be provided by the admitting team. If women remain concerned about undergoing imaging, the obstetric haematology team should be contacted before discharge (contact haematology ST on call phone at QMC site). Women should also be informed of the potential impact on future pregnancies and contraceptive choices of being unable to confirm VTE diagnosis.

  - Unusual site thrombosis
    Thrombosis can occur at other sites during pregnancy. The principals of management are the same as for DVT and PE. Women with unusual site thrombosis should be referred to the obstetric haematology team at presentation, during their inpatient admission (contact haematology ST on call phone at QMC site)

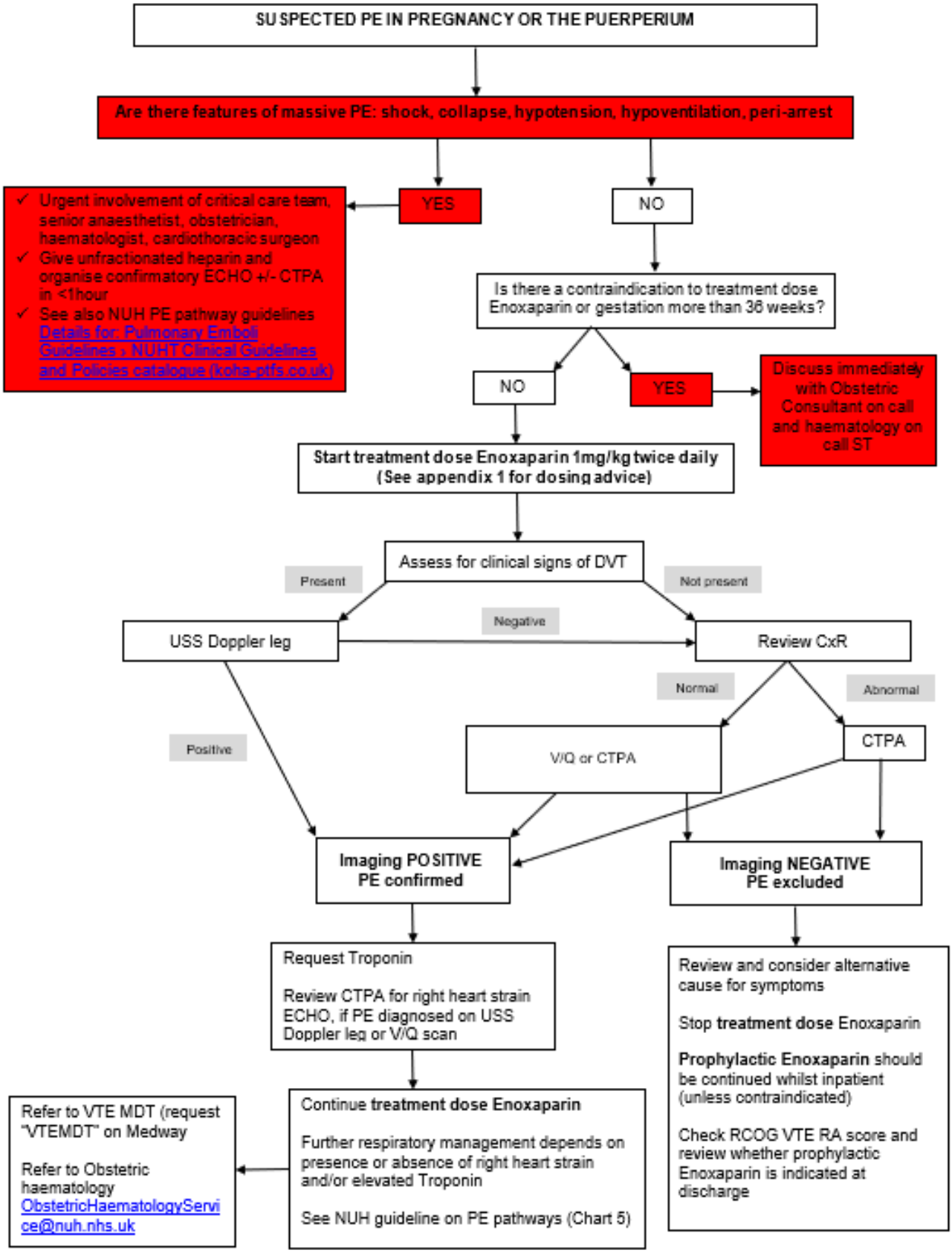
  - Heparin induced thrombocytopenia (HIT)
    HIT is extremely rare during pregnancy and women prescribed LMWH do not require platelet monitoring. However women with a previous diagnosis of HIT should not be prescribed any form of heparin (including LMWH and UFH). First line treatment for VTE is fondaparinux. The obstetric haematology team should be contacted for advice (contact haematology ST on call phone at QMC site). If there is clinical concern about acute HIT, please contact the haematology team as above

