



Coordinated by
FAMILY HEALTH DEVELOPMENT DIVISION
Ministry of Health, Malaysia

PREVENTION & TREATMENT of **THROMBOEMBOLISM** in Pregnancy and Puerperium **A TRAINING MANUAL**

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FOREWORD

Since the establishment of Confidential Enquiries into Maternal Deaths in Malaysia (CEMD) in 1991, the series of reports showed that the maternal deaths due to obstetric embolism had remained consistently high. Blood clot embolism accounts for approximately 55% of the total maternal deaths due to obstetric embolism. In the 2006-2008, 2009-2011, 2012-2014 triennial CEMD reports, there were a total of 39, 37 and 40 maternal deaths respectively that were attributed to blood clot embolism. This is however worrying trend of late, with the number of maternal deaths attributed to blood clot embolisms rising to 24 cases per year for 2015 and 2016.

While amniotic fluid embolism is often unpredictable and non-preventable, venous embolism (which also includes pulmonary embolism) is potentially preventable if appropriate measures are taken in a timely manner. In 2014, the first edition of the **Training Manual on Prevention and Treatment of Thromboembolism in Pregnancy and Puerperium** was published, following a decision made by the National Technical Committee of the CEMD. There has been significant development in the area of venous thromboembolism in pregnancy and puerperium since 2014 and a revision of the earlier training manual was deemed necessary.

Training is one of the cornerstones in bringing about a significant change in our practice, besides guidelines and policy. We are confident that with this training manual, we will mirror the success that we have had with the introduction of the **Training Manual on Management of Postpartum Haemorrhage**.

It is our fervent hope that the revised training manual not only will be able to increase the awareness, knowledge and the skills of our healthcare providers in caring for our obstetric patients but to have a venous thromboembolism screening program in pregnancy and puerperium that is more cost effective. With this enhanced state of preparation, we hope to reduce further maternal deaths due to embolic events.

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ABBREVIATIONS & ACRONYMS

ABG	Arterial Blood Gas	LNG	Levonorgestrel
APH	Antepartum Haemorrhage	LNG-IUD	Levonorgestrel – Releasing Intrauterine Device
ART	Assisted Reproductive Technology	NET	Norethisterone
BMI	Body Mass Index	NSAIDs	Non Steroidal Anti-Inflammatory Drugs
BP	Blood Pressure	O&G	Obstetrics and Gynaecology
CEMD	Confidential Enquiries into Maternal Death	OHSS	Ovarian Hyperstimulation Syndrome
COC	Combined Oral Contraceptives	PIH	Pregnancy Induced Hypertension
CTPA	Computed Tomography Pulmonary Angiogram	PR	Pulse Rate
Cu-IUD	Copper Intrauterine Device	PE	Pulmonary Embolism
CXR	Chest X Ray	POP	Progestogen-Only Pills
DMPA	Depot Medroxyprogesterone Acetate	PPH	Postpartum Haemorrhage
DVT	Deep Vein Thrombosis	PROM	Prelabour Rupture of Membrane
ETC	Etonogestrel	PT/PTT	Prothrombin Time/Partial Thromboplastin Time
FMS	Family Medicine Specialist	RFT	Renal Function Test
GFR	Glomerular Filtration Rate	SLE	Systemic Lupus Erythematosus
GSH	Group, Saved and Hold	SPD	Symphysis Pubis Dysfunction
ICU	Intensive Care Unit	TB	Tuberculosis
IVDU	Intravenous Drug User	UFH	Unfractionated Heparin
IPC	Intermittent Pneumatic Compression	V/Q	Ventilation/Perfusion
LFT	Liver Function Test	VTE	Venous Thromboembolism
LMWH	Low Molecular Weight Heparin		

INTRODUCTION

Obstetric Venous Thromboembolism (VTE) is a leading cause of direct maternal death in Malaysia and in many other developed countries. The annual VTE specific maternal mortality ratio in Malaysia from 2007 to 2016 is between **1.5 to 4.7 per 100,000 live births (Table 1)**. This is comparable to statistics from developed countries. A total of 155 maternal deaths were attributed to VTE in the 10 years period.

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Number of maternal deaths due to pulmonary embolism	7	23	12	15	10	13	12	15	24	24
Specific MMR per 100,000 live births	1.5	4.7	2.4	3.1	2.0	2.5	2.4	2.8	4.6	4.7

Table 1: Number of maternal deaths due pulmonary embolism and specific MMR per 100,000 live births 2007-2016.

Pregnancy increases the risk of VTE by 4 to 6 fold and the risk in the antenatal period is relatively higher in the first trimester and with advancing gestation. The risk in postnatal period is even higher and it may increase by 20 fold if the mode of delivery is by caesarean section. The MEGA study showed that the risk of VTE in the puerperium period is up to 84 fold higher compared to other periods in pregnancy.

The MBRRACE-UK 2015 report looking at VTE specific maternal mortality in the UK from 2009-2013 showed that approximately 70% of these women had significant VTE risk factors, indicating that the large majority of women at significant risk can be identified and as such if managed with thromboprophylaxis, their deaths could potentially have been prevented. The report further states that 52% of the women who died were not compliant to the RCOG VTE guidelines available during that period.

In Malaysia, the Clinical Practice Guidelines on the Prevention and Treatment of Venous Thromboembolism which was published in August 2013 and the 1st edition of the Training Manual for the Prevention and Treatment of Venous

Thromboembolism in Pregnancy and the Puerperium was published in 2014 recommends documented VTE risk assessment or stratification in pregnancy and in the immediate postpartum period. However, besides the state of Sarawak, it is not systematically practiced despite increasing awareness among clinicians.

The above mentioned national guidelines relating to VTE in pregnancy and the puerperium is based on the recommendations of the 2012 RCOG Green Top Guidelines 37a. A more recent 2015 RCOG guideline has since been published which include new risk factors and recommends longer postnatal thromboprophylaxis. The percentage of women requiring thromboprophylaxis is expected to increase further. There are other available guidelines being practiced in other countries, for example the Society of Obstetrics & Gynaecology in Canada (SOGC) and American College of Obstetricians & Gynaecologists (ACOG) recommend VTE prophylaxis only for those with a VTE risk of >1% during pregnancy and the puerperium.

The committee assigned to review the 2nd edition of the National VTE Training Manual has reached a consensus that it is not be practical nor cost effective to follow the 2015 RCOG guidelines and had decided that only women with higher risk of VTE should be given thromboprophylaxis. The committee decided to include only risk factors with an adjusted odds ratio of 3 or more in the risk assessment form. Consequently, the threshold for recommending commencement of thromboprophylaxis in Malaysia, though higher than that of the UK, will still be lower than that of other developed nations like Sweden, Canada or the United States.

VTE in pregnancy is a major but potentially preventable cause of maternal death and morbidity. The impact of a VTE risk screening program as suggested in this training manual would be dependent on the level implementation nationally, both in health clinics and hospitals across Malaysia.

This VTE Training Manual is primarily intended to be used for the training of health care providers both in health clinics and hospitals. Besides recommending a standardized approach for documented VTE risk stratification, the prevention of VTE through lifestyle measures, mechanical and medical thromboprophylaxis will be discussed. This VTE Training Manual will also provide a guide to the diagnosis of VTE and illustrate treatment protocols for suspected and confirmed cases of VTE.

SUMMARY & RECOMMENDATIONS FROM THE MALAYSIAN CEMD REPORT 2012–2014

Summary

There were a total of 69 deaths due to obstetric embolism in the period from 2012 to 2014, with 40 deaths (58.8%) due to blood clot embolism and 29 deaths (41.2%) due to amniotic fluid embolism. The number of deaths was similar to the 2009 to 2011 report with 69 deaths but the number of deaths from obstetric embolism increased slightly from 37 in the previous report to 40 deaths.

The annual cause specific MMR for blood clot embolism were 2.5, 2.4 and 2.8 respectively for 2012 to 2014 and 1.9, 2.0 and 1.7 respectively for Amniotic Fluid Embolism. The mortality ratio for these two conditions per 100,000 live births did not show any significant difference with the ratio determined in the previous reports.

In the current review, associated medical conditions remained as the commonest cause of maternal deaths but blood clot embolism remained as a significant cause of direct maternal deaths.

The majority or 69.1% of the deaths from obstetric embolism occurred in hospitals with the presence of specialists and interestingly, 52.9% of the women who died had caesareans section.

Guidelines on obstetric venous thromboembolism are widely available and these include the 2012 RCOG Green Top Guidelines No. 37a and the Malaysian Clinical Practice Guideline on "*Prevention and Treatment of Venous Thromboembolism (VTE)*" which was published in August 2013. These guidelines proposed performing documented VTE risk screening of all obstetric patients and providing thromboprophylaxis to those at risk.

There should be an audit of the compliance to thromboprophylaxis guidelines in all obstetric units and health clinics where antenatal and postnatal care, are being provided. Efforts in improving awareness and ensuring the universal implementation of existing CPG on VTE in pregnancy, should be improved.

Recommendations

1. There should be research on the linkage between practices such as dietary restrictions and postpartum practices with blood clot embolisms. The role of health education in modifying such practices should also be looked at.
2. There should be a national audit of the implementation and compliance to existing CPG on venous thromboembolism (VTE) in pregnancy and the puerperium.
3. All obstetric units should implement the recommendations stated in training manuals and CPG on the prevention and treatment of VTE in pregnancy and the puerperium.
4. Primary healthcare clinics attending to antenatal mothers should routinely perform VTE risk scoring at antenatal booking as recommended in the *“Training manual: Prevention & Treatment of Thromboembolism in Pregnancy & Puerperium”*. Those who are assessed as intermediate or high risk for VTE should be managed accordingly (or whenever new risk emerges).

OBJECTIVES

General Objective

To develop a comprehensive, updated and evidence based training manual on the prevention and management of venous thromboembolism in pregnancy and puerperium; based on the risk and available resources in Malaysia.

Specific Objectives

1. To appreciate the significance of venous thromboembolism in pregnancy and its association with maternal mortality and morbidity.
2. To highlight the pathophysiology of venous thromboembolism in pregnancy and the importance of prevention.
3. To create awareness on the importance of recognition of risk factors that may predispose to thromboembolic disease in pregnancy in order to appropriately risk stratify patients.
4. To appreciate the signs and symptoms of venous thromboembolism in pregnancy and the available diagnostic modalities and management options.
5. To empower and to train all categories of staffs on the importance of prevention and management of thromboembolism in pregnancy. Patient safety issues are also highlighted in the form of a checklist to ensure completeness.
6. To standardize referral procedures for a woman with suspected venous thromboembolism.

