



**CLINICAL PRACTICE GUIDELINE ON DVT PROPHYLAXIS IN OBSTETRICS AND  
GYNAECOLOGY**

**Statement of Intent**

This clinical practice guideline is not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

These parameters of practice should be considered guidelines, based on the best available evidence at the time of development. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan, must be made by the doctor in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

### Venous Thromboembolism in Obstetrics and Gynaecology

#### Obstetrics

Venous thromboembolism (VTE) encompasses both deep vein thrombosis (DVT) and its acute complication, pulmonary embolism (PE). It is one of the most important preventable causes of death in hospitalised patients. In obstetric practice, PE is the most common direct cause of maternal deaths in developed countries including Singapore. In addition<sup>1 2</sup>, VTE also contributes to significant morbidity in terms of post phleblitic syndrome and chronic venous ulcers.

Thrombotic risk is increased ten fold in pregnancy: this is due to the physiological increase in clotting factors, the enlarging gravid uterus which compresses on pelvic veins and the pelvic vascular endothelial injury which accompany delivery.

The true incidence of VTE in the Asian populations is unknown. Early literature suggested that it was exceedingly rare<sup>3 4</sup>, compared to western populations, in whom venous thromboembolism is an established entity with an annual community prevalence of 1-2 per thousand. There is, however, a growing body of evidence to show that VTE is not so uncommon in this region after all, and that the perceived rarity of VTE has resulted in the condition being grossly underdiagnosed<sup>5</sup>. Local autopsy studies among adult coroner's autopsies in Singapore have demonstrated an increase in prevalence in fatal PEs between the epochs of 1952 and 1966 (1.6 per 1,000 necropsies) and 1989-93 (1.05%)<sup>6</sup>. While this may appear low in contrast to western figures of 4-13%, more recent autopsy reports from Queen Mary Hospital in Hong Kong spanning 30 years show a rising prevalence of pulmonary embolism from 0.75% to 4.7%<sup>7</sup>.

A Hong Kong study showed almost 2 in 1,000 pregnancies and deliveries in Chinese women from Hong Kong were complicated by venous thrombosis or pulmonary embolism, with most occurring postpartum and after caesarean section<sup>8</sup>. However, the most recent Confidential Enquiries into Maternal Deaths for the United Kingdom also showed that the risk of PE is not limited to late pregnancy and the puerperium and those who had undergone caesarean sections: 62% of fatal antenatal PEs occurred in the first trimester, and 10/14 (71%) of postpartum deaths followed vaginal delivery<sup>9</sup>.

### *Clinical features*

While the clinical presentation of deep leg vein thrombosis is typically leg pain and swelling, a significant minority of patients with thrombosis (20%) has no apparent predisposition. The clinical features of venous thromboembolism are often elusive as 75% of patients who present with VTE are asymptomatic and the disease often unsuspected. Deep venous thrombosis in obstetrics more commonly presents with iliofemoral thrombosis which may present as lower abdominal pain rather than lower limb swelling. A high index of suspicion is critical.

### **Gynaecology**

VTE in gynaecology would be relevant in 2 areas: surgery, and hormonal therapy whether it be for contraception or hormone replacement therapy. Surgical risks can be extrapolated from regional studies in general surgery which report a VTE prevalence in the absence of thromboprophylaxis ranging from 3% to 19.1%; this falls well within the quoted prevalence of 6-35% for western populations, granted that these studies may not share similarities in study design and diagnostic tests<sup>10, 11</sup>. Recent studies on VTE prophylaxis done in Singapore have shown that DVT can be easily preventable eg. compression stockings was efficacious in preventing DVT after hysterectomy<sup>12</sup>, prophylactic LMWH prevented the occurrence of DVT for patients undergoing total knee replacements<sup>13</sup> and colorectal surgery<sup>14</sup>.

The thrombogenic properties of oestrogen compounds is well recognized in oral contraceptives, and more recently, also in oral oestrogen-containing hormone replacement therapy (HRT).

Other factors which influence VTE risk in gynaecology include age, immobilization, surgery and malignancy. Recent studies have also shown that chinese populations appear to have a high prevalence of other congenital thrombophilias eg. antithrombin, protein C and protein S deficiencies, although other thrombophilias such as Factor V Leiden mutation and prothrombin gene mutation are extremely rare in chinese populations<sup>15 16 17</sup>.

