Venous Thromboembolism (VTE) Reducing risk

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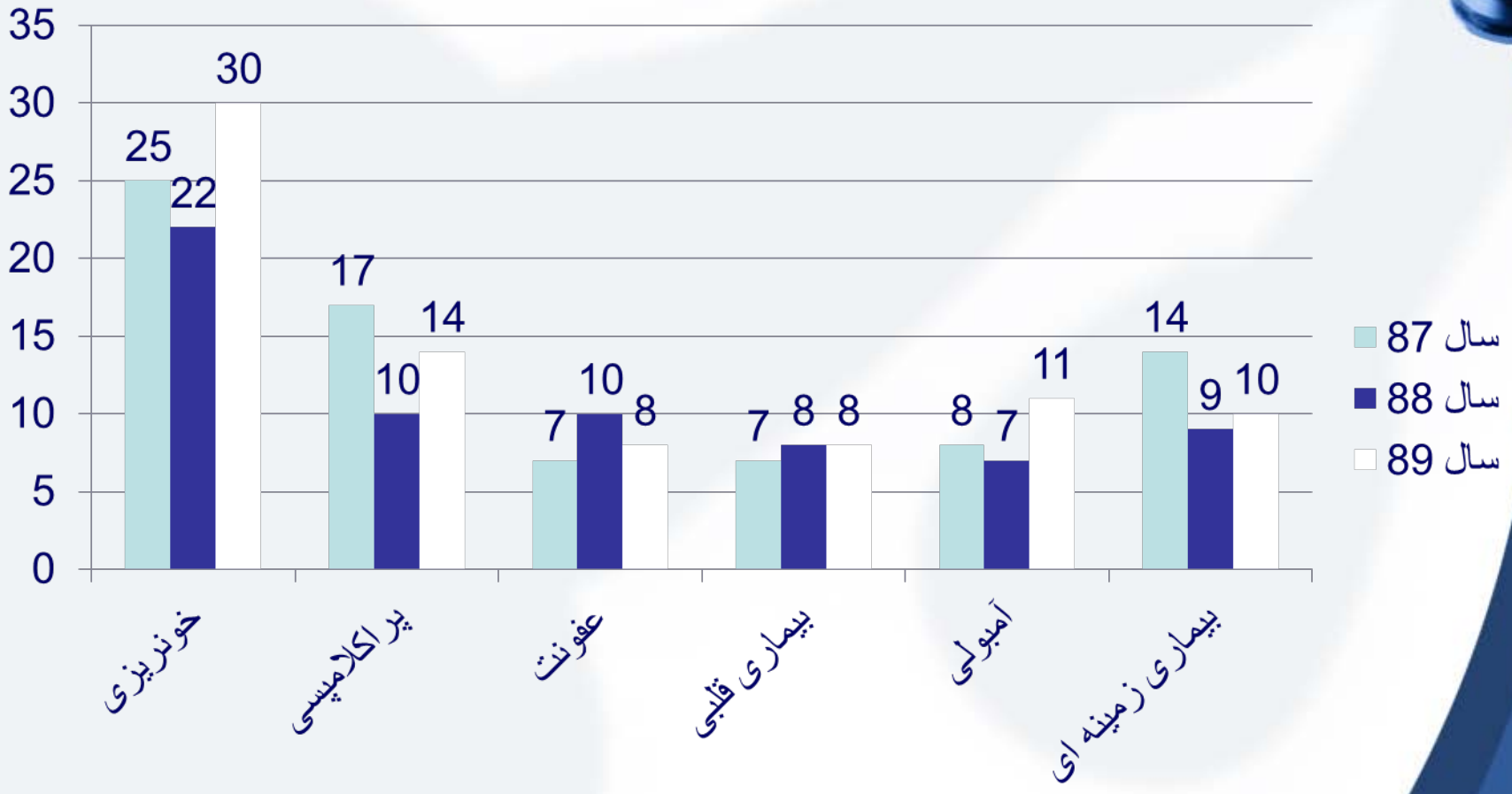
Venous Thromboembolism

- Statistics:
  - UK
  - IRAN

Statistics (UK) :

- Each year 25,000 people in the UK die from venous thromboembolism
- Second most common cause of maternal death overall
- NICE estimates that LMWH reduces VTE risk in medical and surgical patients by 60% and 70%, respectively
- 79% of the women who died from pulmonary embolism in the UK between 2003 and 2005 had identifiable risk factors
- The case fatality rate of pulmonary embolism was 3.5%

درصد مادران فوت شده بر حسب شایعترین علل مرگ مادر



Source: Ministry of Health, Iran

Venous Thromboembolism

- Risk Assessment & Management
- Evidence -Based Medicine

Guideline & Protocols

- UK Guideline (Royal College of Obstetricians and Gynaecologists “RCOG”)
  - www.rcog.org.uk

- وزارت بهداشت، درمان و آموزش پزشكي
  - www.behdasht.gov.ir

Royal College of Obstetricians and Gynaecologists (www.rcog.org.uk)

