Approved by Quality & Patient Care Committee
7 July 2016

THROMBOEMBOLISM PROPHYLAXIS AND TREATMENT

This LOP is developed to guide clinical practice at the Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this LOP

1. AIM

- Appropriately assess thrombo-embolism (TE) and bleeding risk in all women
- Prescribe and administer appropriate TE prophylaxis to all women
- Reduce the risk of thrombo-embolic complications

2. PATIENT

- Woman requiring risk assessment and management for prevention of thromboembolism
- Woman requiring thromboembolism prophylaxis during pregnancy

3. STAFF

Medical, midwifery, nursing

4. EQUIPMENT

Nil

5. CLINICAL PRACTICE

5.1 RISK ASSESSMENT for THROMBOEMBOLISM PROPHYLAXIS

- Perform and record a venous thromboembolism (VTE) risk assessment in each patient before deciding whether or not to use preventive measures and on the most appropriate measures to use
- **Complete and document a thromboembolism risk assessment for all women admitted to RHW within 12 hours of admission**. This should be completed by the admitting doctor or first contact doctor e.g. anaesthetist for operative woman. Based on this risk assessment, prophylaxis should be prescribed
- Review the risk of VTE and the appropriateness of thromboprophylaxis during the woman's hospital stay and following any change in the patient's clinical condition e.g. unexpected surgical intervention, immobility, sepsis, bleeding
- Use Appendix 1 to assess whether a patient is low or high risk for thromboembolism

Notes:

- VTE risk factors are thought to be additive so the presence of multiple risk factors leads to a higher risk of developing VTE
- Thromboprophylaxis is generally not needed for a woman who is fully mobile prior to and during admission and expected to have a length of stay less than 48 hours in the absence of specific patient risk factors for VTE.
- Woman on therapeutic anticoagulation do not require thromboprophylaxis.

The final decision to provide thromboprophylaxis is a clinical decision based on number and type of risk factors balanced against risk of bleeding.

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5.2 IMPLEMENTATION

Medical officers are responsible for:

- Undertaking assessment of risk for VTE (appendix 1)
- Prescribing VTE thromboprophylaxis, both anticoagulant drugs and mechanical prophylaxis, on the medication chart according to VTE risk and clinical circumstance.
- Reviewing as necessary a patient's risk for VTE and adjusting thromboprophylaxis as required when re-prescribing medications.
- Monitoring the safety of woman under their care prescribed VTE thromboprophylaxis.

Nursing and midwifery staff are responsible for:

- Ensuring that admitting or team medical officer has been notified to complete a VTE risk assessment and prescription for all women within 12 hours of admission
- Administering anticoagulant agents and application of mechanical prophylaxis as prescribed

All staff are responsible for:

- Reporting the occurrence of VTE or any adverse effects of thromboprophylaxis

There are 6 steps to ensuring all women at risk of VTE receive appropriate thromboprophylaxis

Step 1. Complete and document a risk assessment for VTE: see Appendix 1
Record the patient's BMI in the clinical notes by the person conducting the risk assessment. For obstetric woman use calculated (or estimated) pre pregnancy BMI which should be documented on the antenatal card/records for all women.

Step 2. Assess if the patient has any contraindications to anticoagulant drugs.
Include: recent or current bleeding, high risk of bleeding, thrombocytopenia (platelets <50,000x10 ^{9}/L), significant bleeding disorder (severe platelet dysfunction, underlying coagulopathy or coagulation factor abnormalities), allergy.

Step 3. Prescribe chemical prophylaxis (anticoagulants) if indicated

Step 4. Assess if the patient has any contraindications to mechanical prophylaxis.
Include: morbid obesity where correct fitting of stockings cannot be achieved, inflammatory conditions of the lower leg, severe peripheral arterial disease, severe peripheral neuropathy, severe oedema or lymphoedema of the legs, extreme leg deformity, recent skin graft or local surgery, significant risk of falls.

Step 5. Apply mechanical prophylaxis
Graduated compression stockings (GCS) (usually for ambulant woman) and Thrombo-Embolic Deterent (TED) stockings (for those on bed rest). RHW stocks one brand which is suitable for both.
IPC: Intermittent pneumatic compression boots as prescribed.

Step 6. Review the patient regularly.

Refer to educational notes for special considerations

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6. DOCUMENTATION
Integrated clinical notes
Medication chart

7. EDUCATIONAL NOTES
The likelihood of developing a venous thromboembolism (VTE) is increased by well-recognised risk factors. The majority of episodes (>70-80%) of VTE follow provoking factors such as admission to hospital for medical or surgical illness. Thromboprophylaxis measures, including anticoagulant drugs (also called chemical prophylaxis), mechanical thromboprophylaxis and early mobilisation, are proven effective interventions in reducing the morbidity and mortality associated with development of deep venous thrombosis (DVT) and pulmonary embolism (PE) in hospitalised woman.