As in obstetrics, objective testing is a necessity as clinical diagnosis alone is inaccurate and fatality can occur as the first clinical presentation in untreated patients. In post-

mortem studies, 60-70% of patients who died from fatal PE were misdiagnosed and not suspected to have PE during life. There is no data to show any racial differences in clinical features and presentations of VTE.

The rationale for thromboprophylaxis in obstetrics and gynaecology is justified on the grounds that:

- VTE is the leading cause of maternal mortality, and deaths of these women who are relatively young are largely preventable in the majority of cases if appropriate prophylaxis had been given. VTE is also increased in pelvic surgery, as well as patients receiving hormonal therapy in its various forms eg. Contraception, HRT.
- VTE is clinically silent in most cases, and that the majority of PE fatalities had unrecognized preceding DVT or submassive PE. Limiting anticoagulation treatment in only clinically apparent cases would therefore have limited impact in preventing deaths in otherwise healthy individuals, particularly obstetric patients.
- Treatment of established DVT, which requires full anticoagulation in therapeutic doses, carries more haemorrhagic risks and is more costly than prophylactic anticoagulation;
- Screening and treatment for asymptomatic thrombosis does not appear cost-effective;
- The most efficient way to prevent fatal and non-fatal DVT/PE is to use routine prophylaxis in moderate and high-risk hospital patients.

## Levels of Evidence and Grades of Recommendations

Recommendations in clinical practice guidelines should be based on good evidence. The definitions of the levels of evidence and the grading of recommendations in guidelines should emulate those used by the Scottish Intercollegiate Guidelines Network (SIGN), which originate from the US Agency for Health Care Policy and Research. These are set out in the following tables:

Level	Type of Evidence
<b>Ia</b>	Evidence obtained from meta-analysis of randomised controlled trials.
<b>Ib</b>	Evidence obtained from at least one randomised controlled trial.
<b>IIa</b>	Evidence obtained from at least one well-designed controlled study without randomisation.
<b>IIb</b>	Evidence obtained from at least one other type of well-designed quasi-experimental study.
<b>III</b>	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
<b>IV</b>	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Grade	Recommendation
<b>A</b> (evidence levels Ia, Ib)	Required – at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing specific recommendation.
<b>B</b> (evidence levels IIa, IIb, III)	Required – availability of well conducted clinical trial studies but no randomised clinical trials on the topic of recommendation.
<b>C</b> (evidence level IV)	Required – evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.
<b>GPP</b> (Good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

## **Development and Aims of This Consensus Statement**

The major aim of this consensus statement is to assist obstetricians and clinicians in :

- Identifying patients at increased risk of venous thromboembolism in obstetrics and gynaecology
- Strategies for thromboprophylaxis

This should be reviewed periodically and changes made accordingly as more primary data becomes available.

### **Obstetrics**

Pregnancy itself increases the risk of VTE by as much as ten fold, and therefore women who have additional risk factors are at particular risk during pregnancy<sup>18 19</sup>. These women should be offered prepregnancy counselling with a prospective management plan as thrombotic risk exists from the start of the first trimester but the majority of booking antenatal visits are made at the end of the first trimester.

**C All women should have an assessment of risk factors for VTE in early pregnancy or before pregnancy. The assessment should be repeated in the event of hospitalisation or the onset of any other intercurrent problems.**

**B Women with previous VTE should be screened for inherited and acquired thrombophilia according to local protocols ideally before pregnancy.**

### **Risk factors for VTE in Obstetrics and Gynaecology**

#### Patient factors

- Age over 35 years (>40 years for gynaecology patients)
- Obesity
- Parity > 4
- Dehydration eg. Hyperemesis gravidarum
- Gross varicose veins
- Previous VTE
- Thrombophilia
  - Congenital eg. antithrombin deficiency, protein C deficiency, protein S deficiency, Factor V Leiden, prothrombin gene variant
  - Acquired eg. antiphospholipid syndrome, positivity for lupus anticoagulant , anticardiolipin antibodies
- Severe infection, e.g. pyelonephritis
- Immobility (> 4 days bed rest)
- Pre-eclampsia
- Excessive blood loss
- Paraplegia
- Sickle cell disease
- Ovarian hyperstimulation syndrome
- Inflammatory disorders e.g. inflammatory bowel disease
- Some medical disorders, e.g. nephrotic syndrome, certain cardiac diseases, myeloproliferative disorders, essential thrombocythaemia, polycythaemia vera