DEFINITION & PATHOPHYSIOLOGY OF THROMBOEMBOLISM

Definition

Thromboembolism describes a spectrum of disorders characterized by thrombosis.

If it happens in the venous circulation, it is described as venous thromboembolism and as a sequel, if it happens in the lung; it is defined as pulmonary embolism.

Obstetric embolism traditionally incorporates both thrombosis and amniotic fluid embolism. Obstetric thromboembolism is limited to thrombosis in pregnancy and puerperium.

Physiology of Haemostasis

1. Hemostasis is a complex process that requires the interplay of multiple physiological pathways. Cellular and molecular mechanism interact to seal damaged blood vessels with localized clot formation preventing significant bleeding.
2. The three mechanisms of primary haemostasis include:
 - a. Vasoconstriction (usually lasting a few minutes).
 - b. Primary platelet aggregation.
 - c. Fibrin deposition.
3. The subsequent activation of the coagulation cascade (intrinsic pathway) re-enforces the clot.
4. Anticoagulation mechanisms keep the clot size in check. It is subsequently responsible for the dissolution of the clot following healing of the vascular endothelium.
5. The normal balance between coagulation and anticoagulation is key to normal haemostasis.

Pathophysiology of Thrombosis

1. Thrombosis occurs when there is disruption of the Virchow's triad; namely endothelium injury, stasis of blood and a hypercoagulable state.

2. Modifications to haemostasis in pregnancy renders blood hypercoagulable despite normal coagulation profile in-vitro.
3. In addition to the modifications in pregnancy, certain conditions specific to pregnancy further contribute to thrombogenesis.

Example: Pre-eclampsia promotes thrombogenesis via several mechanisms:

- **Haemoconcentration:** Increased vascular permeability causes intravascular fluid shift to the extravascular compartment.
- **Vascular endothelial injury:** It is postulated that the systemic deposition of inflammatory complements cause vasculitis thus inviting thrombogenesis.

The diagnosis prompts hospital admission, further limiting the mobility of affected patients.

Modifications in Pregnancy

1. Pregnancy is a hypercoagulable state. These changes are observed from the first trimester and for at least 6 postpartum weeks.
2. There is a peak in coagulation immediately postpartum and tends to tail off after the 3rd postpartum week.
3. Venous stasis is exaggerated in pregnancy with venodilation, compression of the gravid uterus on the inferior vena cava and the impression of the left infundibulopelvic vessels on the iliac vein.

Clotting factors that increase in pregnancy	Clotting factors that fall in pregnancy
Factor VIII	Antithrombin
Factor IX	Protein S
Factor X	Reduce is fibrinolytic activity
Fibrinogen levels rise by 50%	

Table 2: Modifications of clotting factors in pregnancy.

RISK FACTORS AND PREVENTION OF VTE

A. Risk Factors & Score for Venous Thromboembolism in Pregnancy & Puerperium

Types of risk	Specific Risk	Risk score
Pre-existing	Previous thromboembolism.	4
	High risk thrombophilia.	3
	Medical comorbidities. (e.g. - malignancies, cardiac failure, active SLE, active TB, IVDU, nephrotic syndrome, diabetic nephropathy, thalassemia major or intermedia post splenectomy)	3
	Obesity: BMI $\geq 40\text{kg/m}^2$	2
	BMI 30-39 kg/m^2	1
	Current smoker (≥ 10 per day).	1
	Family history of VTE .	1
	Low risk thrombophilia (factor V Leiden, High FVIII).	1
Obstetric risk	Caesarean section (elective & emergency).	2
	Pre-eclampsia.	1
	Rotational instrumental delivery.	1
	Prolonged labour (>24 hours).	1
	PPH ($\geq 1,000\text{mls}$) or requires blood transfusion.	1
	Stillbirth (current).	1
	IVF (1 st trimester risk only).	1
Transient*	Surgical procedures (excluding episiotomy 1 st and 2 nd degree perineal tear repair, evacuation of retained products of conception).	4
	Hyperemesis gravidarum/OHSS.	4
	Immobility/Dehydration/Admission beyond 3 days.	1
	Systemic/Postpartum infection.	1

Types of risk	Specific Risk	Risk score
	Long distance travel (>4 hours).	1

***Note:** Thromboprophylaxis is recommended during the transient period. Consider stopping once the transient risks are deemed no longer significant.

Table 3: Risk factors & score for venous thromboembolism in pregnancy and puerperium.

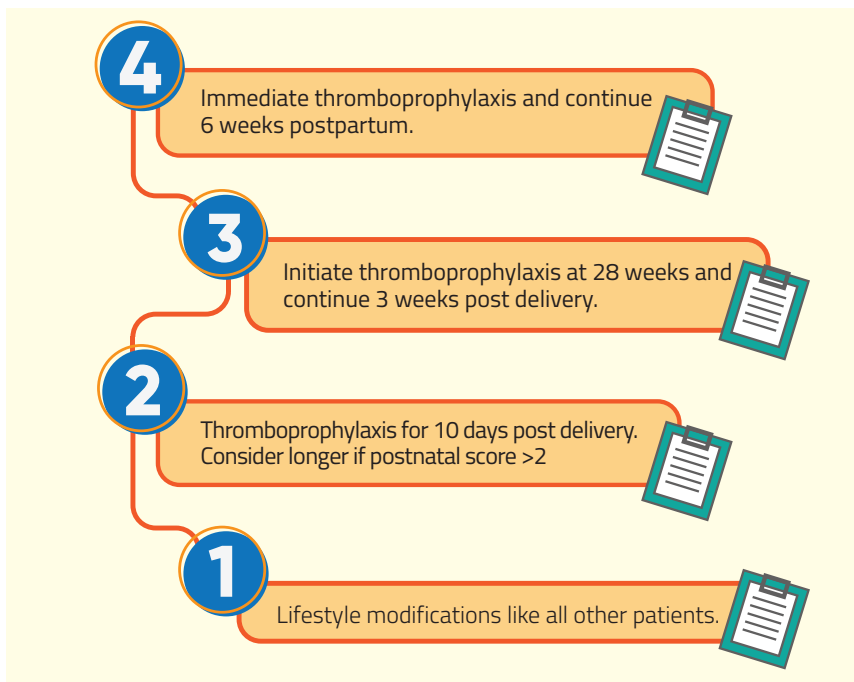
B. Prevention of Obstetric Thromboembolism

1. All women should have a documented thromboembolism risk assessment during

Pre-pregnancy	Booking	Admission/ New illness	Immediate postpartum
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Note: This should be in a form of a numerical score. This can be performed by all categories of trained health care professionals.

2. All women should be risk stratified into four groups and below are the recommendations



Note:

1. All patients should be counselled on lifestyle modifications and VTE prevention.
2. All patients with a score of 3 or more should be assessed at 3 weeks post delivery on the need for longer thromboprophylaxis. This can be done by the FMS or medical officer.
3. Women with previous VTE or underlying thrombophilia should be managed in collaboration by a haematologist and ideally seen in the pre-pregnancy clinic.
4. Women with anti-thrombin III deficiency and anti-phospholipid syndrome require higher prophylactic dose.

3. Thromboprophylactic agents of choice

i) Low Molecular Weight Heparin (LMWH)

- a. LMWH is the agent of choice for thromboprophylaxis. It is more convenient with regards to daily administration, with a proven safety profile in pregnancy and does not require frequent monitoring of platelets. It is safe in breastfeeding but may require dose adjustment in patients with renal impairment.
- b. It should be administered based on the pre-pregnancy or booking weight.

Body weight (kg)	Enoxaparin	Dalteparin	Tinzaparin
<50kg	20mg daily	2,500 units daily	3,500 units daily
50-90kg	40mg daily	5,000 units daily	4,500 units daily
91-130kg	60mg daily	7,500 units daily	7,000 units daily
131-170kg	80mg daily	10,000 units daily	9,000 units daily
>170kg	0.6mg/kg/day	75 units/kg/day	75 units/kg/day

- c. LMWH is contraindicated in patients with
 - i. Significant risk of bleeding.
 - ii. History of drug allergy to LMWH.

ii) Unfractionated Heparin (UFH)

- a. This is the anticoagulant of choice in patients with massive pulmonary embolism or in patients with cardiorespiratory compromise.

- b. UFH may also be used in the peripartum period in patients who are at an increased risk of thrombosis, haemorrhage or where regional anaesthetic techniques may be required.
- c. The recommended dosage of UFH as prophylaxis is 5,000 units 12 hourly for a patient weighing between 50–90kg. Currently, there is lack of evidence in terms of efficacy and safety for those in extreme weights (<50kg and >90kg).
- d. Patients on UFH will require platelet monitoring every 2–3 days from days 4–14 or until heparin is stopped.

iii) Fondaparinux

There is still insufficient evidence with regards to the safety of Fondaparinux in pregnancy as it crosses the placenta and is excreted in minute amounts in breast milk. Current recommendations suggest that it should only be used in cases where there is hypersensitivity towards heparins. It also has a longer half-life and there is no known antidote.

iv) Non-vitamin K Antagonist Oral Anti-Coagulants (NOACs)

NOACs should be avoided in pregnant women due to the lack of clinical evidence.

4. Timing of initiation

This depends on the patient's thromboembolism risk scoring.

- i. Those with an antenatal score of 4 or more should have it initiated as soon as possible.
- ii. Those with an antenatal score of 3 should have it initiated after 28 weeks.
- iii. It can be initiated post delivery between 4–6 hours following delivery/caesarean section.

5. Labour & delivery

- i. There is no contraindication for vaginal delivery for patients on LMWH, but vigilance for PPH is recommended.
- ii. Patients should be advised to omit their LMWH dose if they have signs or symptoms of labour or bleeding and to seek medical attention immediately.

- iii. Regional analgesia should be avoided until at least 12 hours from the last prophylactic dose of LMWH.

6. Postpartum thromboprophylaxis

- i. The first thromboprophylactic dose of LMWH should be given as soon as possible after delivery provided there is no postpartum haemorrhage and regional analgesia has not been used.
- ii. LMWH should not be given for 4 hours after use of spinal anaesthesia or after the epidural catheter has been removed and the catheter should not be removed within 12 hours of the most recent injection.
- iii. If a woman develops a haemorrhagic problems while on LMWH, the treatment should be stopped and expert haematological advice sought.
- iv. Breastfeeding is not contraindicated in patients taking LMWH. In certain high risk patients who need longer thromboprophylaxis, the options of conversion to warfarin can be discussed in the post partum period.