Prescription of thromboprophylaxis is a clinical decision based on balancing benefits of prevention of VTE and risks of bleeding related to antithrombotic medications

SPECIAL CONSIDERATIONS

Woman undergoing surgery

- Remove GCS prior to transfer to Operating Theatre (OT)
- Omit chemical prophylaxis prior to OT as charted.
- Apply IPC in OT and continue until either removal before discharge from recovery or following mobilisation in the ward as charted.

Anticoagulation during pregnancy
Pregnancy is associated with a small but significant increase in risk of VTE. In some women this risk is considered significant enough to warrant anticoagulation therapy antenatally. Such treatment should be individualised but the following table (Table 1) gives guidelines for suggested prophylaxis regimes. See Table 2 for dosage regimes

Ideally such counseling should be offered prior to conception. If a decision is made to initiate thromboprophylaxis antenatally, this should begin as early in pregnancy as practical.
In most cases, anticoagulation will be with Low molecular weight heparin (LMWH) although aspirin and/or warfarin may be used for certain patient groups.

Woman undergoing **neuraxial anaesthesia or analgesia**.
In order to minimise the risks of haemorrhage and spinal cord damage it is important to manage chemical thromboprophylaxis carefully. There should be a **minimum of 12 hours from LMWH dosing** or **6 hours from low dose unfractionated heparin dosing** for any neuraxial procedure (including spinal anaesthesia, insertion or removal or manipulation of epidural catheter). After neuraxial procedures (including spinal anaesthesia, insertion or removal or manipulation of epidural catheter) a **minimum of 2 hours** must elapse before administration of chemical thromboprophylaxis.

Woman with renal impairment
Renal clearance is the primary mode of elimination for several anticoagulants including enoxaparin, fondaparinux and rivaroxaban. With reduced renal function, these drugs may accumulate and increase the risk of bleeding. While the published data linking renal impairment, drug accumulation and increased bleeding is weak and inconclusive it is sensible to recommend for a woman with creatinine clearance <30mL/min either :

1) Unfractionated heparin 2500 units SC BD or
2) Enoxaparin 20mg SC daily

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Specific haematological advice may be advisable in selected women.

Creatinine clearance is calculated using the below formula:

$$\frac{[140 - \text{age}] \times \text{weight (kg)}}{0.815 \times \text{serum creatinine (micromol/L)}} \times 0.85$$

Woman at extremes of body weight and age
LMWH is dosed according to body weight. In general:

- reduce dose of enoxaparin by 50% if >80 years or body weight is <40kg
- consider increased dose in women weighing >100kg

Extended duration prophylaxis
Certain women may require extended duration prophylaxis up to 6 weeks after admission. These include:

- woman with previous history of VTE
- obstetric woman with thrombophilia(s)
- woman with certain gynaecological cancers eg clear cell cancer
- woman with ongoing excess VTE risk e.g. ovarian hyperstimulation

Women assessed and requiring extended thromboprophylaxis on discharge must have their thromboprophylaxis plans documented and an appropriate follow up schedule provided. It is desirable that such women are able to self adminsiter anticoagulant drugs if necessary.

ANTICOAGULANT MEDICATIONS AND PROCEDURES

Heparin

- Consists of heparin chains of varying molecular weights (MW). It is also referred to as unfractionated heparin (UFH) or heparin sodium
- Enhances the activity of naturally occurring antithrombin III which then inactivates thrombin and other proteases involved in blood clotting, most notably factor Xa
- Administered intravenously (bolus or continuous) or subcutaneously
- Short biologic half-life of approximately one hour
- Renal clearance
- The effect of standard heparin is measured by the APTT
- Adverse reactions: bleeding, thrombocytopenia (benign or HITS), rarely alopecia and osteoporosis
- Overdosage: protamine sulfate can be given to counteract the action of heparin
- Heparin does not cross the placenta during pregnancy

Low Molecular Weight Heparin (LMWH)

- Include enoxaparin and dalteparin
- Compared with unfractionated heparin, LMWH has less of an effect on thrombin compared to heparin, but maintains the same effect on Factor Xa
- Administered subcutaneously once or twice daily
- Longer half-life than unfractionated heparin (3-6 hours after subcutaneous injection)
- Undergo renal clearance

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- Produce a more predictable anticoagulant response than unfractionated heparin which reflects their better bioavailability, longer half-life, and dose independent clearance
- No need for monitoring of the APTT. If necessary, monitor with antiXa levels.
- Adverse reactions: bleeding (< unfractionated heparin), allergic reactions (e.g., pruritus, rash, fever, injection site reaction, hives), skin necrosis, anaphylactoid reactions and thrombocytopenia (< unfractionated heparin)
- Overdosage: poorly responsive to protamine sulphate
- LMWH does not cross the placenta