- On oral contraception or hormone replacement therapy (HRT) (for gynaecology patients)

### Surgery

- Caesarean section –elective, emergency and intrapartum
- Surgical procedure in pregnancy or puerperium, e.g. evacuation of retained products of conception, postpartum sterilisation
- Long-haul travel
- Prolonged labour \*
- Midcavity instrumental delivery \*
  - Immobility after delivery \*

\* risk factors specific to postpartum VTE only

### Gynaecology

**C All gynaecological patients scheduled for surgery should have a pre-operative risk assessment for VTE in order that a prospective management plan with respect to thromboprophylaxis is made.**

## Recommended Thromboprophylaxis

### Obstetrics

#### Obstetric Patients – prophylaxis in pregnancy, during labour and puerperium

Expert haematological advice or referral to a joint obstetric and haematology clinic should be sought in cases when the antenatal team are uncertain about thromboprophylaxis.

**GPP Regardless of their risk of VTE, immobilisation of women during pregnancy, labour and the puerperium should be minimised and dehydration should be avoided.**

#### Women with a previous VTE

These women are at increased risk of recurrent VTE in the next pregnancy (RR 3.5 95% CI 1.6 –7.8)<sup>20</sup>. This risk is further increased if the woman has thrombophilia or if her previous VTE was in an unusual site or was unprovoked. As discussed in Risk Assessment above, these women should have a careful history taken and be screened for both inherited and acquired thrombophilia, ideally before pregnancy. Specialist haematologist consultation is recommended in view of the effects of pregnancy on the results of a thrombophilia screen eg. Protein S levels may be physiologically suppressed in pregnancy.

#### *Women with a previous VTE and no thrombophilia*

These women should be offered prophylaxis with low molecular weight heparin (LMWH) for six weeks after delivery. The issue of antenatal thromboprophylaxis is controversial. There is some evidence that if the previous VTE was associated with a temporary risk factor, such as trauma, antenatal anticoagulation is not required<sup>21</sup>. However, if the previous VTE was oestrogen-related (occurred in pregnancy or as a result of the combined oral contraceptive pill), it would seem clinically intuitive that antenatal thromboprophylaxis with LMWH would be warranted, especially if additional risk factors such as obesity were present<sup>22</sup>. Moreover, women with more than 1 previous VTE, or those with a family history of VTE (first degree relative) or if the VTE occurred in an

unusual site eg. axillary or superior vena caval veins, then antenatal thromboprophylaxis with LMWH should be offered, as these may indicate thrombophilic state which is undetectable by current methods available thrombophilia screening tests.

**C Women with previous VTE should be offered prophylaxis with low molecular weight heparin (LMWH) for six weeks after delivery.**

**C Women with a previous recurrent VTE (two or more), or a previous VTE which occurred in pregnancy, or with a family history of VTE in a first-degree relative or whose episode of VTE was in an unusual site eg. axillary vein or SVC), should be offered thromboprophylaxis with LMWH antenatally and for at least 6 weeks postpartum.**

*Women with previous VTE and known hereditary thrombophilia.*

Pre-existing thrombophilia increases the risk of VTE in pregnancy, however, the degree of risk varies with the type of thrombophilia, with particularly high relative risks for those with combined or complex thrombophilic deficiencies eg. relative risk for VTE is 107 for combined Factor V Leiden and prothrombin mutation, compared to 7 for Factor V Leiden alone. Current evidence would support that women with previous VTE and an identifiable thrombophilia should receive antenatal thromboprophylaxis with LMWH, continuing onto postpartum prophylaxis for 6 weeks. Expert haematological advice should also be sought for those with symptomatic thrombophilia, with regards to dosages of prophylaxis required.

**B Women with previous VTE and thrombophilia should be offered thromboprophylaxis with LMWH antenatally and for at least six weeks postpartum.**

### **Women with thrombophilia without previous VTE**

There is a paucity of prospective data examining the incidence of VTE in women with thrombophilia who get pregnant. Data from retrospective studies show a varying degree of risks depending on the type of thrombophilic deficiency. However, women with combined defects, those who are homozygous for defects, or who have antithrombin deficiency are at particularly high risk of developing VTE in pregnancy<sup>23 24 25 26 27</sup>. These women should receive antenatal and at least 6 weeks postpartum thromboprophylaxis

with LMWH. Those in lower risk categories should at least receive 6 weeks of postpartum thromboprophylaxis with LMWH; the question of antenatal thromboprophylaxis for these women should involve consultation with a haematologist.