DIAGNOSIS OF VENOUS THROMBOEMBOLISM

All women suspected to have thromboembolism should have an objective testing performed to confirm or negate the diagnosis of thromboembolism.

Treatment should be initiated while awaiting confirmatory test.

D-dimer is not recommended to be performed in the investigation of acute thromboembolism.

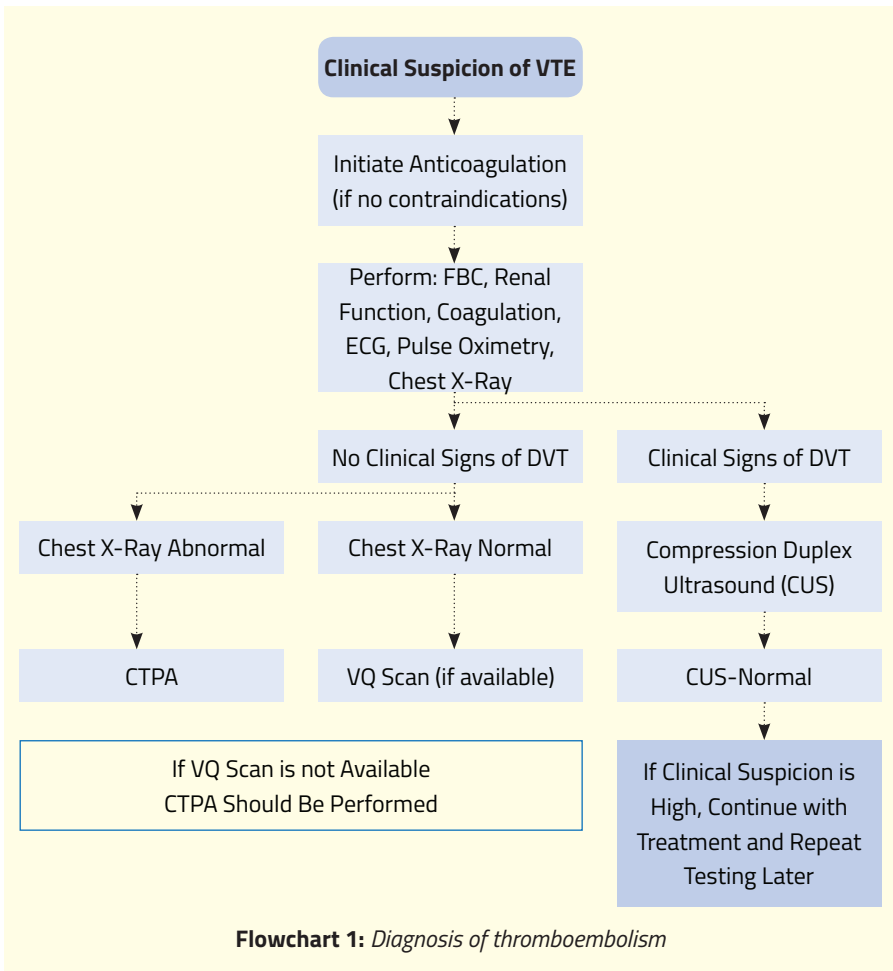
Thromboembolism can present with a myriad of clinical symptoms and signs.

The health care provider should actively enquire about the symptoms and look for the signs suggesting these conditions.

Venous Thromboembolism	Pulmonary Embolism
<p>Symptoms</p> <ol style="list-style-type: none"> 1. Unilateral swelling of limb. 2. Claudication pain. 3. Heavy ache in the limb. 	<ol style="list-style-type: none"> 1. Sudden onset of shortness of breath. 2. Chest pain – dull, worsened on inspiration. 3. Non productive cough (occasionally blood stained).
<p>Signs</p> <ol style="list-style-type: none"> 1. Swelling – non pitting. 2. Increased warmth of lower limb. 3. Reduced capillary filling. 4. Fever. 	<ol style="list-style-type: none"> 1. Tachypnoeic. 2. Tachycardia. 3. Cyanosis (if severe). 4. Cardiorespiratory compromise or sudden collapse.
<p>Investigations</p> <ol style="list-style-type: none"> 1. Full blood count, renal, liver function and coagulation. 2. Pulse oximetry. 3. Compression duplex ultrasonography (<i>Modality of choice. Focus should be on the ilio-femoral and popliteal vessels.</i>) 4. Venogram Although this is the gold standard, it is associated with radiation risk and is rarely utilized in pregnancy. 	<ol style="list-style-type: none"> 1. Arterial blood gas (ABG). 2. Chest radiograph. 3. ECG <i>There may be sinus tachycardia. S1,Q3TIII are rarely seen in pregnancy. In severe cases, right axis deviation, right bundle branch block and peaked P wave in Lead II may be evident.</i> <ol style="list-style-type: none"> i. CTPA (CT Pulmonary Angiogram) Has significant breast radiation exposure. Likely to be normal if chest x-ray is normal.

Venous Thromboembolism	Pulmonary Embolism
	ii. Lung ventilation-perfusion scan (V/Q) Lifetime risk for paediatric cancers is rare.

Note: VTE more commonly involves the ilio-femoral vessels of the lower limb as compared to lower popliteal vessels in the non pregnant patient.



CTPA	V/Q scan
<p>Advantages</p> <ul style="list-style-type: none"> ▪ More readily available. ▪ Low radiation to fetus. ▪ May diagnose other pathology such as pneumonia, pulmonary oedema and aortic dissections. 	<ul style="list-style-type: none"> ▪ Higher negative predictive value. ▪ Low radiation to maternal breast.
<p>Disadvantages</p> <ul style="list-style-type: none"> ▪ May not detect small periphery embolism. ▪ Slight increases risk of maternal breast cancer. ▪ Neonatal hypothyroidism. 	<ul style="list-style-type: none"> ▪ Very small increased risk of childhood cancer.

Table 3: *Difference between CTPA & V/Q scan*

MANAGEMENT OF ACUTE VENOUS THROMBOEMBOLISM

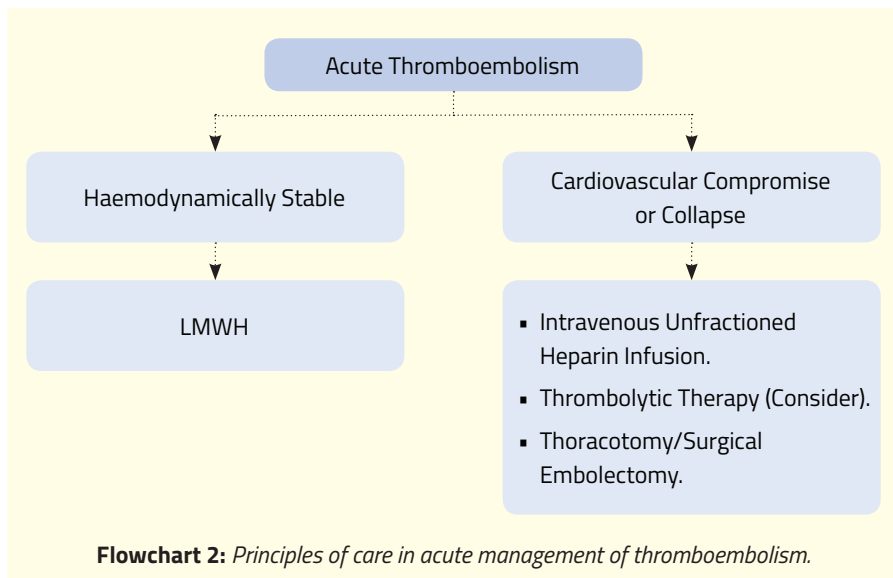
Think of thromboembolism in any women who is

- i. Unwell
- ii. Has cardiovascular compromise
- iii. Maternal collapse

1. Thromboembolism is a medical emergency associated with significant morbidity and mortality. An O&G specialist should be consulted if there is a clinical suspicion of thromboembolism and treatment should be initiated as soon as possible. The patient than can be referred to the regional tertiary hospital with O&G Specialist for further confirmatory investigations. Once the diagnosis is confirmed, the patient should be co-managed with a haematologist or physician.
2. Women who complain of sudden calf pain (usually unilateral) and swelling should be assessed for possibility of deep vein thrombosis (DVT).
3. Women who complain of sudden onset of chest symptoms (dull ache on inspiration or sharp pleuritic pain, shortness of breath or cough without haemoptysis) should be assessed for possibility of pulmonary thromboembolism (PTE). Such cases should be referred to O&G specialist immediately.
4. Lower limb deep vein thrombosis (ilio-femoral) is more common in pregnancy. Outside pregnancy DVT occurs more in the superficial calf (popliteal and foot) regions. The preponderance of DVT of the left lower limb to right is almost 9:1 in pregnancy.
5. Treatment should be commenced immediately after specialist consultation. A multidisciplinary approach involving a haematologist or a physician is essential.
 - a. All suspected cases of DVT/PTE should have treatment commenced upon clinical suspicion of VTE. Objective confirmation of thromboembolism should be performed once modality and its expertise become available. Diagnosis should not delay commencement of treatment.
 - b. Thrombophilia screening (acquired and inherited) is not necessary prior to commencement of heparin treatment. Investigations for thrombophilia

can be carried out later after completion of treatment.

- c. Definitive diagnosis should be pursued via an objective method of testing without undue delay after commencement of treatment.



Clinically Stable	Clinically Unstable
Treatment dose of LMWH (weight adjusted) No routine monitoring of Anti-Xa activity unless:	Heparin infusion
1. Extreme of weight.	1. Loading Dose – 80 units/kg.
2. Develops new thrombus.	2. Maintenance – 18 units/kg/hour and monitor APTT.
3. Renal impairment.	Thoracotomy
	Surgical embolectomy

- d. In patients who are haemodynamically stable; LMWH is the treatment of choice.
- e. LMWH is superior to UFH in terms of efficacy with a more predictable half life.

