# Venous thromboembolism in obstetrics

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# Venous thromboembolism

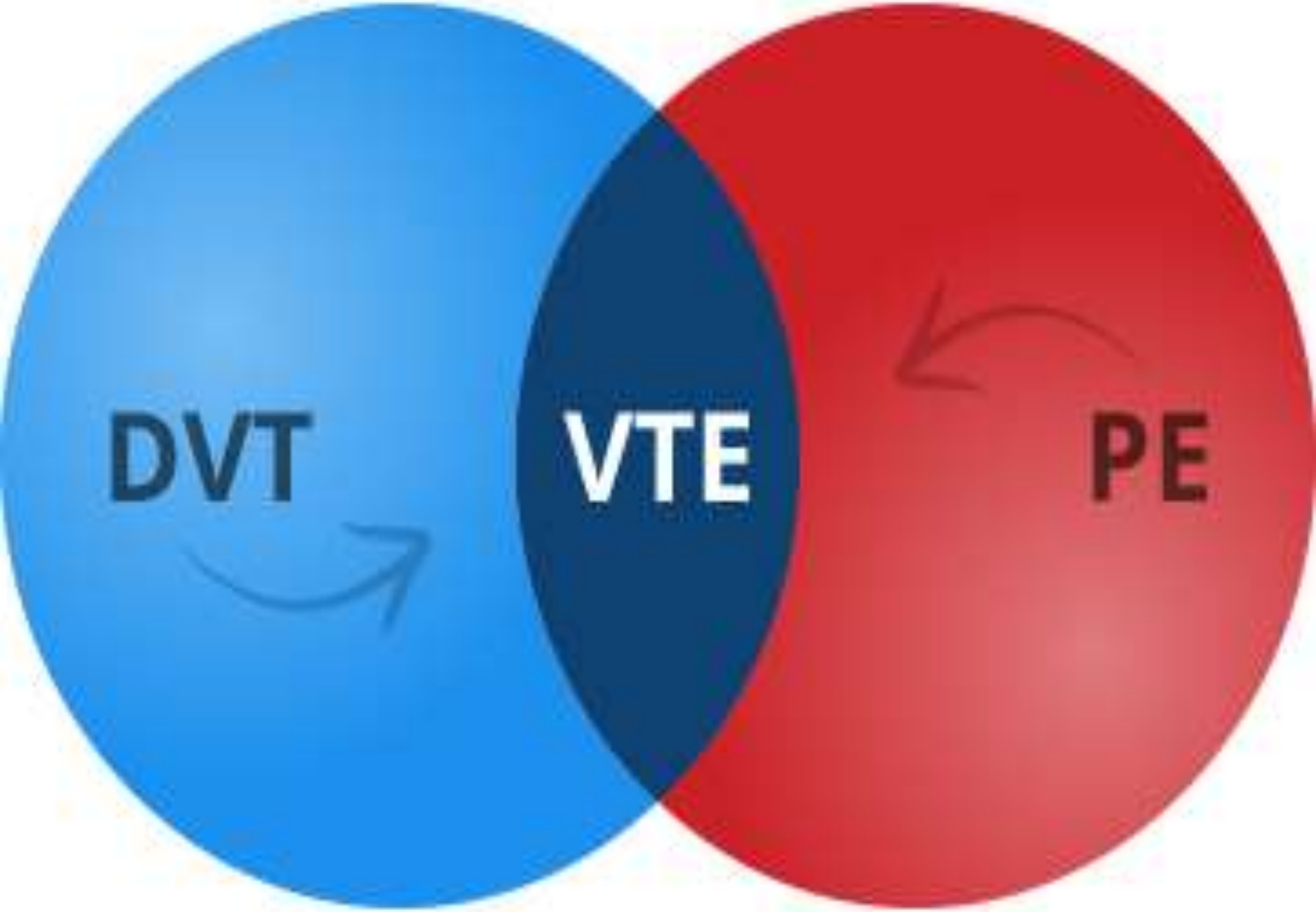
VTE is one of the main direct causes of **maternal death** in the UK