**B Women with asymptomatic hereditary or acquired thrombophilia should receive at least 6 weeks of postpartum thromboprophylaxis with LMWH. Depending on the specific thrombophilia and the presence of other risk factors, they may qualify for antenatal thromboprophylaxis. Those with combined defects, or who are homozygous for thrombophilic defects, or with antithrombin deficiency should receive antenatal thromboprophylaxis with LMWH as they are at especially high risk for VTE during pregnancy and the puerperium.**

#### **Women with antiphospholipid syndrome (acquired thrombophilia)**

Antiphospholipid syndrome (APS) is defined as the presence of lupus anticoagulant or anticardiolipin antibodies of medium-high titre on two occasions eight weeks apart, in association with a history of thrombosis (arterial or venous) or adverse pregnancy outcome (three or more unexplained miscarriages before 10 weeks of gestation, a fetal death after 10 weeks of gestation or a premature (less than 35 weeks) birth due to severe pre-eclampsia or intrauterine growth restriction<sup>28</sup>.

#### *APS and previous VTE*

These women have a up to 70% risk of recurrence of thrombosis in pregnancy, and therefore should receive antenatal low dose aspirin and LMWH and postnatal thromboprophylaxis with LMWH<sup>29</sup>.

**C Women with antiphospholipid syndrome should receive low dose aspirin antenatally to reduce the risk of pregnancy complications, and postpartum thromboprophylaxis with LMWH.**

#### *APS with history of recurrent miscarriages*

There is evidence that antenatal low dose aspirin and LMWH in prophylactic doses improves obstetric outcomes in this subset of patients. It is recommended that they also continue to receive at least three to five days of postpartum thromboprophylaxis<sup>30</sup>.

**A Women with APS and recurrent miscarriages should also receive antenatal thromboprophylaxis with LMWH from the diagnosis of pregnancy.**

*APS with previous history of severe early onset pre-eclampsia*

Low dose aspirin has been shown to improve pregnancy outcome in APS. Meta-analyses of low dose aspirin have demonstrated its safety in pregnancy and that it decreases the risk of pre-eclampsia by 15% in high risk patients<sup>31</sup>. While they may not require LMWH antenatally, it is recommended that they should receive postpartum thromboprophylaxis for at least 3-5 days.

**C Women with antiphospholipid syndrome should receive low dose aspirin antenatally to reduce the risk of pregnancy complications, and postpartum thromboprophylaxis with LMWH.**

*Positive antibody titres with no previous VTE or “APS classifiable” pregnancy loss*

These patients do not satisfy the definition of having APS and therefore may not require LMWH or low dose aspirin. This should be discussed with the patient with regards to risks associated with therapy against an unquantifiable protection, if any, against VTE and other APS-related adverse obstetric outcomes<sup>32 33 34</sup>.

**Women with neither previous VTE or thrombophilia**

This will form the vast majority of obstetric patients. All antenatal patients should be screened for risk factors according to Table 1.

Early mobilisation +/- compression stockings should be considered for women with one or 2 of the above risk factors.

In women with 3 or more of the above risk factors, postpartum pharmacological prophylaxis with LMWH should be considered until patient is fully ambulant.

Clinical judgement is required with regard to the weighing of the above risk factors eg an extremely obese woman admitted to the antenatal ward may justify antenatal thromboprophylaxis.

### **Women undergoing caesarean section**

As caesarean section carries a higher risk of VTE compared to vaginal delivery, all women undergoing caesarean section should be individually assessed for their risk of developing VTE, and be categorised as low, moderate or high risk. A scoring system, taking into account other factors eg. Age, weight, should be used, as shown in the following table.