- f. UFH is associated with more side effects; especially with its association with thrombocytopenia and the need for frequent monitoring.
- g. The following LMWHs are recommended in pregnancy:

Enoxaparin	Adequate safety data
Tinzaparin	Adequate safety data

- h. Women who are allergic to heparins or have developed heparin resistance (antibodies) should be treated with heparinoids.
 - i. There is limited data of safety and efficacy of Fondaparinux in pregnancy.
 - j. LMWH (subcutaneous).
 - i. Routine monitoring of platelet counts is not indicated.
 - ii. Anti-Xa level monitoring is not indicated unless when the weight is less than 50kg or more than 90kg. The target level is 0.5-1.2.
 - iii. Sampling should be done 4 hours post dose.
 - k. UFH.
 - i. Subcutaneous: 10,000 BD to be adjusted to achieve a PTT 1.5-2.5 control.
 - ii. Intravenous:
 - a. Bolus: 80 units/kg
 - b. Infusion: 18 units/kg/hour
 - iii. aPTT target: 1.5 to 2.5 control.
 - iv. Platelet counts to be monitored daily during IV treatment and weekly for 4 weeks then monthly during SC treatment. Heparin-induced thrombocytopenia is a rare idiosyncratic complication of UFH.
 - l. In women who are unable to tolerate heparins, heparinoids such as danaparoid sodium or fondaparinux can be used.
6. Duration of treatment
- a. Total of 3 months of treatment is recommended.
 - b. In pregnancy therapeutic doses is to be continued through pregnancy till 6 weeks postpartum. At 6 weeks postpartum therapy should be extended to complete a minimum total treatment duration of 3 months.

7. Peripartum

- a. Women should be advised to stop LMWH 24 hours before a planned delivery (induction or caesarean).
- b. Women should be advised to omit injection at onset of labour and to seek a review by a medical personnel in the following:
 - i. Leaking liquor
 - ii. APH
 - iii. Contractions
- c. Regional anaesthesia is contraindicated if the last therapeutic dose was less than 24 hours ago OR if the last prophylactic dose was less than 12 hours ago. If a patient on therapeutic doses of anticoagulant undergoes caesarean section, placement of drainage tubes should be considered.
- d. Postpartum
 - i. Active management of 3rd stage.
 - ii. PPH prophylaxis should be instituted: Blood grouped and saved, IV access and 40 units oxytocin infused after delivery of placenta.
 - iii. Therapeutic dose can be recommenced 4 hours postpartum (also for operative delivery).
 - iv. Epidural placement should be delayed until at least 24 hours after the last dose and epidural removal should be more than 12 hours after the last injection.
 - v. Use of warfarin for maintenance therapy may be considered.
 - vi. Women should be counselled that both heparins and warfarin are safe during breastfeeding.

8. Adjunct treatment

- a. Raise affected limb.
- b. Compression stockings for at least 2 years in the affected limb.
- c. Analgesia (avoid NSAIDs especially after 32 weeks).
- d. Consider caval filter if:
 - i. Recurring despite adequate anticoagulation.
 - ii. Non-resolving or worsening emboli.

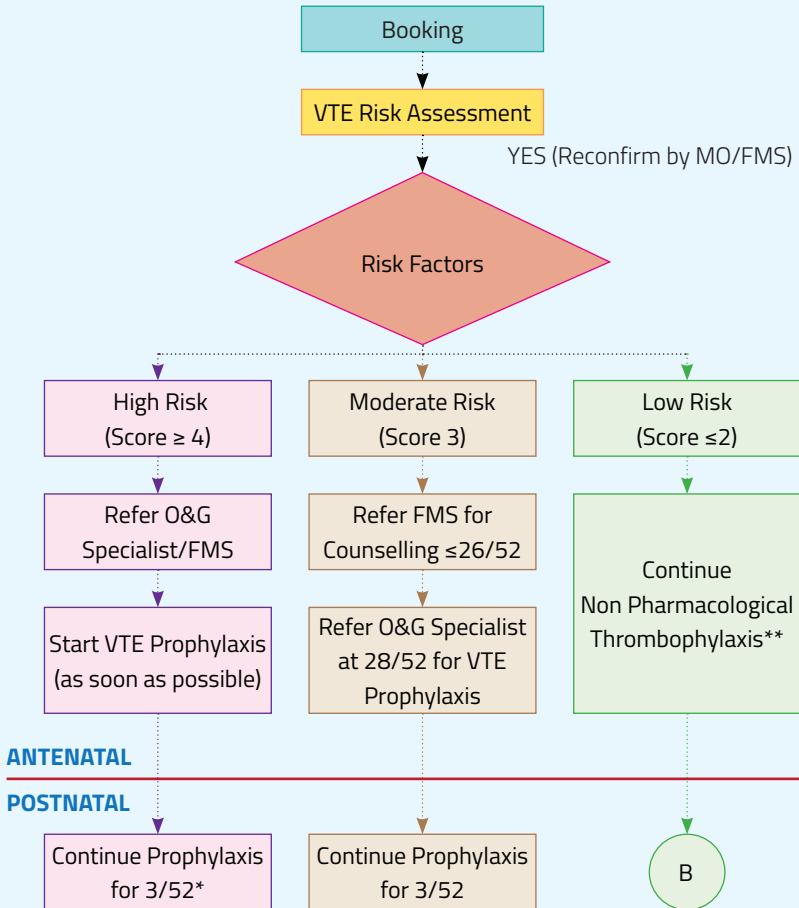
9. In severe cases of PTE with cardiorespiratory compromise
 - a. Consider thrombolytic therapy (streptokinase or urokinase) although no clear survival benefits have been established. Complications include 3-5% non-fatal maternal haemorrhage and 2% fetal demise.
 - b. If all fails, to consider thoracotomy after cardiothoracic input.
10. Prevention of post-DVT limb syndrome
 - a. 60% of women develop this condition characterized by chronic swelling and pain.
 - b. Wearing graduated compression stockings (DVT stockings) for 2 years on the affected limb reduces this by more than half.

VTE RISK ASSESSMENT IN PRIMARY HEALTH CARE

All women should have their VTE risk assessment done during pre-pregnancy, booking, inter-current illness and immediate postnatal period.

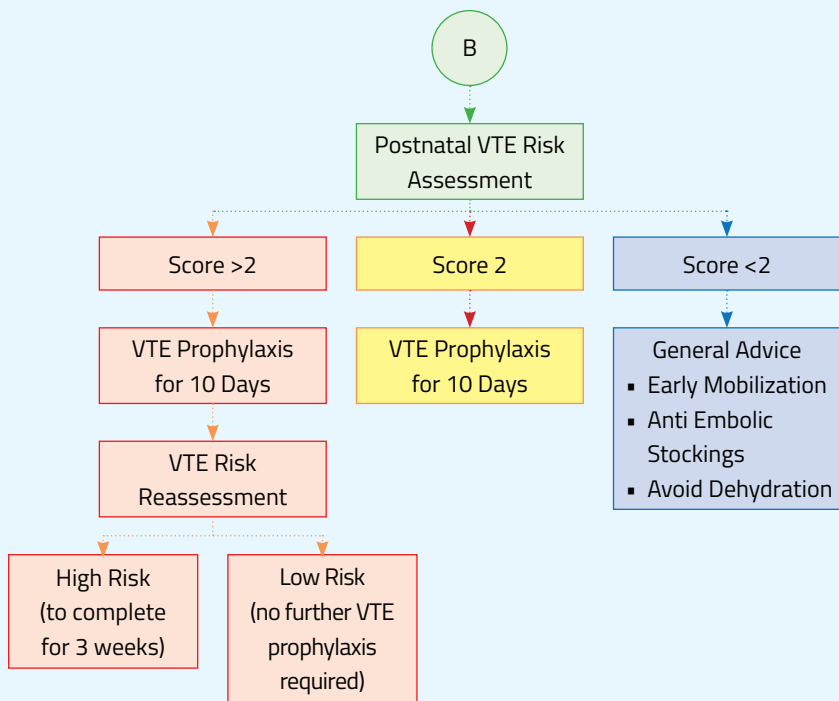
IN GENERAL

1. All antenatal mothers attending Health Clinics for booking must be assessed for VTE risk using a VTE checklist.
2. Patients with an antenatal score of 3 or more requiring thromboprophylaxis should be discussed/referred to an O&G specialist/FMS.
3. All mothers who delivered in the hospital, alternative birthing center, health clinics, home delivery or birth before arrival should have a documented VTE risk assessment.
4. All patients at low risk should be advised on non-pharmacological thromboprophylactic measures such as anti-embolic stockings, avoidance of dehydration and early ambulation.
5. Initiation of pharmacological thromboprophylaxis can be undertaken when the thromboprophylactic agents are available.



* Consider additional 3 weeks prophylaxis in certain high risk patients (at the discretion of O&G specialist).

** Non pharmacological thromboprophylaxis measures e.g. anti embolic stockings, avoid dehydration, early mobilization.



REFERRAL PATHWAYS

A. Patients with Risk Factors

Pre-pregnancy

- a. Patients who are contemplating pregnancy who have a significant risk of developing DVT or PE during pregnancy should be referred to the pre pregnancy clinic where risks can be discussed and appropriate management instituted. This should include patients with:
 - i. Previous history of VTE/PE
 - ii. Thrombophilia
 - iii. Antiphospholipid syndrome
 - iv. Other risk factors – obesity, elderly, hypertensive, those planning IVF/ICSI to conceive, smokers, varicose veins, paraplegia etc.
- b. These patients should be referred early to pre-pregnancy clinic and should be seen by a specialist.

Antenatal

- a. Mothers in the antenatal period should be routinely assessed for risks of VTE in the clinic at booking, when she develops new VTE risk factors and during admissions.
- b. The initial assessment at booking, can be performed by nurses. If the score is 3 or more, these mothers should be referred to the medical officer to confirm the risks. This initial referral to the medical officer should be immediate if possible or within 72 hours. Referral by phone is acceptable in certain situations.
- c. Risks assessment during admission should be done by the medical officer.
- d. Mothers requiring thromboprophylaxis in the antenatal period, should be referred to a FMS or O&G specialist.
- e. Initiation of thromboprophylaxis should be done in a hospital if LMWH or unfractionated heparins are not available in health clinics
- f. Patients who are assessed as having low risk should be counselled appropriately and can continue with their normal antenatal care unless otherwise indicated.

Postpartum

- a. All patients should have their risks reassessed in the immediate postpartum period, if they are assessed as low risk antenatally. This is especially important for patients who may have had:
 - i. Caesarean section.
 - ii. Instrumental delivery.
 - iii. Complicated/prolonged labour.
 - iv. Sepsis.
 - v. Complications during labour e.g. Eclampsia, PPH.

B. Patients suspected to have VTE or PTE

This is an obstetric emergency. Patients who are suspected to have VTE or PE should be referred immediately to the nearest Hospital.