It includes deep vein thrombosis (**DVT**) and pulmonary embolism ( **PE** )

VTE is a common lethal disorder that affects **hospitalized and non-hospitalized** patients, recurs frequently and results in long-term complications

The risk of VTE is :

- **antenatally 4-5 X** higher than in non-pregnant women
- **postpartum 20 X** higher than in non-pregnant women


DVT
VTE
PE

Majority of women with VTE in pregnancy have **clinical symptoms** !!

**DVT** → leg swelling and unilateral pain +- lower abdominal pain

**PE** → dyspnea, chest pain, hemoptysis and collapse

# Investigations ?? (DVT)

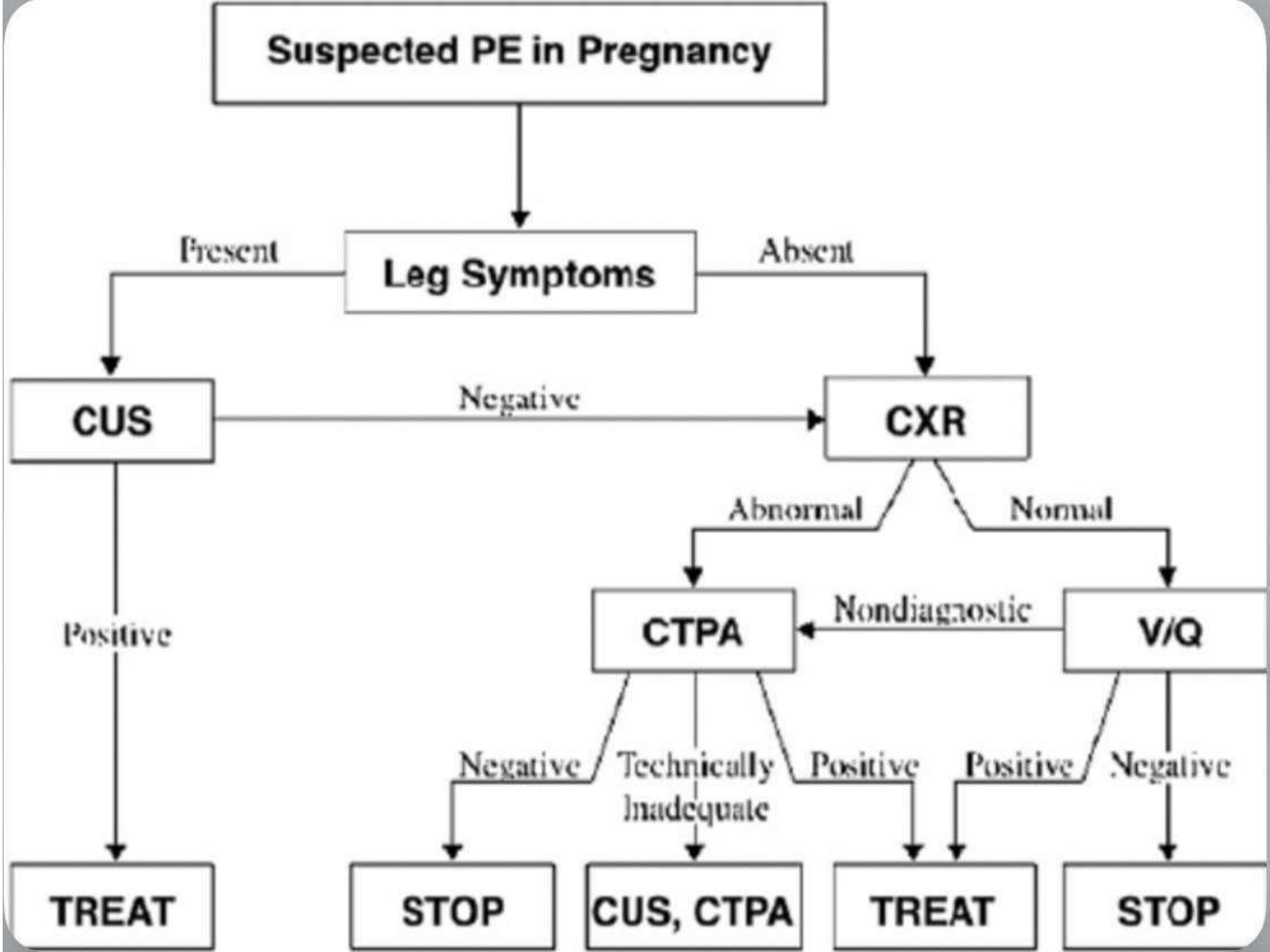
- **Compression duplex ultrasound**

- If ultrasound is **negative** + **low** level of clinical suspicion➔ **stop** anticoagulant treatment.

- If ultrasound is **negative** + **high** level of clinical suspicion➔ **repeat** ultrasound on **days 3 and 7.**

# Investigations ?? (PE)

- ECG
- CXR
- Compression duplex US
- V/Q scan
- CTPA (CT pulmonary angiography).


Suspected PE in Pregnancy
Leg Symptoms
Present
Absent
CUS
Negative
CXR
Abnormal
Normal
Positive
CTPA
Nondiagnostic
V/Q
Negative
Technically Inadequate
Positive
Positive
Negative
TREAT
STOP
CUS, CTPA
TREAT
STOP

A.D.A.M.

# Obstetric thromboprophylaxis risk assessment and management

**All women should undergo a documented assessment of risk factors for VTE in early pregnancy or prepregnancy**

**Risk assessment** should be repeated when:

- admitted to hospital for any reason