Warfarin

- Oral anticoagulant
- Indirect antagonist of Vitamin K, which is required for synthesis of the active clotting factors II (prothrombin), VII, IX, and X in the liver
- Initial warfarinisation is challenging, and maintaining stable anticoagulation is often difficult because of the influence of poor nutritional status, liver disease, variable oral intake and absorption, drug to drug interactions
- Long half-life: hours-days
- The dose will vary according to the International Normalised Ratio (INR)
- Adverse effects: bleeding, less commonly: hypersensitivity, rash, alopecia, diarrohea, skin necrosis, jaundice, and hepatic dysfunction
- Overdosage: effects may be reversed by administration of Vitamin K, clotting factor replacement (Prothrombinex) or and fresh frozen plasma depending on the INR and the presence of bleeding complications
- Warfarin crosses the placenta and is associated with teratogenesis and haemorrhagic complications in the fetus

Novel oral anticoagulants (NOACs):

- Rivaroxaban (Xarelto) and Apixaban (Eliquis) are direct reversible competitive antagonists of activated factor X. Dabigatran (Pradaxa) is a direct reversible competitive antagonist of thrombin. Their main advantages are a rapid onset of anticoagulant effect, more predictable pharmacokinetics, and a lower potential for clinically important interactions with food, lifestyle and other drugs. Unlike warfarin, there are no readily available and validated tests for measuring the anticoagulant effect of the newer oral anticoagulants and routine clinical monitoring of all patients on these drugs is still essential,
- Rivaroxaban can be prescribed on the Pharmaceutical Benefits Scheme (PBS) to treat acute symptomatic deep vein thrombosis (DVT) without symptomatic pulmonary embolism (PE) and to prevent recurrent venous thromboembolism (VTE). [For dosing information see MIMS.]
- These agents should be used with caution in patients with severe renal or hepatic impairment (dabigatran does not undergo hepatic metabolism and may be safe in patients with hepatic disease).
- These drugs are contraindicated in children, and pregnant or lactating women.

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Antiplatelet agents

- Irreversibly decrease platelet aggregation and inhibit thrombus formation.
- They include:
  - Cyclooxygenase inhibitors
    - Aspirin
  - Adenosine diphosphate (ADP) receptor inhibitors
    - Clopidogrel
    - Ticlopidine
  - Phosphodiesterase inhibitors
    - Cilostazol
  - Glycoprotein IIB/IIIA inhibitors (intravenous use only)
    - Abciximab
    - Eptifibatide
    - Tirofiban
    - Defibrotide
  - Adenosine reuptake inhibitors
    - Dipyridamole
- Long half-life: weeks
- Adverse effects: bleeding, gastric irritation and peptic ulcer, tinnitus
- Overdosage: supportive treatment
- Antiplatelet agents may be used with caution in pregnancy.

NON-DRUG THERAPIES FOR PREVENTION OF THROMBOEMBOLISM

Include:

- GCS including TEDs and Intermittent Pneumatic Compression (IPC) devices (thigh or knee length)

Adverse reactions:

- GCS may cause reduced blood flow, pressure ulcers or increased chance of slipping or falls
- IPC can exacerbate ischemic disease and therefore may be contraindicated in woman with peripheral arterial disease or arterial ulcers.

8. RELATED POLICIES/ PROCEDURES/ CLINICAL PRACTICE LOP:

- Heparin (UFH) : Prescribing, administration and monitoring including HITs
- Warfarin : Prescribing, administration and monitoring
- Regional anaesthesia
- Bridging anticoagulation: Management of longterm anti-coagulation or antiplatelet therapy in the peri-operative period
- Hyperemesis Gravidarum and Nausea and Vomiting in Pregnancy –Management
- Ovarian hyperstimulation syndrome
- Neuraxial (intrathecal and/or epidural) opioid analgesia
- Heparin sodium for intravenous administration

9. RISK RATING: Medium- review every 3 years

10. NATIONAL STANDARD: Medication safety

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REVISION & APPROVAL HISTORY

Reviewed and endorsed Therapeutic & Drug Utilisation Committee 21/6/16
Reviewed and endorsed Maternity Services LOPs group June 2013
Approved Quality & Patient Safety Committee 15/4/11
Reviewed February 2011 and replaced the following :
SE Health, Venous Thromboembolism (VTE)
Thromboprophylaxis – approved Quality Council 21/2/05
Thromboprophylaxis at Caesarean Section Guidelines – approved Quality Council 19/9/05
Thromboprophylaxis in Pregnancy Guideline – approved Quality Council 16/10/06
Thromboprophylaxis for Vaginal Delivery and Post-Partum Guideline – approved Quality & Patient Safety Committee 15/10/09