Flowchart 1: Suspected DVT in pregnancy

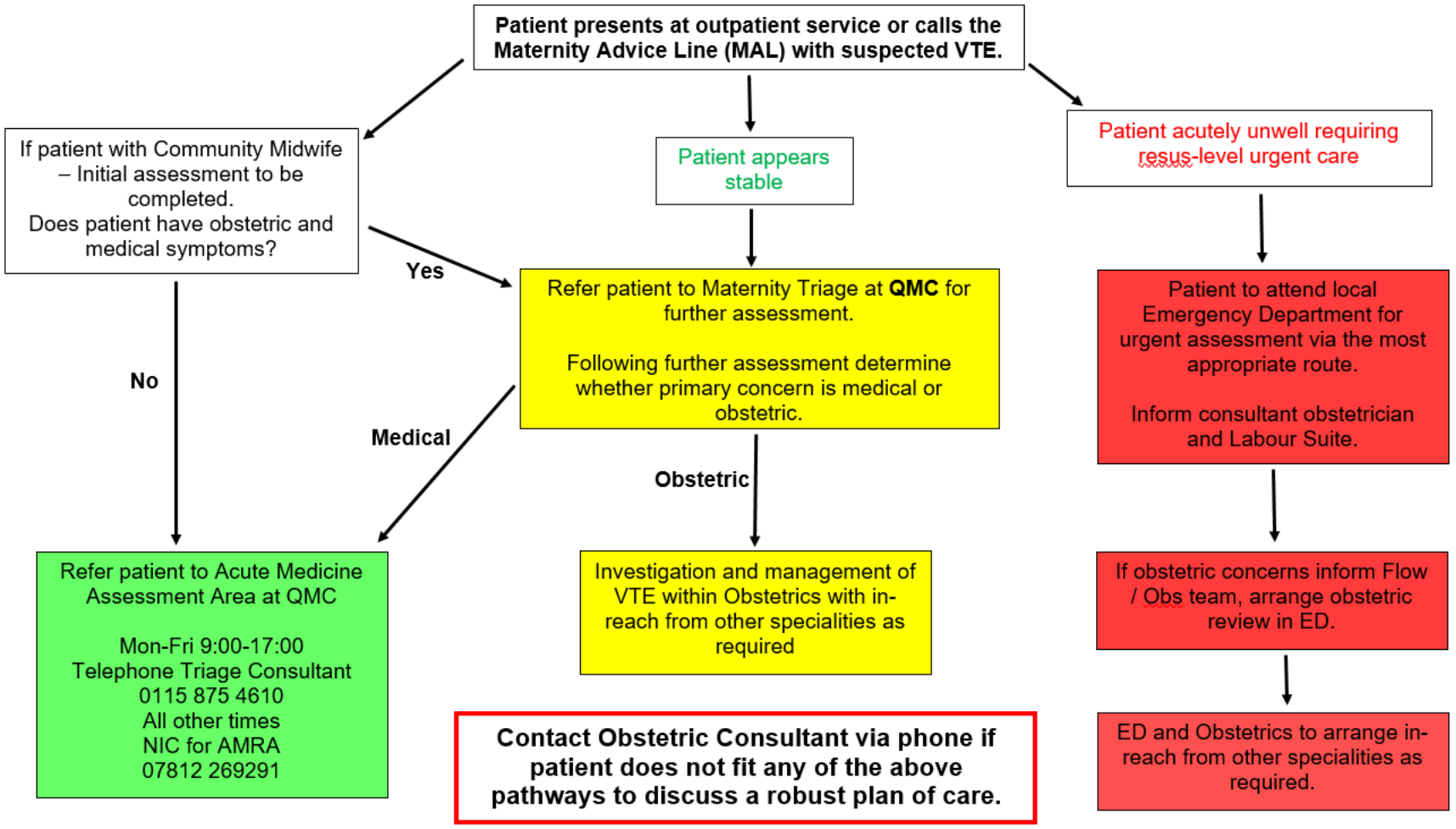


See also NUH PE pathway guidelines (Chart 5) Details for: Pulmonary Emboli Guidelines › NUHT Clinical Guidelines and Policies catalogue (koha-ptfs.co.uk)

Flowchart 2: Suspected PE in pregnancy



Appendix 1: Maternity advice line SOP



Appendix 2: Dosing of enoxaparin in pregnant patients

Current weight	Therapeutic Dose of Enoxaparin*Δ
Less than 50 kg	40mg twice daily
50 - 69kg	60mg twice daily
70 - 89kg	80mg twice daily
90 - 109kg	100mg twice daily
110 – 125kg	120mg twice daily
More than 125 kg	Discuss with haematologist

*The dosing advice above is for patients with creatinine clearance (CrCl) >30ml/min. If CrCl is less than 30ml/min, please seek pharmacist advice before prescribing

Δ Enoxaparin should be rounded to the nearest syringe size. Do **not** instruct patients to squirt dose out of the syringe.

References

Royal College of Obstetricians and Gynaecologists. Thromboembolic Disease in Pregnancy and the Puerperium: Acute Management. Green top Guideline No 37b, 2015

MMBRACE-UK Saving Lives Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2019 – 2021

Lactmed Drugs and Lactation Database (LactMed®) - NCBI Bookshelf (nih.gov)