- develops other intercurrent problems
- intrapartum or immediately postpartum

# Risk factors :

## ** Pre-existing risk factors →

**Previous VTE**

**Thrombophilia** (see next)

**Medical comorbidities** (see next)

**Age > 35 years**

**Smoking**

**Paraplegia**

**Obesity** (BMI ≥ 30 kg/m2) either prepregnancy or in early pregnancy -- more risk for PE

**Parity ≥ 3**

**Gross varicose veins** (symptomatic or above knee or with associated phlebitis, oedema/skin changes)

# Thrombophilias

- ***Heritable*** (found in 20-50% of pregnancy-related VTE)
  - **Antithrombin deficiency (high risk)**
  - Protein C deficiency
  - Protein S deficiency
  - Factor V Leiden
  - Prothrombin gene mutation

- ***Acquired***
  - **Antiphospholipid antibodies (high risk)**
  - Persistent lupus anticoagulant and/or persistent moderate/high titre anticardiolipin antibodies and/or $\beta^2$-glycoprotein 1 antibodies)

# Medical comorbidities

Cancer

heart failure

active SLE

inflammatory polyarthropathy or IBD

nephrotic syndrome

Type I diabetes mellitus with nephropathy

sickle cell disease

current intravenous drug user

# ** Obstetric risk factors →

Multiple pregnancy

Current pre-eclampsia

Caesarean section

Prolonged labour (> 24 hours)

Mid-cavity or rotational operative delivery

Stillbirth

Preterm birth

PPH (> 1 litre/requiring transfusion)