**Table 1: Risk Assessment Profile and Thromboprophylaxis Regimen**

<b>Risk group</b>	<b>Risk factors</b>	<b>Prophylaxis</b>
<b>Low risk</b>	Uncomplicated pregnancy Elective caesarean section	Early mobilisation and attention to hydration
<b>Moderate risk</b>	Emergency caesarean section Age greater than 35 Obesity Pre-eclampsia Para 4 or more Gross varicose veins (to be continued until fully mobile) Current infection Prolonged immobility Major current illness	LMWH and/or graded compression (TED) stockings
<b>High risk</b>	Three or more moderate risk factors or Absolute indication Personal history of: (to be continued until the fifth postoperative day or fully mobile if longer) <ul style="list-style-type: none"><li>▪ DVT or pulmonary embolus</li><li>▪ Thrombophilia</li><li>▪ Antiphospholipid syndrome</li><li>▪ Paralysis of the lower limbs</li><li>▪ Extended major pelvic surgery</li></ul>	LMWH and TED stockings

### 5.3g **Epidural anaesthesia and pharmacological thromboprophylaxis**

Patients on LMWH antenatally and who wish epidural anaesthesia in labour, or epidural or spinal anaesthesia for caesarean section, should stop pharmacological prophylaxis when labour starts. In general terms, an epidural or spinal block should not be given for 10-12 hours after LMWH administration<sup>35 36</sup>. However, the risk benefit ratio must be taken into account in the decision regarding timing of epidural or spinal anaesthesia. LMWH should not be given within two hours of epidural or spinal anaesthesia or of catheter removal.

**C In pregnant women who have requested epidural anaesthesia during labour, stop the administration of LMWH when labour starts.**

**C LMWH can be administered or readministered three hours after atraumatic epidural or spinal anaesthesia, or removal of an epidural catheter.**

**GPP Patients should be warned to discontinue self-injections of LMWH as soon as they believe themselves to be in labour, and not restart until evaluation in hospital**

## Gynaecology

### Gynaecological surgical patients for elective major surgery

- Early mobilisation + compression stockings +/- pneumatic pumps for patients with:
  - Absence of past history and family history of venous thrombosis;
  - Absence of thrombophilia and diseases associated with hypercoagulable states
  - Absence of all other risk factors
  
- Pharmacologic peri-operative prophylaxis indicated for patients with:
  - Presence of thrombophilia and diseases associated with hypercoagulable states
  - Past history and family history of venous thrombosis
  - Major cancer surgery
  - 3 or more risk factors as listed in above.

### **Mechanical methods**

Graduated compression stockings and intermittent pneumatic compression devices have been shown to be effective in DVT prophylaxis in moderate risk surgical patients. It is not been evaluated in medical patients, but the efficacy shown in surgical patients can be reasonably extrapolated.

They do not increase the risk of bleeding and can be safely used for patients with high-risk of bleeding. However they are contraindicated for patients with severe leg ischaemia.

### **Pharmacological methods**

Unfractionated Heparin, Low Molecular Weight Heparins, Warfarin, Dextran have been proven to be useful in preventing DVT/PE. Warfarin is teratogenic and should be avoided if possible during pregnancy, a possible exception being made for patients with prosthetic heart valves, in which case warfarin should be avoided at least between 6 and 12 weeks and after 36 weeks gestation. LMWH is preferred to unfractionated heparin in pregnancy, as there is more safety data<sup>37 38 39</sup>, particularly with respect to heparin induced thrombocytopenia<sup>40</sup>, osteopaenia<sup>41 42 43</sup> and bleeding complications. Moreover, LMWHs are easy to administer and in most cases monitoring of clotting times is not required.

Low Molecular Weight Heparins (LMWH). Examples of LMWH in clinical use in Singapore include:

- Fraxiparine – 0.2 ml daily if bodyweight < 50 kg, 0.3 ml daily if bodyweight > 50 kg till fully mobilised.
- Clexane – 20 mg daily till fully mobilised. For pregnant women >50kg, in whom thrombotic risks are increased, a 40mg daily dose may be more efficacious.

The platelet count should be checked before and one week after the introduction of LMWH.

## **Pharmacological methods for Obstetrics Patients**

*Patients who need postpartum prophylaxis*

**C Postpartum, the first dose of s/c LMWH should be given 6 hours after delivery.**

6 hours after delivery and when haemostasis secured and after removal of epidural catheter, start low molecular weight heparin – s/c Fraxiparine 0.2 ml OM if body weight below 50 kg and 0.3 ml OM if body weight above 50 kg, or s/c clexane 20-40 mg OM.

*Patients who need postpartum prophylaxis for at least 6 weeks*

**C Where the patient does not wish to continue self-injecting, LMWH can be replaced by warfarin starting on the first or second postpartum day. The LMWH can be withdrawn when the INR has been within the target range (INR 2-3) for 2 consecutive days.**

Continue low molecular weight heparin until INR reaches 1.5. Maintain INR at 2.0 for 6 weeks postpartum. Some women may prefer s/c Low Molecular Weight Heparin for 6 weeks instead of Warfarin.