FOR REVIEW : JULY 2021

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Table 2

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TABLE 1 – ANTENATAL AND POSTNATAL RECOMMENDATIONS FOR ANTICOAGULATION[14]

Woman's Details	Antenatal Recommendation	Postnatal Recommendation
• Positive family history* (FH) VTE but no personal history VTE	Observation	Nil
• Positive FH* VTE but no personal history VTE with high risk thrombophilia**	Consider prophylactic LMWH especially if other risk factors	Prophylactic LMWH 6 weeks
• Single prior provoked VTE, no other persistent risk factors*	Observation	Prophylactic LMWH 6 weeks
• No personal or FH of VTE but high risk thrombophilia**	Consider prophylactic LMWH	Prophylactic LMWH 6 weeks
• Single prior provoked VTE with persistent risk factors*	Consider prophylactic LMWH	Prophylactic LMWH 6 weeks
• Single prior VTE associated with Combined Oral Contraceptive Pill (OCP) or pregnancy	Prophylactic LMWH	Prophylactic LMWH 6 weeks
• Single prior unprovoked VTE • Prior recurrent provoked VTE	Prophylactic LMWH	Prophylactic LMWH 6 weeks
• Recurrent unprovoked VTE • Antithrombin deficiency • Pre-pregnancy therapeutic anticoagulation	Therapeutic LMWH	Therapeutic LMWH 6 weeks or usual Pre-pregnancy anticoagulation
• Mechanical cardiac valve	Consider Warfarin or therapeutic LMWH + aspirin	Warfarin long term

*Risk factors: thrombophilia, family history in 1^{o} relative, immobility, varicose veins
**High risk thrombophilia: Factor V Leiden homozygous, antithrombin deficiency, protein C and S deficiency, or .combined defects

TABLE 2. DOSE REGIMENS

	Prophylaxis dose (SC)	Treatment dose (IV)
Unfractionated heparin	5000 units BD or TDS	Complex, see IV Heparin LOP

LMWH	Prophylactic dose (SC)	Therapeutic dose (SC)
Enoxaparin (Clexane)	40 mg daily	1.5 mg/kg/daily or 1 mg/kg BD
Dalteparin (Fragmin)	5000 units daily	100 units/kg BD

Note: women at extremes of weight and or impaired creatinine clearance may require dose adjustment

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APPENDIX 1 – RECOMMENDED RISK ASSESSMENT AND MANAGEMENT FOR INPATIENT VTE PREVENTION

OBSTETRIC		
LOW	**HIGH**	
	Moderate Risk	***High Risk***
Vaginal delivery	Age ≥ 35	Emergency Caesarean section
Age < 35	BMI ≥ 30	Thrombophilia
BMI < 30	FH of TE in 1° relative	Varicose veins with phlebitis
Early mobilisation	Admission to ACC	PH of TE
	Immobility	
Elective Caesarean section	Pre-eclampsia	
Minor surgery	Varicose veins	
	Hyperemesis gravidarum	

GYNAECOLOGY AND BREAST		
LOW	**HIGH**	
	Moderate Risk	***High Risk***
Minor/day surgery	Age ≥ 60	Cancer
Age < 60	BMI ≥ 30	PH of TE
BMI < 30	FH of TE in 1° relative	Thrombophilia
Early mobilisation	Major surgery	Ovarian hyperstimulation

Abbreviations: BMI: body mass index; FH: family history; PH: personal history; TE: thromboembolism;

Definitions :

Thrombophilia: Factor V Leiden hetero - or homozygous; Antithrombin III deficiency; anticardiolipin antibody positive, lupus inhibitor positive; Protein S def.; Protein C def.; prothrombin gene hetero- or homozygous.

Minor surgery: ERPC, vaginal repair, MROP or gynaecological surgery including hysteroscopies, any benign case < 1 hour, day only surgery

Major surgery**:** procedures requiring laparotomy, surgery for gynaecological cancer, gynaecological surgery (including laparoscopic) > 1 hour and/or requiring an overnight stay in hospital.

THE RISK OF VTE MUST BE BALANCED AGAINST THE RISK OF BLEEDING AND TREATMENT MODIFIED ACCORDINGLY

MANAGEMENT	
Low risk	Early mobilisation and avoidance of dehydration
≥ 2 moderate risk factors	As above for low risk +intra-operative IPC +post-operative GCS +enoxaparin 40mg SC daily or unfractionated heparin 5000 units SC BD or TDS
High risk	As above for low and moderate risk +post-operative IPC until mobile (Gynae only) +consider extended duration prophylaxis

Abbreviations : IPC: intermittent pneumatic compression; GCS: graduated compression stockings/TEDS