# ** New onset/transient risk factors→

**Reversible,mostly later:** needs ongoing indivisual risk assessment

Any surgical procedure in pregnancy or puerperium
Bone fracture
Hyperemesis & dehydration
OHSS
ART (IUI, IVF)
Admission or immobility
Current systemic infection
wound infection
Long-distance travel (> 4 hours)

| Thrombophilic defect | Pregnancy (%/pregnancy, 95% CI) | Antenatal (%/pregnancy, 95% CI) | Postpartum (%/pregnancy, 95% CI) |
|---|---|---|---|
| Antithrombin, protein C or protein S deficiency[82] | 4.1 (1.7–8.3) | 1.2 (0.3–4.2) | 3.0 (1.3–6.7) |
| Antithrombin deficiency type 1 (range)[83–87]* | 15–50 | 0–40 | 11–28 |
| V Leiden heterozygous[82] | 2.1 (0.7–4.9) | 0.4 (0.1–2.4) | 1.7 (0.7–4.3) |
| Prothrombin gene mutation heterozygous[82] | 2.3 (0.8–5.3) | 0.5 (0.1–2.6) | 1.9 (0.7–4.7) |
| V Leiden homozygous or compound heterozygosity V Leiden and prothrombin gene mutation (range)[88,89] | 1.8–15.8 | 0–5 | 1–10 |

*These data are from a population-based study, not a family-based study

**Risk factors for VTE**

| Pre-existing risk factors | Tick | Score |
|---|---|---|
| Previous VTE (except a single event related to major surgery) | | 4 |
| Previous VTE provoked by major surgery | | 3 |
| Known high-risk thrombophilia | | 3 |
| Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user | | 3 |
| Family history of unprovoked or estrogen-related VTE in first-degree relative | | 1 |
| Known low-risk thrombophilia (no VTE) | | 1[a] |
| Age (> 35 years) | | 1 |
| Obesity | | 1 or 2[b] |
| Parity ≥ 3 | | 1 |
| Smoker | | 1 |
| Gross varicose veins | | 1 |
| **Obstetric risk factors** | | |
| Pre-eclampsia in current pregnancy | | 1 |
| ART/IVF (antenatal only) | | 1 |
| Multiple pregnancy | | 1 |
| Caesarean section in labour | | 2 |
| Elective caesarean section | | 1 |
| Mid-cavity or rotational operative delivery | | 1 |
| Prolonged labour (> 24 hours) | | 1 |
| PPH (> 1 litre or transfusion) | | 1 |
| Preterm birth < 37[+0] weeks in current pregnancy | | 1 |
| Stillbirth in current pregnancy | | 1 |
| **Transient risk factors** | | |
| Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation | | 3 |
| Hyperemesis | | 3 |
| OHSS (first trimester only) | | 4 |
| Current systemic infection | | 1 |
| Immobility, dehydration | | 1 |

Any woman with : (RFs other than previous VTE)

**>= 4** current RFs → prophylactic LMWH antenatally and 6 weeks postnatally (after risk assessment)

**3** current RFs → prophylactic LMWH from 28 weeks and 6 weeks postnatally (after risk assessment)

**2** current RFs → prophylactic LMWH for at least 10 days postpartum

**1** current RF → mobilization and hydration

## Appendix I: Obstetric thromboprophylaxis risk assessment and management

**Antenatal assessment and management (to be assessed at booking and repeated if admitted)**

Any previous VTE except a single event related to major surgery

→ **HIGH RISK**

**Requires antenatal prophylaxis with LMWH**

**Refer to trust-nominated thrombosis in pregnancy expert/team**

Hospital admission

Single previous VTE related to major surgery

High-risk thrombophilia + no VTE

Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy, nephrotic syndrome, type I DM with nephropathy, sickle cell disease, current IVDU

Any surgical procedure e.g. appendicectomy

OHSS (first trimester only)

→ **INTERMEDIATE RISK**

**Consider antenatal prophylaxis with LMWH**

Obesity (BMI > 30 kg/m$^2$)

Age > 35

Parity ≥ 3

Smoker

Gross varicose veins

Current pre-eclampsia

Immobility, e.g. paraplegia, PGP

Family history of unprovoked or estrogen-provoked VTE in first-degree relative

Low-risk thrombophilia

Multiple pregnancy

IVF/ART

→ **Four or more risk factors: prophylaxis from first trimester**

**Three risk factors: prophylaxis from 28 weeks**

Transient risk factors: Dehydration/hyperemesis; current systemic infection; long-distance travel