**C There is no contraindication to breast feeding when the mother is being treated with LMWH, warfarin or other coumarins.**

*Patients who need antenatal prophylaxis*

Refer to haematologist, high risk pregnancy obstetrician or obstetric physician.

## **Contraindications to pharmacological thrombo-prophylaxis**

- Patients with known bleeding disorders e.g. haemophilia, von Willibrand's Disease, thrombocytopenias and platelet dysfunction
- Acquired coagulopathy secondary to liver diseases, drugs, uraemias etc;
- Strong family history of bleeding disorders
- Underlying pathology which predispose to bleeding e.g. peptic ulcers, haemangiomas
- Neuro-surgery and eye surgery.(However in patients with very high risk of thrombosis, pharmacological thrombo-prophylaxis can be considered a few days after the surgery when there is reduced risk of bleeding and before the patient is ambulant)
- Heparin allergy
- Heparin induced thrombocytopenia

**Where anticoagulants are contraindicated, graduated elastic compression stockings should be worn for at least 6 weeks following delivery. This may be combined with low dose aspirin. C**

## **Contraindications to compression stockings and pneumatic leg pumps**

- Severe peripheral vascular disease and leg ischaemia

### **Combined oral contraceptive (COC) pills**

The risk of VTE in users of the combined second and third generation oral contraceptive pill (COCs) is increased three fold (15/100,000 women per year)<sup>44</sup> and six fold (30/100,000 women per year)<sup>45</sup> respectively, compared to the background rate of spontaneous VTE in non-pregnant healthy women (5/100,000 women per year). The risk is higher in women with thrombophilias<sup>46</sup>.

This has to be taken in perspective in the event of pregnancy ensuing as a result of not using contraception, as the risk of VTE in pregnancy is 100 cases per 100,000 maternities.

Peri-operative VTE risks are increased from 0.5% to 1% for pill users<sup>47</sup>; however, the benefits of stopping the pill 4-6 weeks before surgery to prevent VTE has to be weighed against the possibility of an unwanted pregnancy, the risk of surgery and anaesthesia on a pregnancy, and the risks of a subsequent pregnancy termination. Counselling of alternative contraceptive methods is essential.

Timing of restarting COC should involve individual assessment according to risk factors and postoperative complications and patient mobility. Perioperative prophylaxis is given in accordance with the recommendations made above. In emergency surgery, routine VTE prophylaxis should be given as these patients' risk of VTE is greater.

### **Progestogen-only contraceptives**

Low dose progestogen-only contraceptive preparations are not at increased risk of VTE, and indeed may be substituted for women with previous VTE or who are at high risk of VTE. However, higher doses of progestogens used for other non-contraceptive therapeutic indications eg. menstrual disorders, are associated with a 5-6 fold increased risk of VTE<sup>48 49</sup>.

### **Hormone replacement therapy (HRT)**

Recent studies have confirmed that HRT, including the selective oestrogen receptor modulator, raloxifene, increase the risk of VTE threefold, particularly in the first year of use i.e 30 cases per 100,000 women per year for users compared to 10 per 100,000 women per year for non-users<sup>50</sup>. Additional factors such as age<sup>51</sup>, obesity, thrombophilias and coronary heart disease increase the risks further<sup>52</sup>. While it is uncertain if HRT is a risk factor for perioperative VTE, most HRT users will merit routine prophylaxis<sup>53</sup>.

There is good evidence that HRT will increase the recurrence of VTE in users with a personal history of VTE, especially if they have thrombophilic defects. For such women, and those who have known thrombophilic defects with no personal history of VTE, but who wish to use HRT, referral to a specialist centre with expertise in thrombophilia is recommended. Transdermal preparations may be preferred as they have a lesser effect on haemostasis compared to oral HRT.