They should be coded RED

Patients should be sent to the nearest Hospital accompanied by an appropriately trained staff. This should be a medical officer where possible. If an Obstetric Retrieval Team is available at a nearby hospital, this Retrieval Team should be optimized.

The patient should be stabilized prior to transfer.

If available, the first dose of anticoagulant should be given by the attending doctor prior to transfer.

During transfer the following equipment should be available.

1. Vital signs monitor including pulse oxymeter.
2. Oxygen and high flow mask.
3. Equipment and drug for maternal resuscitation.

On arrival at hospital:

District Hospital without Specialist

Medical Officers should fully assess the patient. After assessment, the case should be discussed with the obstetrician/physician/hematologist at the nearest Specialist Hospital. Decision should then be made:

1. If the VTE is suspected, treatment should be initiated.
2. If there is a need to further investigate.
3. If the patient should be transferred to the nearest Specialist Hospital.

Hospital with Specialist

Patient should be reassessed.

Treatment should be initiated if the diagnosis is probable and without waiting for further investigations.

Patient should be managed by a multidiscipline team consisting a radiologist, hematologist, physician and anaesthetist. In cases of Pulmonary Embolism, patient will need to be monitored in Intensive Care or in a High Dependency Unit.

CONTRACEPTION & VENOUS THROMBOEMBOLISM

The combined contraceptive pill is associated with a risk of VTE of 15 per 100,000 women years as compared to 5 per 100,000 women years in non users.

This risks further increases to 25 per 100,000 women years in contraceptives containing desogestrel or gestodene. Risks are also higher with combinations that have a higher dose of ethinylestradiol.

This chapter will address contraceptive needs for women at risks of VTE as well as for women with a history of VTE/PTE and will reference the WHO Medical Eligibility Criteria for Contraceptive Use (WHO, MEC, 5th edition, 2015).

In General

1. Women who have a higher risk of VTE or with a history of venous thromboembolism should avoid the combined hormonal contraception (COC and CIC).
2. Progestogen only contraception are safe. Examples include:
 - a. Progestogen-only pill (POP)
 - b. Depot Medroxyprogesterone Acetate (DMPA) and Norethisterone
 - c. The LNG implants
3. Intrauterine devices can be used once the uterus has returned to normal size or in post miscarriage patients.
4. Barrier methods are safe.

CASE DISCUSSIONS

Case 1. Postnatal DVT (*high index of clinical suspicion*)

A 32 year old G6P3+1 @ 38w2d, with booking BMI 23.8kg/m², with non significant personal medical nor antenatal history, presents in spontaneous labour on 22/7/2013. She delivers a healthy baby with EBL 250ml at 11pm of 22/7/2013.

During the postnatal round the next morning (about 11 hour post-SVD), patient complained of left lower limb soreness, examination of which was unremarkable – not swollen, not warm, no redness, except for slight soreness on deep compression. Vital signs were stable, ECG did not show any changes. However CUS revealed short segment DVT of left saphenofemoral vein.

She was started on S/C LMWH and subsequently bridged with warfarin for a total of 3 months. A repeat CUS showed resolved DVT.

1. What was her VTE risk factor? Would she require thromboprophylaxis?
None; no.
2. What led the attending doctor to request for CUS?
Left lower limb soreness, high index of suspicion.
3. What is the calculation for treatment dose of LMWH?
**Tinzaparin: 175u/kg daily;
Enoxaparin according to weight or 1mg/kg BD or 1.5mg/kg daily.**
4. Was a repeat CUS after completion of treatment necessary?
No, thrombus may remain to be present, especially if calcified. Request for any imaging test is based on clinical assessment.
5. Lesson learned from this patient?
Enquire ALL patients of VTE symptoms, irrespective of risk scoring.

Case 2. Postnatal DVT (*management in district hospital*)

A 23 year old G2P1 at term underwent an EMLSCS for non-reassuring fetal status and received postnatal thromboprophylaxis with LMWH for 7 days (as was the protocol then). Her BMI was 38.7kg/m² on booking, and had no significant personal or antenatal history.

By postnatal day 24, patient contacted her nurse. Upon visiting the patient at home, patient revealed that she had been having fever for 4 days, left leg swelling for 2 days and generally felt unwell. Examination by nurse at home was not remarkable but she brought the patient to the nearest district hospital nevertheless since patient complained of feeling unwell.

In the ED, patient was found to be tachycardic at 108bpm, however there was no fever or tacypnoea. Her left calf measured 42.5cm as compared to her right calf of 39.5cm. ED MO then made the diagnosis of possible DVT and referred to O&G Specialist on call of a tertiary hospital. Despite being told to send the patient to the specialist hospital immediately, the ED MO waited for results before sending the patient. ECG showed sinus tachycardia, her ABG and blood investigations were normal.

Patient subsequently had a confirmation by CUS showing long segment left lower limb DVT. She was treated accordingly.

1. What were her VTE risk scores?
Score 3 (BMI >30kg/m² score 1; EMLSCS score 2).
2. Was the duration of postnatal thromboprophylaxis adequate?
Yes. RCOG 2009 guidelines stated 7 days prophylaxis. However since the latest updated guidelines of 2015, it has now being extended to 10 days.
3. What were the signs & symptoms that should draw your attention to diagnosis of DVT?
Patient's complaint of leg pain & fever, difference in calf circumference, tachycardia.
4. What would you have done differently if you were the ED MO in the district hospital?
Start treatment before transferring patient (if instructed by O&G Specialist), send patient without waiting for investigation, do not delay in transfer.
5. Lesson learned from this patient?
Act promptly once VTE is suspected – Specialist should be clear in the directive to start treatment first (LMWH is generally available in non-specialist district hospital), investigation to follow later. Need to enhance nurses' capability in VTE management.

Case 3. Postnatal PE (*clinical signs*)

A 36 year old G2P1+2 at term was admitted on 5/1/17 for IOL for hypertension complicating pregnancy. On 8/1/17, 4 hours after entering active phase of labour, she was noted to have temperature 37.6°C with HR104 bpm and a non reactive CTG, hence posted for EMLSCS. Her LSCS was uneventful with an EBL of 300ml.

Two hours post-operation, noted temperature increased to 38.9°C with HR116 bpm. Septic workout performed and IV antibiotics commenced. S/C Unfractionated heparin 7500u BD was started 6-hours post operation as per department protocol and patient's choice (declined LMWH).

Patient's fever settled on 10/1/17 after 2 days of antibiotic, however there was persistent tachycardia. Having ruled out anemia and thyroid dysfunction, she was then subjected to ECG (sinus tachycardia, no S1Q3T3), and ABG (which revealed hypoxia). A decision was made to rule out Pulmonary Embolism, she was switched from UFH to treatment dose of LMWH, while arrangement was made for CTPA the next day. By the same evening, her leptospirosis result came back as positive and antibiotic was optimized.

CTPA reported a Right Pulmonary Embolism involving the segmental branches of right middle and low lobe. Bilateral lower lobes plate atelectasis and right lower lobe pleural base consolidation.

She was bridged with warfarin and planned for 3 months of treatment.

1. What were her VTE risk factor(s)?
Prolonged admission (>3days), BMI 30.5kg/m² on admission, EMLSCS.
2. Would you have considered antenatal thromboprophylaxis in view of her VTE risk?
As she was already being induced, only compression stockings were prescribed with advice for ambulation in ward and maintenance of good hydration. Pharmacological thromboprophylaxis was commenced only after delivery.
3. What would be your choice of thromboprophylaxis agent?
LMWH is superior than UFH.
4. What are the lessons learned from this patient?
Maintain high index of suspicion. Do not assume VTE does not occur in patient already started on thromboprophylaxis (in this patient - UFH).
Start treatment first before performing CTPA (as this often required preparation eg fasting).

Case 4. Postnatal PE (*risk factors, clinical signs*)

A 36 year old Para 5, a known active smoker (>10 sticks/day), with booking BMI of 25.2kg/m², and no other significant personal or antenatal history, delivers on 14/12/2015 and had PPH of 1.2L. She had been complaining of left lower limb swelling since postpartum 1 week and thus went to her nearest health clinic. However she was dismissed as having musculoskeletal pain. She subsequently went to GP twice without any improvement.

By postpartum day 24, she went again to the same health clinic and seen by the same MO, this time with worsening leg symptoms (swelling and pain), again she was dismissed with pain killers.

On postpartum day 29 (12/1/2016), she came to the ED of her nearest hospital with worsening leg swelling and pain, with additional complaint of shortness of breath and chest pain. A diagnosis of left DVT with possible Pulmonary Embolism was made and treatment with LMWH was commenced before any imaging tests were done.

Venous Doppler study revealed long segment DVT of left lower limb with IVC extension. CTPA reported thrombosis of the left descending pulmonary artery with pulmonary infarction.

She recovered well with LMWH.

1. What were her VTE risk factors and what were her risk scores?
Current smoker (>10/day), PPH >1L. Total score 2.
2. Would she require thromboprophylaxis? If so when and for how long?
Postnatally for 10 days.
3. Would you test for thrombophilia for this patient? What are the indications for thrombophilia testing?
Not for this patient as this was a provoked VTE by pregnancy.
Women with unprovoked VTE should be tested for antiphospholipid antibodies.
Women with a family history of VTE and either antithrombin deficiency or where the specific thrombophilia has not been detected, should be tested for antithrombin deficiency.
4. Will CTPA results influence your management? If so, how?
Not necessary as DVT has been confirmed and it will not change the management.
5. How will you manage her next and subsequent pregnancy in terms of VTE risk?
Start thromboprophylaxis from first trimester itself, and to continue for 6 weeks postpartum.
6. Lessons learned?
Always assess obstetric patient for VTE risk. Her VTE risk score of 2 calls for postpartum thromboprophylaxis for 10 days. Pulmonary Embolism occurs in 15-24% of untreated DVT with 15-30% mortality risk. However, if treated DVT, the risk of developing Pulmonary Embolism drops to 4.5%, with a mortality risk of 1%.

Case 5. Antenatal DVT (*labour management*)

A 37 year old G6P4+1, BMI 23kg/m², without any significant family or personal medical history, was diagnosed to have left DVT at 13 weeks gestation. Self injecting LMWH at home, she injected at 12pm on 25/6/2016 and subsequently came in active labour and had a spontaneous vaginal delivery at 4pm, 4 hour after injection. She was later subjected to MRP for retained placenta. Total EBL was 450mls. No protamine was required.