**Fewer than three risk factors**

→ **LOWER RISK**

**Mobilisation and avoidance of dehydration**

**Table 3.** Suggested thromboprophylactic doses for antenatal and postnatal LMWH

| Weight | Enoxaparin | Dalteparin | Tinzaparin (75 u/kg/day) |
|---|---|---|---|
| < 50 kg | 20 mg daily | 2500 units daily | 3500 units daily |
| 50–90 kg | 40 mg daily | 5000 units daily | 4500 units daily |
| 91–130 kg | 60 mg daily* | 7500 units daily | 7000 units daily* |
| 131–170 kg | 80 mg daily* | 10 000 units daily | 9000 units daily* |
| > 170 kg | 0.6 mg/kg/day* | 75 u/kg/day | 75 u/kg/day* |
| High prophylactic dose for women weighing 50–90 kg | 40 mg 12 hourly | 5000 units 12 hourly | 4500 units 12 hourly |

*may be given in 2 divided doses

# During labour and delivery ??!

**Stop** LMWH if any **vaginal bleeding** or once **labour** begins – then reassess on admission to hospital

**Avoid regional techniques** if possible until: **>12** hrs after previous **prophylactic** dose or **>24** hrs after the last **therapeutic** dose

**Don't give** LMWH for **4 hrs** after use of spinal anesthesia or removal of epidural catheter and **don't remove** the catheter within **12 hrs** of the most recent injection

If a women having **elective CS** → give her the dose of LMWH **on the day prior** to delivery and **omit any morning dose** of the operation day

Give the first thromboprophylactic dose of LMWH **ASAP after delivery** provided there is no PPH and regional anesthesia has not been used

# Postnatal assessment and management

# (to be assessed on delivery suite)

# High risk

Any previous VTE

Anyone requiring antenatal LMWH

High-risk thrombophilia

Low-risk thrombophilia + FHx

**At least 6 weeks postnatal prophylactic LMWH**

# INTERMEDIATE RISK

Caesarean section in labour

BMI ≥ 40 kg/m2

Readmission or prolonged admission (>=3 days) in the puerperium

Any surgical procedure in the puerperium except immediate repair of the perineum

Medical comorbidities

**At least 10 days postnatal prophylactic LMWH**

# Low risk

## If one of the following:

**Age > 35 years** **Obesity (BMI ≥ 30 kg/m2)** **Parity ≥ 3**
**Smoker** **Elective caesarean section** **Family history of VTE**
**Low-risk thrombophilia** **Gross varicose veins** **Current systemic infection**
**Immobility, e.g. paraplegia, PGP, long-distance travel** **Current pre-eclampsia**
**Multiple pregnancy** **Preterm delivery in this pregnancy (< 37 weeks)**
**Stillbirth in this pregnancy** **mid-cavity rotational or operative delivery**
**Prolonged labour (> 24 hours)** **PPH > 1 litre or blood transfusion**

**Note : if >= 2 RFs → intermediate risk**

## Early mobilisation and avoidance of dehydration

## Postnatal assessment and management (to be assessed on delivery suite)

- Any previous VTE
- Anyone requiring antenatal LMWH
- High-risk thrombophilia
- Low-risk thrombophilia + FHx

→ **HIGH RISK**
**At least 6 weeks' postnatal prophylactic LMWH**

- Caesarean section in labour
- BMI ≥ 40 kg/m²
- Readmission or prolonged admission (≥ 3 days) in the puerperium
- Any surgical procedure in the puerperium except immediate repair of the perineum
- Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy; nephrotic syndrome, type I DM with nephropathy, sickle cell disease, current IVDU