**C Women starting COC, higher dose progestogens, oral HRT or raloxifene should be advised of the small absolute risk of VTE. Individual risk assessment in terms of family and personal history of VTE and additional risk factors should be made.**

**C A personal history of VTE is a contraindication to the use of COC and oral HRT.**

**C A family history of VTE (first degree relative) is a relative contraindication to the use of COC, higher dose progestogens, oral HRT and raloxifene, regardless of the results of thrombophilia screening.**

**C In current or recent users of COC, higher progestogen, oral HRT or raloxifene who are undergoing surgery, it is recommended that health care givers:**

- **Discuss the risks and benefits of stopping these hormones pre-operatively**
- **Arrange alternative contraception if COC is to be discontinued**
- **Consider thromboprophylaxis according to overall risk factors**
- **Give VTE thromboprophylaxis routinely in emergency surgery**

**Obstetrics**

**C All women should have an assessment of risk factors for VTE in early pregnancy or before pregnancy. The assessment should be repeated in the event of hospitalisation or the onset of any other intercurrent problems.**

**B Women with previous VTE should be screened for inherited and acquired thrombophilia according to local protocols ideally before pregnancy.**

**GPP Regardless of their risk of VTE, immobilisation of women during pregnancy, labour and the puerperium should be minimised and dehydration should be avoided.**

**C Women with previous VTE should be offered prophylaxis with low molecular weight heparin (LMWH) for six weeks after delivery.**

**C Women with a previous recurrent VTE (two or more), or a previous VTE which occurred in pregnancy, or with a family history of VTE in a first-degree relative or whose episode of VTE was in an unusual site eg. axillary vein or SVC), or who have significant residual clot burden from the previous VTE, should be offered thromboprophylaxis with LMWH antenatally and for at least 6 weeks postpartum.**

**B Women with previous VTE and thrombophilia should be offered thromboprophylaxis with LMWH antenatally and for at least six weeks postpartum.**

**B Women with asymptomatic hereditary or acquired thrombophilia should receive at least 6 weeks of postpartum thromboprophylaxis with LMWH. Depending on the specific thrombophilia and the presence of other risk factors, they may qualify for antenatal thromboprophylaxis. Those with combined defects, or who are homozygous for thrombophilic defects, or with antithrombin deficiency should receive antenatal thromboprophylaxis with LMWH as they are at especially high risk for VTE during pregnancy and the puerperium.**

**C** In pregnant women who have requested epidural anaesthesia during labour, stop the administration of LMWH when labour starts.

**C** LMWH can be administered or readministered three hours after atraumatic epidural or spinal anaesthesia, or removal of an epidural catheter.

**GPP** Patients should be warned to discontinue self-injections of LMWH as soon as they believe themselves to be in labour, and not restart until evaluation in hospital

**C** Women with APS and a history of VTE should also receive antenatal thromboprophylaxis with LMWH, and the postpartum thromboprophylaxis should be for at least 6 weeks.

**A** Women with APS and recurrent miscarriages should also receive antenatal thromboprophylaxis with LMWH from the diagnosis of pregnancy.

**C** Women with antiphospholipid syndrome should receive low dose aspirin antenatally to reduce the risk of pregnancy complications, and postpartum thromboprophylaxis with LMWH.

**C** Postpartum, the first dose of s/c LMWH should be given 6 hours after delivery.

**C** Where the patient does not wish to continue self-injecting, LMWH can be replaced by warfarin starting on the first or second postpartum day. The LMWH can be withdrawn when the INR has been within the target range (INR 2-3) for 2 consecutive days.

**C** There is no contraindication to breast feeding when the mother is being treated with LMWH, warfarin or other coumarins.

### **Gynaecology**

**C** All gynaecological patients scheduled for surgery should have a pre-operative risk assessment for VTE in order that a prospective management plan with respect to thromboprophylaxis is made.

**C Women starting COC, higher dose progestogens, oral HRT or raloxifene should be advised of the small absolute risk of VTE. Individual risk assessment in terms of family and personal history of VTE and additional risk factors should be made.**

**C A personal history of VTE is a contraindication to the use of COC and oral HRT.**

**C A family history of VTE (first degree relative) is a relative contraindication to the use of COC, higher dose progestogens, oral HRT and raloxifene, regardless of the results of thrombophilia screening.**

**C In current or recent users of COC, higher progestogen, oral HRT or raloxifene who are undergoing surgery, it is recommended that health care givers:**

- **Discuss the risks and benefits of stopping these hormones pre-operatively**
- **Arrange alternative contraception if COC is to be discontinued**
- **Consider thromboprophylaxis according to overall risk factors**
- **Give VTE thromboprophylaxis routinely in emergency surgery.**

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This consensus statement is produced on behalf of the College of Obstetricians and Gynaecologists, Singapore by:

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Valid until 2008  
unless otherwise indicated

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