1. What were her VTE risk factors?

None, according to the new VTE Checklist. (Previous checklist: age & parity are risk factors)

2. What are your measures for such patient during delivery? And why?

Vigilant against PPH – low threshold for extra uterotonics, tranexamic acid, and other methods such as uterine tamponade.

Protamine sulphate (antidote) may be necessary and should be readily availability.

In the event of EMLSCS, intraperitoneal may be beneficial. Discuss with anaesthetist regarding the appropriate anaesthesia as regional anaesthesia would be contraindicated.

Peaked bioavailability of LMWH is 4-6 hours after injection, thus this patient had the highest risk of bleeding when she delivered 4 hours after LMWH injection. However, LMWH has lower risk of bleeding among the different types of anticoagulants.

3. How long will the patient require further DVT treatment?

A minimum of 3 months anticoagulation is required and should cover the 6 weeks of puerperium.

4. How will you manage her next and subsequent pregnancies in terms of VTE risk?

Start thromboprophylaxis from first trimester itself/as soon as pregnancy is confirmed and to continue for 6 weeks postpartum.

5. Lessons learned?

Reinforced the importance of withholding any anticoagulant treatment once a patient has any signs & symptoms of labour (contraction, show, leaking), and seek medical attention soonest possible. Be vigilant against PPH when patient goes into labour. Patient education and empowerment is important.

Case 6. Antenatal PE (*investigation, doctors*)

A 23 year old G1P0 with booking BMI 29kg/m² is admitted at 38w for IOL for GDM and PIH. She developed chest tightness, shortness of breath and nausea on day 5 of admission. ABG showed good oxygenation, ECG was not suggestive of PE and CUS of lower limbs were negative. In view of persistent symptoms and without other differential diagnosis, she was started on treatment with LMWH for Pulmonary Embolism. IOL was withheld for a few days, and patient subsequently had to undergo EMLSCS for poor progress, which was uneventful and with EBL 400mls. A CTPA performed post-delivery showed filling defects in basal segmental branches of left descending pulmonary artery, i.e. pulmonary embolism of left lower lobe.

She was given 6 months of anticoagulants.

1. What were her VTE risk factors?
Antenatally - prolonged admission (>3days); BMI >30kg/m².
Postnatally – additional risk in EMLSCS.
2. How would you have managed her pregnancy and delivery?
IOL should be withheld for a few days for clots/thrombus to be stabilised. Resume IOL thereafter. There is no indication for LSCS for Pulmonary Embolism as LSCS imposes higher risk of Pulmonary Embolism. At all time, be vigilant against PPH when patient is in active phase of labour.
3. Would CTPA be necessary and when?
Any VTE event must be confirmed by imaging test. CTPA can be done after starting anticoagulant. As in this patient, it was performed after delivery.
4. Lesson learned from this patient?
Maintain high index of suspicion, thorough investigation to rule out any VTE event even if a patient is being induced or in early labour as VTE can happen in any phase of pregnancy. CTPA can be done after commencing anticoagulants once situation allows.

Case 7. Postnatal PE (*high index of suspicion, doctors*)

A 37 year old G3P2 admitted to antenatal ward on 23/2/2016 evening for management of IUD with placenta previa. Her booking BMI was 30.4kg/m² and did not have any family or significant past medical history. As her fetus was in a transverse lie and placenta being PP major, it was decided for LSCS. Her baseline coagulation profile (performed for IUD) was normal.

ELLSCS was carried out on 25/2/2016 morning under spinal anaesthesia. Patient desaturated the minute placenta was delivered and immediately she was converted to general anaesthesia. She lost 500ml in OT and was transferred to ICU as amniotic fluid embolism (AFE) was suspected. Repeated coagulation done later showed DIVC (Intraoperation: APTT57.2, PT18.4, INR1.47; 1 hour post operation: APTT82.2, PT24.3, INR2.11). In ICU, about post-operative 2 hours, patient bled a further 1,000ml and Massive Transfusion Protocol (MTP) was activated (transfused 4 RBCs, 4 FFP, 4 Platelet Concentrate). Pulmonary Embolism was also suspected as AFE is thrombogenic, a CTPA was performed and showed thrombus in the segmental branch of the right descending pulmonary artery.

She was started on anticoagulants once there was no further evidence of bleeding. And patient recovered well.

1. What were her VTE risk factors?

Antenatally: BMI>30kg/m², Stillbirth

Postnatally: ELLSCS

2. And when would you consider thromboprophylaxis?

Antenatal thromboprophylaxis was indicated after the diagnosis of IUD was made upon admission. In the event of planned LSCS, LMWH could still be served the day before the scheduled LSCS.

3. Lessons learned from this patient?

Maintain high index of suspicion even in the event of AFE. AFE is thrombogenic, Pulmonary Embolism should be anticipated and proceed with the necessary investigation such as CTPA if there is clinical suspicion.

Case 8. Postnatal PE Mortality (*high index of suspicion, doctors*)

A young mother in her second pregnancy, who had a booking weight of 94kg, had an emergency caesarean section for poor progress in a district specialist hospital. Intra-operatively was uneventful. She was started on subcutaneous unfractionated Heparin 5,000 units twice daily in the ward. Over the night, she complained of on and off cough.

During the morning ward rounds, the specialist noted that the patient was dyspnoeic with chest discomfort and was hypoxic. The patient had to be intubated and transferred to a tertiary hospital. Upon arrival at the tertiary hospital 4 hours later, she was managed in the intensive care unit and was ventilated. ECG, chest x-ray and bedside echocardiogram were performed which suggested massive pulmonary embolism and the patient became haemodynamically unstable. She was then given thrombolysis and was on triple inotropic support. She developed multi-organ failure and died 2 days later.

Learning points:

1. There is inadequate efficacy data for Heparin for women above 90kg. Alternative thromboprophylaxis drug should have been used for this lady.
2. There is a delay in suspecting pulmonary embolism as she developed some of the clinical signs and symptoms over the night. It was only suspected during the morning rounds by the specialist when she deteriorated.
3. Anticoagulation was not started in the district hospital despite the clinical suspicion of pulmonary embolism (blood clot embolism) as recommended in Clinical Practice Guidelines. It was also not started immediately in the tertiary hospital. Anti-coagulation should be started on suspicion and should not be delayed until confirmation of diagnosis.

Case 9. Antenatal PE Mortality

A 40 year old lady in her second pregnancy at 10 weeks gestation underwent a laparotomy in a tertiary hospital for acute pelvic pain. She had a right salpingoophorectomy for a gangrenous ovarian cyst. She was discharged well on the third post-operative day and she returned to her home town about 300km away. She was not screened for VTE risk thus thromboprophylaxis was not given. On the 10th post-operative day she complained of sudden shortness of breath and presented to a district hospital without specialist.

She gave a history of bilateral calf pain a few days earlier. She was transferred immediately to a specialist hospital located about an hour away after consulting the O&G specialist. On arrival in the specialist hospital, a CT pulmonary angiogram was performed an hour later which confirmed the presence of saddle pulmonary embolism. She was then started on anticoagulation with a low molecular weight heparin. She was managed in the intensive care unit and was given a thrombolytic agent when she became unstable. However, she succumbed to her illness 16 hours later.

Learning points:

1. VTE risk scoring should be performed when she was admitted to the ward for surgery and upon discharge from the ward. Had risk assessment been made, the patient should have been started on thromboprophylaxis. Risk scoring is sometimes not done in the gynaecology wards where early pregnancy cases are managed. This should be avoided by education of the care givers.
2. The first dose of anticoagulation should have been started in the district hospital based on the suspicion of pulmonary embolism, before she was transferred to the specialist hospital.
3. Anticoagulation should not have been delayed until after the confirmation of pulmonary embolism by CT pulmonary angiogram.

Case 10. Post Abortion PE Mortality

26 year old G4P3, booked for antenatal care at 15 weeks with BMI 24.6. 1 month later, she was diagnosed to have lupus nephritis with systemic and mucocutaneous involvement. At 19 weeks gestation, she was admitted to hospital for 1 week for control of her hypertension. Patient was not given thromboprophylaxis during her hospital stay.

1. What are her VTE risk factors? Would she require thromboprophylaxis?

Active SLE, hospital admission.

Yes, thromboprophylaxis is indicated.

She developed pulmonary embolism 6 days after discharge at 20+6 weeks. With worsening maternal condition, she was subjected to termination of pregnancy at 22+2 weeks. After starting on LMWH, she was bridged with warfarin. She was discharged on day 26 post miscarriage without LMWH, and with INR 1.8. Her warfarin dose was increased accordingly.

2. How would you manage her anticoagulant?

LMWH should be continued while waiting for target INR to be reached (bridging with warfarin).

By day 38 post abortion, patient became symptomatic with shortness of breath. She was brought in dead to ED. Her family refused post-mortem examination. Massive pulmonary embolism could not be ruled out.

PRE AND POST TEST

Pre/Post Test

[Total score – 20/Pass mark – 14/20]

1. Obstetric thromboembolism is the leading cause of direct maternal death in Malaysia. **[1 Mark]**

True/False

2. What is the incidence of VTE in the third trimester? **[1 Mark]**

.....

3. List 5 antenatal risk factors for venous thromboembolism (VTE). **[5 Marks]**

a. c.

b. d.

e.

4. What are the 3 common signs and symptoms of DVT? **[3 Marks]**

a. c.

b.

5. What are the 3 common signs and symptoms of pulmonary embolism? **[3 Marks]**

a. c.

b.

6. If a patient with risk factors for VTE presents with symptoms that are highly suggestive of venous thromboembolism, should treatment be initiated before awaiting investigations? **[1 Mark]**

True/False

7. Should a D-dimer test be performed to diagnose acute VTE? **[1 Mark]**

True/False

8. Name one investigation that is recommended if the patients presents with symptoms suggestive of pulmonary embolism? **[1 Mark]**

.....

9. What is the recommended medication of choice of the patient has venous thromboembolism and is hemodynamically stable? **[1 Mark]**

.....

10. List three contraceptive options for patients with a history of VTE in pregnancy? **[3 Marks]**

a..... C.....

b.....

APPENDICES

A. Anti Embolic Stockings

Anti embolic stockings are mechanical devices used as a preventive measure against the formation of thrombosis and embolus. This graduated compression stockings come in a variety of lengths and sizes. The graduated compression applies pressure to the legs in varying amounts, with the most compression furthest away from the heart, namely the ankle and then lessening the compression further up the leg.