→ **INTERMEDIATE RISK**
**At least 10 days' postnatal prophylactic LMWH**

**NB If persisting or > 3 risk factors consider extending thromboprophylaxis with LMWH**

- Age > 35 years
- Obesity (BMI ≥ 30 kg/m²)
- Parity ≥ 3
- Smoker
- Elective caesarean section
- Family history of VTE
- Low-risk thrombophilia
- Gross varicose veins
- Current systemic infection
- Immobility, e.g. paraplegia, PGP, long-distance travel
- Current pre-eclampsia
- Multiple pregnancy
- Preterm delivery in this pregnancy (< 37+0 weeks)
- Stillbirth in this pregnancy
- Mid-cavity rotational or operative delivery
- Prolonged labour (> 24 hours)
- PPH > 1 litre or blood transfusion

**Two or more risk factors** → **INTERMEDIATE RISK** (above)

**Fewer than two risk factors** → **LOWER RISK**
**Early mobilisation and avoidance of dehydration**

Antenatal and postnatal prophylactic dose of LMWH

Weight < 50 kg = 20 mg enoxaparin/2500 units dalteparin/3500 units tinzaparin daily
Weight 50–90 kg = 40 mg enoxaparin/5000 units dalteparin/4500 units tinzaparin daily
Weight 91–130 kg = 60 mg enoxaparin/7500 units dalteparin/7000 units tinzaparin daily
Weight 131–170 kg = 80 mg enoxaparin/10000 units dalteparin/9000 units tinzaparin daily
Weight > 170 kg = 0.6 mg/kg/day enoxaparin/ 75 u/kg/day dalteparin/ 75 u/kg/day tinzaparin

# Treatment options :

**low-molecular-weight heparin** (LMWH) immediately ?!!

Therapeutic dose ?

**IV UFH** & **MDT** if massive PE with cardiac compromise (if confirmed – **immediate thrombolysis**) or at term

**Elevation of the leg** & **mobilisation** with **graduated elastic compression stockings** should be encouraged

**IVC filter** if iliac vein VTE or if proven DVT with recurrent PE despite adequate anticoagulation

# **The maintenance treatment** of DVT or PE?

Treatment with therapeutic doses of subcutaneous LMWH should be employed **during the remainder of the pregnancy** and for **at least 6 weeks postnatally** and **until at least 3 months of treatment** has been given in total.

(note : before discontinuing treatment the continuing risk of thrombosis should be assessed)

Warfarin → should **not** be used in the treatment of VTE in pregnancy

New anticoagulants → with consideration

# Thromboprophylactic agents :

## ** LMWH →

- The agent of choice for antenatal & postnatal.
- Doses are based on weight (the booking or most recent wt)
- No need to monitor platelet count or anti-Xa levels
- Reduce the dose if with renal impairement
- Safe in breastfeeding

## ** Unfractionated heparin (UFH) →

- Used if very high risk of thrombosis peripartum where increased risk of hemorrhage or where regional anesthesia may be required
- If used after CS, Monitor PLT count every 2-3 days from day 4-14 or until heparin is stopped

# ** Low dose aspirin →

Not recommended for this aim in obstetric patients

# ** Warfarin →

Its use is restricted in pregnancy to the few situations where heparin is unsuitable (eg: with **mechanical heart valves**)

Women receiving long-term anticoagulation with warfarin can be *converted from LMWH to warfarin postpartum* when the risk of hemorrhage is reduced, usually 5-7 days after delivery

Safe in breastfeeding

**** Danaparoid →**

Needs consultant hematologist with expertise in haemostasis and pregnancy

**** Fondaparinox →**

If women intolerant of heparin compounds

Its use in pregnancy should be in conjunction with a consultant hematologist with expertise in haemostasis and pregnancy

**** Dextran →**

Avoid it antenatally and intrapartum – bcz of the risk of anaphylactoid reaction

**** Oral thrombin and Xa inhibitors →**

Non-vitamin K antagonist oral anti-coagulant (NOACs) should be avoided in pregnant women

Not recommended in breastfeeding

## ** Anti-embolism stockings →

Use it properly with appropriate size and providing graduated compression with a calf pressure of 14-15 mmHg

Use it for women who are hospitalized and have a contraindication to LMWH in pregnancy and the puerperium

## **Contraindications or precautions** to LMWH use:

- Known bleeding disorder .
- Active antenatal or postpartum bleeding
- Women considered at increased risk of major haemorrhage (e.g. placenta praevia)
- Thrombocytopenia (platelet count < 75 × 109)
- Acute stroke in previous 4 wks (haemorrhagic or ischaemic)
- Severe renal disease
- Severe liver disease
- Uncontrolled hypertension (>200/120)

# Recurrent miscarriages

- >= 3 consecutive miscarriages < 24 wks
- Prev = 1%
- risk factors

**1- genetic factors (3-4%)**

cytogentic analysis for the misc

abnormal → karyotyping for both paretns (txn / deletion)

tt: refer to genetics / PGD

**2- anti-phospholipid syndrome (15%)**

**clinical criterea :**

>= 3 consec misc < 10 wks

>=1 misc > 10 wks

>=1 preterm birth < 34 wks

**lab criterea :**

anti-phospholipid abs

anti-cardiolipin abs

anti B2 GP 1 abs

TT: Aspirin / LMWH / psychological support

**3- anatomical factors (10%)**

arcuate / bicornuate / septate

usu. 2nd TM

dx: US , Hysteroscopy

tt: hysteroscopic resection ?!!

**4- endocrine factors**

DM / thyroid disorders / PCOS

tt: refer to endocrinology

**5- unexplained (50%)**

75% continue normally without any pharmacological treatment

start aspirin / LMWH / psychological support since +ve pregnancy test

# MCQ 1

A 28-year-old woman with a BMI of 25 kg/m2 books into the antenatal clinic at 12 weeks. Two years previously she had a confirmed iliofemoral thrombosis in her left leg after major knee surgery

**Your advice regarding thromboprophylaxis should be :**

A. To use **LDA** throughout pregnancy and for 6 weeks postpartum
B. To use LMWH throughout pregnancy and for 6 weeks postpartum
C. To use LMWH from 28 weeks and for 6 weeks postpartum
D. To use **LDA** and **LMWH** throughout the pregnancy and for 6 weeks postpartum
E. To use **LMWH** only if other risk factors arise in pregnancy

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# MCQ 2

A 36-year-old woman, para 5, attends the antenatal clinic for a review at 20 weeks of gestation. A general exam reveals a BMI of 41 kg/m2 and varicose veins. Her anomaly scan and booking bloods are normal.

**Your advice regarding thromboprophylaxis should be :**

A. To use **LDA** throughout pregnancy and for 6 weeks postpartum
B. To use LMWH throughout pregnancy and for 6 weeks postpartum
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E. To use **LMWH** only if other risk factors arise in pregnancy

# MCQ 3

- A 25-year-old lady , G2P1 , delivered an alive baby girl by elective CS due to breech presentation , her BMI is 23 kg/m2 , non-smoker .

**Your advice regarding thromboprophylaxis should be :**

A. To use **LDA** for 6 weeks postpartum
B. To use **LMWH** for 6 weeks postpartum
C. To use **LMWH** for 10 days postpartum
D. To use **LDA** and **LMWH** for 6 weeks postpartum
E. Hydration and mobilization

# MCQ 3

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C. To use **LMWH** for 10 days postpartum
D. To use **LDA** and **LMWH** for 6 weeks postpartum
**E. Hydration and mobilization**

# MCQ 4

- Which of the following antibodies carries the highest thromboembolic risk and more responsible for recurrent VTE :

A- factor V leiden heterozygous

B- protein s deficiency

C- anti-thrombin 3 deficiency

D- antinuclear antibodies

E- protein c deficiency

# MCQ 4

- Which of the following antibodies carries the highest thromboembolic risk and more responsible for recurrent VTE :