Despite the absence of clear evidence that the use of anti embolic stockings reduces maternal mortality due to DVT or PE, it is still recommended for women whose VTE risk is not high enough to warrant pharmacological thromboprophylaxis or those who refuses to use pharmacological agents.



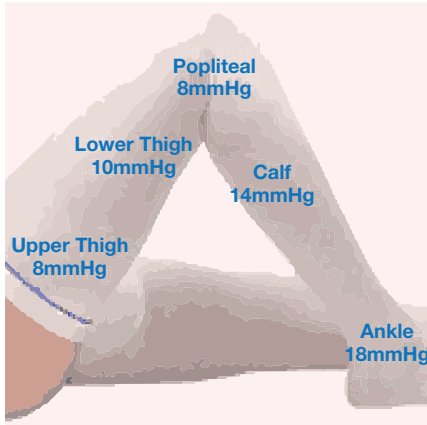
Above knee anti-embolic stockings.



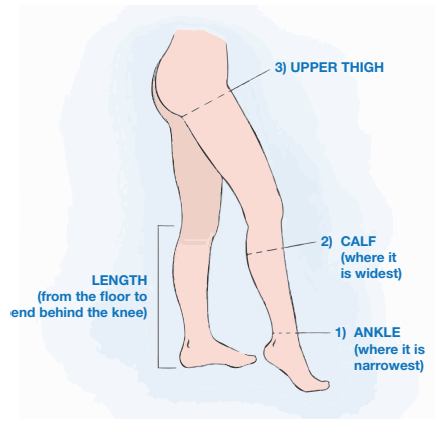
Below knee embolic stockings.

Measurement

1. Measure widest circumference of calf while standing using a flexible tape.
2. Measure from the bottom of the heel to the bend of the knee along the back of the leg.
3. For the thigh high stocking, measure the thigh circumference and from bottom of the heel to the gluteal furrow along the back of the leg.



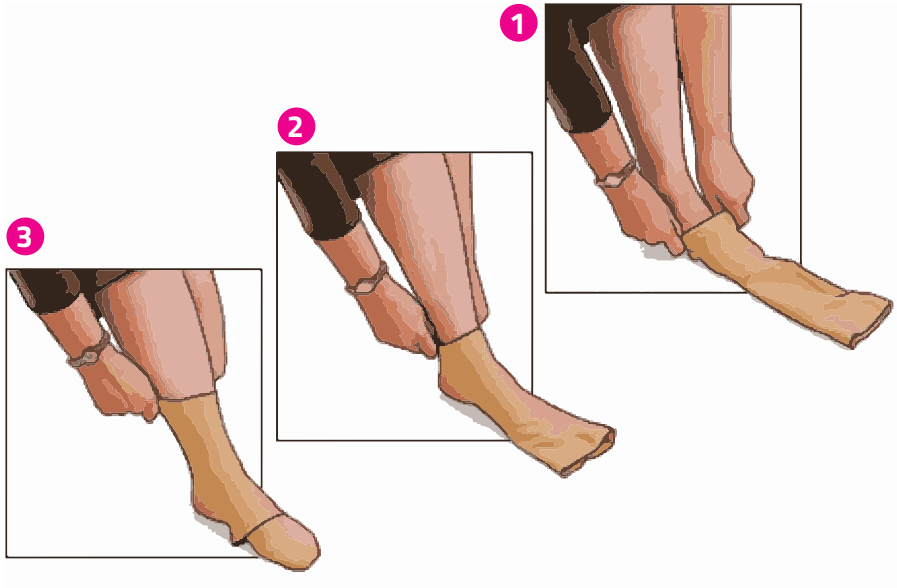
Appropriate calf pressures



Application

Due to the tough elastic material of anti-embolic stockings, many people have trouble wearing compression stockings. There are some tips to apply.

1. First, turn the upper part of the stocking inside out to the heel and gently slide the stocking down to the foot part.
2. Now carefully slip one foot in.
3. Gently pull the remaining part of the compression stocking over the heel.
4. Use the palms of hands to massage the stocking up toward the knee. Try not to pull at the upper edge of the compression stocking.
5. Now use the same steps for the other leg.
6. Compression thigh high stocking: Use the steps above until the compression stocking is by the knee. Using the palms of hands, ease the stocking upward (don't pull on the upper edge of the stocking) until it reaches upper thigh.



B. Intermittent Pneumatic Compression (IPC)

IPC consists of a garment which is fitted to the calf or foot and inflated by a pump. As the garment inflates with air, it compresses the veins and pushes the blood back to the heart. The garment deflates again after a few seconds. This action mimics the squeezing action on the veins by the calf or foot muscle. IPC is a safe, natural and effective alternative may sometimes be used in combination with medications for high risk patients.

The compression will continue to alternate from limb to limb. If the garments are too loose or too tight, the patient may experience some pain, numbness or tingling.

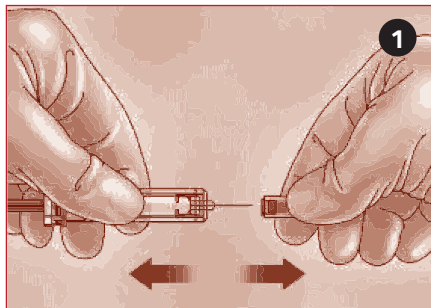
Garments

A garment, which has an inflatable section at the back, is wrapped around each calf. The garment connects to the pump that has a pre-set pressure and cycle for inflating and deflating. The pump inflates them once a minute on each leg. Garments come in various sizes and are fitted according to the size of the patient's leg. Some garments are designed for the calf and thigh area together.

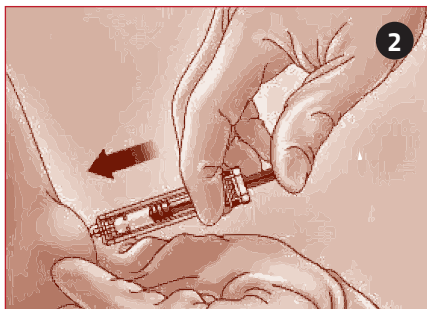


Calf, thigh and foot garments can be worn in any combination as per the patient photographed below. IPC should be applied just before surgery and needs to be maintained until the patient is walking properly again, usually after about 3 days. It is essential to keep the device working at all times, including while the patient sleeps, to keep the blood moving.

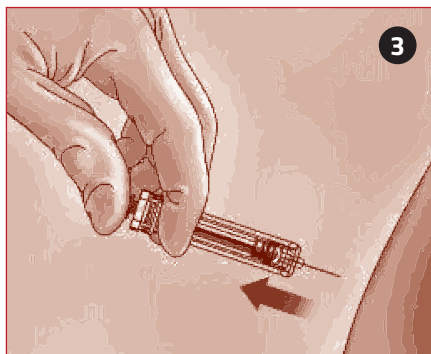
C. Administration of Subcutaneous LMWH



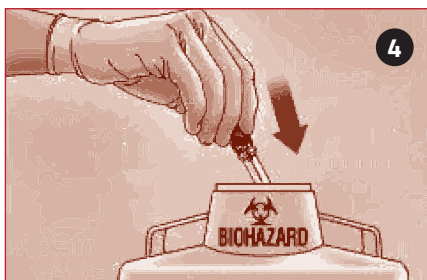
Carefully remove the needle guard covering the needle.



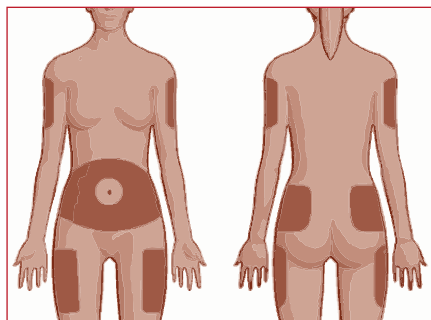
Pinch a fold of skin with other hand. Insert the needle fully into the skin fold at a 90° angle. Press down the plunger slowly over 10-15 seconds. Continue to hold the skin fold during injection.



Pull the needle out of the skin. Do not rub the injection site.



Dispose the used syringe.



Do not inject within 5cm from umbilicus and above iliac crests or near scars or bruises
Clean the area with sterile alcohol swab and allow to dry before injection.

D. Odds Ratio for VTE Risk Factors

Risk Factor	Adjusted Odd Ratio	95% CI
Heart disease	43.4	35.0–53.9
Previous VTE	24.8	17.1–36
PPH + surgery	12	3.9–36.9
Immobility	10.8	4.0–28.8
SLE	8.7	5.8–13
Transfusion	7.6	6.2–9.4
Sickle cell	6.7	4.4–10.1
Stillbirth	6.24	2.77–14.1
Post-partum infection	6.1	5.0–7.5
Pre-eclampsia with FGR	5.8	2.1–16
BMI >30kg/m ²	5.3	2.1–13.5
Hyperemesis	4.4	2.4–8.4
ART	4.3	2.0–9.4
Multiple pregnancy	4.2	1.8–9.7
PPH >1L	4.1	2.3–7.3
Caesarean section	3.6	3.0–4.3
Smoking >10 per day	3.4	2.0–5.5
Pre-eclampsia	3.1	1.8–5.3
Pre-term delivery	2.69	1.99–3.65
Varicose veins	2.4	1.04–5.4
Parity ≥3	2.4	1.8–3.1
Age >35	1.4	1.0–2.0