A- factor V leiden heterozygous

B- protein s deficiency

**C- anti-thrombin 3 deficiency**

D- antinuclear antibodies

E- protein c deficiency

# MCQ 5

- **Traneximic acid :**

A- is an antifibrinolytic

B- is used as a third line drug for tt of menorrhagia

C- increases tissue plasminogen activator activity

D- reduces menstrual blood loss by 90%

E- can cause dysmenorrhea

# MCQ 5

- **Traneximic acid :**

A- is an antifibrinolytic

B- is used as a third line drug for tt of menorrhagia

C- increases tissue plasminogen activator activity

D- reduces menstrual blood loss by 90%

E- can cause dysmenorrhea

# MCQ 6

- **Warfarin** in pregnancy, all are true except :

A- it is teratogenic

B- it crosses the placenta

C- epidural anesthesia is better to be avoided

D- is contraindicated in breastfeeding

E- should be avoided after 36 weeks of gestation

# MCQ 6

- **Warfarin** in pregnancy, all are true except :

A- it is teratogenic

B- it crosses the placenta

C- epidural anesthesia is better to be avoided

D- is contraindicated in breastfeeding

E- should be avoided after 36 weeks of gestation

# MCQ 7

- A 42 YO patient is seen at 18 week GA with chest pain, mild SOB, and a swollen left leg. Blood investigations, CXR and ECG are normal. Duplex US at the same day confirms left femoral DVT. Your next step:

A- D-dimer

B- CTPA

C- MRI

D- start UFH

E- start therapeutic dose LMWH

# MCQ 7

- A 42 YO patient is seen at 18 week GA with chest pain, mild SOB, and a swollen left leg. Blood investigations, CXR and ECG are normal. Duplex US at the same day confirms left femoral DVT. Your next step:

A- D-dimer

B- CTPA

C- MRI

D- start UFH

E- start therapeutic dose LMWH

# MCQ 8

- Which of the following conditions lets you **consider thromboprophylaxis during pregnancy** even without any other risk factor ?

A- diabetes

B- sickle cell disease

C- IUGR

D- thalassemia

E- obesity type 2

# MCQ 8

- Which of the following conditions lets you **consider thromboprophylaxis during pregnancy** even without any other risk factor ?

A- diabetes

B- sickle cell disease

C- IUGR

D- thalassemia

E- obesity type 2

# MCQ 9

A 25-year-old lady , delivered an alive baby boy by normal vaginal delivery , her BMI is 42 kg/m2 , non-smoker .

**Your advice regarding thromboprophylaxis should be :**

A. To use **LDA** for 6 weeks postpartum
B. To use **LMWH** for 6 weeks postpartum
C. To use LMWH for 10 days postpartum
D. To use **LDA** and **LMWH** for 6 weeks postpartum
E. To use **LMWH** only if other risk factors arise in pregnancy

# MCQ 9

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A. To use **LDA** for 6 weeks postpartum

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**C. To use LMWH for 10 days postpartum**

D. To use **LDA** and **LMWH** for 6 weeks postpartum

E. To use **LMWH** only if other risk factors arise in pregnancy

# MCQ 10

- A 22 weeks pregnant lady who will travel from Dubai to Amman to celebrate wedding of her brother. Her BMI is 22 and this is her first pregnancy. Whats the **preventive measure for VTE ?**

A- heparin

B- warfarin

C- hydration, movement in aeroplan

D- nothing

E- LMWH for 10 days

# MCQ 10

- A 22 weeks pregnant lady who will travel from Dubai to Amman to celebrate wedding of her brother. Her BMI is 22 and this is her first pregnancy. Whats the **preventive measure for VTE ?**

A- heparin

B- warfarin

C- hydration, movement in aeroplan

D- nothing

E- LMWH for 10 days

Born

To Leave

a " "

# GOOD LUCK

# IN YOUR EXAM


Thank
You