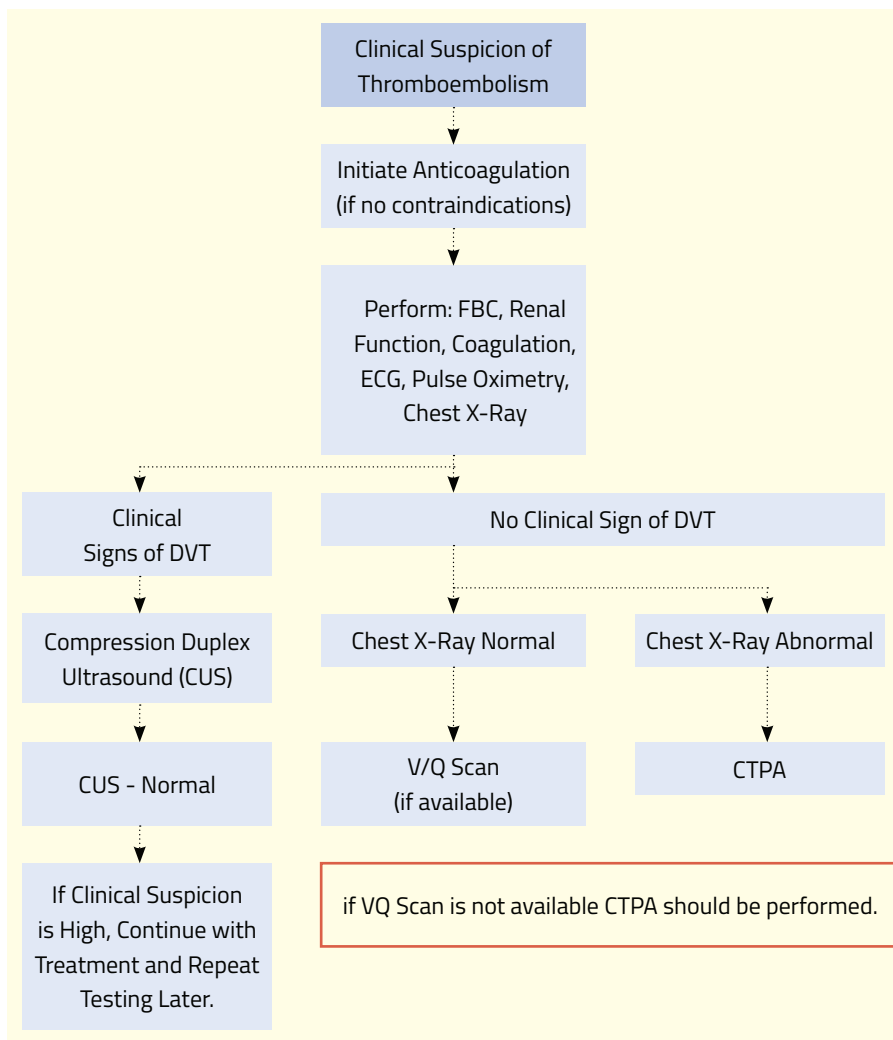
E. Pregnancy and Puerperal VTE Risk Checklist

VTE Risk Factors	VTE Score	Tick		
		Pre-Pregnancy/ Booking	Admission New Illness	Post Delivery
Date				
Pre-existing risk factors				
Previous VTE	4			
High risk thrombophilia	3			
Medical comorbidities (e.g. - malignancies, cardiac failure, active SLE, active TB, IVDU, nephrotic syndrome, diabetic nephropathy, thalassemia major or intermedia post splenectomy)	3			
Obesity: BMI $\geq 40 \text{ kg/m}^2$	2			
BMI 30-39 kg/m^2	1			
Family history of VTE	1			
Low risk thrombophilia (factor V Leiden, High FVIII)	1			
Current smoker (≥ 10 per day)	1			
Obstetric risk factors				
Caesarean section (emergency & elective)	2			
Pre eclampsia	1			
IVF (1 st trimester risk only)	1			
Rotational instrumental delivery	1			
PPH ($\geq 1,000 \text{ mls}$) or requires blood transfusion	1			
Stillbirth (current)	1			

VTE Risk Factors	VTE Score	Tick		
		Pre-Pregnancy/ Booking	Admission New Illness	Post Delivery
Prolonged labour (>24 hours)	1			
*Transient risk factors				
Surgical procedures (excluding episiotomy, 1 st & 2 nd degree perineal repair, evacuation of retained products of conception)	4			
Hyperemesis gravidarum/OHSS	4			
Systemic/Postpartum infection	1			
Immobility/Dehydration/ Admission beyond 3 days	1			
Long distance travel (>4 hours)	1			
Total score				
Name & stamp				

***Note:** Thromboprophylaxis is recommended during the transient period. Consider stopping once the transient risks are deemed no longer significant.

F. Suggested Algorithm for The Management of VTE



Flowchart 1: *Diagnosis of thromboembolism*

Note: Although V/Q scan has a higher sensitivity of detecting pulmonary embolism; especially when the CXR is normal, in hospitals without such facilities, consider CTPA as the imaging modality of choice.

G. Post Natal Home Visit Monitoring

Home Visit Postnatal Monitoring Chart

- As taken from *Rekod Kesihatan Ibu KIK/1(a)/96 (Pindaan 2012)*.
- Section on VTE (DVT/Pulmonary Thromboembolism) risk is highlighted.

Tarikh Keluar Hospital: Tarikh maklumat diterima:

Keadaan Ibu	Tarikh/ Hari											Lawatan ke Klinik	
		0	1	2	4	5	6	8	10	20	1/12	2/12	
Tekanan Darah													
Suhu Badan													
Nadi													
Lokia													
Payudara													
Tinggi Rahim													
Perineum													

Gejala dan Tanda-tanda DVT/Pulmonary Thromboembolism*

Sakit/Bengkak di Kaki													
Sakit Dada													
Susah Bernafas													
'Redness/Inflammation of Lower Limbs'													
'Calf Tenderness' (sakit betis)													

Masalah dan Pengendalian Postnatal Ibu:

.....

*Postnatal mothers with any of the above clinical signs and symptoms of DVT/pulmonary embolism must be 'Coded Red' and referred to the Medical Officer or Family Medicine Specialist immediately.

H. Medical Eligibility Criteria for Contraceptive Use

	COC/P/ CVR	CIC	POP	DMPA/ NET-EN	LNG/ETG/ Implants	CU-IUD	LNG-IUD
History of High Blood Pressure during Pregnancy (where current blood pressure is measurable and normal)	2	2	1	1	1	1	1
Deep Vein Thrombosis/ Pulmonary Embolism (DVT/PE)							
a. History of DVT/PE	4	4	2	2	2	1	2
b. Acute DVT/PE	4	4	3	3	3	1	3
c. DVT/PE and established on anticoagulant therapy	4	4	2	2	2	1	2
d. Family History (first degree relatives)	2	2	1	1	1	1	1
e. Major Surgery							
i. with prolonged immobilization	4	4	2	2	2	1	2
ii. without prolonged immobilization	2	2	1	1	1	1	1
f. Minor Surgery without Immobilization	1	1	1	1	1	1	1
Known Thrombogenic Mutations (e.g. factor V Leiden; prothrombin mutation; protein S, protein C and antithrombin deficiencies)	4 ^a	4 ^a	2 ^a	2 ^a	2 ^a	1 ^a	2 ^a

I. Radiological Imaging Risks in Pregnancy

Table 1: Summary of suspected in-utero induced deterministic Radiation Effects.

Menstrual or Gestational Age (weeks)	<50mGy	50-100mGy	>100mGy
0-2	None	None	None
3-4	None	Probably none	Possible spontaneous abortion.
5-10	None	Potential effects are scientifically uncertain and probably to subtle to be clinical detectable.	Possible malformations increasing in likelihood as dose increases.
11-17	None	Potential effects are scientifically uncertain and probably too subtle to be clinically detectable.	Increased risk of deficits in IQ or mental retardation that increase in frequency and severity with increasing dose.
18-27	None	None	IQ deficits not detectable at diagnostic doses.
>27	None	None	IQ deficits not detectable at diagnostic doses.

Adapted from ACR Practice Guideline for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation, ACR Practice Guideline 2014.

Table2: Approximate foetal doses from common diagnostic procedures.

Examination	Mean (mGy)	Maximum (mGy)
<u>Conventional X-Ray Examination:</u>		
Abdomen	1.4	4.2
Chest	<0.01	<0.01
Intravenous Urogram	1.7	10
Lumbar Spine	1.7	10
Pelvis	1.1	4
Skull	<0.01	<0.01
Thoracic Spine	<0.01	<0.01
<u>Fluoroscopic Examination:</u>		
Barium Meal (upper GI)	1.1	5.8
Barium Enema	6.8	24
<u>Computed Tomography:</u>		
Abdomen	8.0	49
Chest Including CTPA	0.06	0.96
Head	<0.005	<0.005
Lumbar Spine	2.4	8.6
Pelvis	25	79

Adapted from Pregnancy and Medical Radiation; ICRP publication 84, Annals of the ICRP Vol. 30, No. 1 2000.

Standard Operating procedure for Consent Taking in Pregnant or Potentially Pregnant Patient going for Radiological Procedure.

J: Training Programme

VTE Training Program for Doctors

Duration (min)	Lecture	Topic	Speaker
15		Pre test	Faculty
30	1	VTE and Maternal Mortality	O&G
30	2	Lessons Learned from Temerloh Hospital Obstetric VTE Registry	O&G
20	3	Pathophysiology of Obstetric VTE	O&G
20	4	Risk factors and VTE Checklist	O&G/FMS
30	5	Compression therapy – prevention and treatment of DVT	OT
30	6	Pharmacological thromboprophylaxis for Obstetric VTE	O&G/Hematologist
20	7	Clinical presentation of DVT & PE	FMS
20	8	Unusual site thrombosis e.g. Cerebral Thrombosis	Hematologist
20	9	Investigation for VTE	Hematologist/O&G
30	10	Imaging Modalities for VTE in Pregnancy	Radiologist
20	11	Acute management of VTE at community level (including referral)	FMS/O&G
30	12	Acute management of VTE in Specialist Hospital	Hematologist/O&G
30	13	Are all heparins the same?	Hematologist
15	14	Discharge communication – from hospital to health clinic	Hospital Nurse /O&G
20	15	Contraceptive consideration in VTE	FMS/O&G
45		Case Studies	Faculty
15		Post test	Faculty

VTE Training Program for Paramedics

Duration	Lecture	Topic	Speaker
15		Pre test	Faculty
30	1	Pathophysiology of Obstetric VTE	O&G
45	2	Risk factors and VTE Checklist	O&G/FMS
30	3	Compression Therapy – Prevention and Treatment of DVT	OT
20	4	Pharmacological Thromboprophylaxis for Obstetrics VTE	O&G/Hematologist
20	5	Clinical Presentation of DVT & PE	FMS
20	6	Unusual Site Thrombosis e.g. Cerebral Thrombosis	Hematologist
20	7	Diagnosis of VTE	Hematologist/O&G
30	8	Acute Management of VTE at Community Level (including referral)	FMS/O&G
30	9	Acute Management of VTE in Specialist Hospital	Hematologist/O&G
20	10	Discharge Communication – from Hospital to Health Clinic	Hospital Nurse
30	11	Post-Discharge Follow Up Care	Health Nurse
30	12	Roles of Community Nurses – Health Education, Nursing Care	Health Nurse
20	13	Contraceptive Consideration in VTE	FMS/O&G
45		Case Studies	Faculty
15		Post Test	Faculty

FURTHER READING

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