وزارت بهداشت، درمان و آموزش پزشکی

Benefits of following the guideline

- دستورالعمل پیشگیری از ترومبوآمبولی وریدی در بارداری و پس از زایمان
- http://behdasht.gov.ir/uploads/VTE_prevention-Guideline._pdf_151337.pdf

- **Protecting patients (Safety)**

&

- **Protecting doctors (Medico-legal)**

Examples of VTE risk assessment:

- 40 years old , BMI=42, Pre-eclampsia, smoker, emergency c/section, previous history of PE, family history of DVT in mother, Anti-thrombin deficiency

- 22 years old, BMI=21, NVD, mobile

Risk Factors

- **Pre-existing**
- **Obstetric**
- **New-onset/transient & Potentially reversible**

Risk Factors (Pre-existing):

- Previous venous thromboembolism
- Thrombophilia:
  - *Heritable*:
    - Antithrombin deficiency
    - Protein C deficiency
    - Protein S deficiency
    - Factor V Leiden
    - Prothrombin gene G20210A
  - *Acquired (antiphospholipid syndrome)*:
    - Persistent lupus anticoagulant
    - Persistent moderate/high-titre anticardiolipin antibodies or β2 glycoprotein 1 antibodies
- Medical comorbidities :e.g. heart or lung disease, SLE, cancer, inflammatory conditions (inflammatory bowel disease or inflammatory polyarthropathy), nephrotic syndrome (proteinuria > 3 g/day), sickle cell disease
- Intravenous drug user
- Age > 35 years
- Obesity (BMI > 30 kg/m2)
- Parity ≥ 3
- Smoking
- Gross varicose veins (symptomatic or above knee or with associated phlebitis, oedema/skin changes)
- Paraplegia

Risk Factors (Obstetric):

- Caesarean section
- Pre-eclampsia
- Multiple pregnancy, assisted reproductive therapy
- Prolonged labour
- PPH (> 1 litre) requiring transfusion

Risk Factors (New-onset/transient & Potentially reversible):

- Surgical procedure in pregnancy or puerperium (e.g. ERPC, appendicectomy, postpartum sterilisation)
- Hyperemesis, dehydration
- Ovarian hyperstimulation syndrome
- Admission or immobility (≥ 3 days' bed rest) e.g. symphysis pubis dysfunction restricting mobility
- Systemic infection (requiring antibiotics or admission to hospital) e.g. pneumonia, pyelonephritis,
- postpartum wound infection
- Long-distance travel (> 4 hours)

Adjusted Odds Ratio for Risk Factors

Risk factor	AOR	95% CI	Comment
Previous VTE[23]	24.8	17.1–36	
Age > 35[15,22]	1.3[14]	1.0–1.7	n = 603
	1.4[21]	1.0–2.0	pn = 256
Obesity, body mass index > 30[6,22–24]	2.65[5]	1.09–6.45	n = 143 an PE
	5.3[23]	2.1–13.5	n = 129
	4.4[22]	3.4–5.7	
	1.7[21]	1.1–2.6	pn = 256
Body mass index >25[13,22]	1.8[12]	1.3–2.4	an = 268
	2.4[12]	1.7–3.3	pn = 291
	1.7[21]	1.2–2.4	pn = 256
Weight:			
90–120 kg[31]	1.93	1.10–3.39	an
> 120 kg	4.32	1.26–14.84	an
Weight gain in pregnancy > 21 kg[13] (compared with 7–21 kg)	1.6	1.1–2.6	pn = 291
Parity:			
1[16]	4.03	1.6–9.84	n = 143 an PE
2[15]	1.5	1.1–1.9	n = 603
3 or more[14]	2.4	1.8–3.1	n = 603
Smoking:	2.1[12]	1.3–3.4	an = 268
10–30/day[13,15,26]	3.4[12]	2.0–5.5	pn = 291
	1.4[14]	1.1–1.9	n = 603
	2.5[25]	1.3–4.7	n = 90
'current smoker'[24]	2.7[23]	1.5–4.9	n = 129
Sickle cell[22,36]	6.7[22]	4.4–10.1	
	2.5[138]	1.5–4.1	DVT
	1.7[138]	0.9–3.1	PE

Adjusted Odds Ratio for Risk Factors

Systemic lupus erythematosus[23]	8.7	5.8–13	
Anaemia[23]	2.6	2.2–2.9	
Varicose veins[26]	2.4	1.04–5.4	
Immobility[13]	7.7	3.2–19	an
	10.8	4.0–28.8	pn
Pre-eclampsia[13,15]	2.9[14]	2.1–3.9	
	3.1[12]	1.8–5.3	pn
Pre-eclampsia + fetal growth restriction[13]	5.8[12]	2.1–16	
Hyperemesis[13]	2.5	2–3.2	
Assisted reproductive therapy[13]	4.3	2.0–9.4	an
Twins[13,15]	2.6[12]	1.1–6.2	an
	1.8[14]	1.1–3.0	n = 603
Multiple pregnancy[22]	4.2	1.8.–9.7	an = 109
Preterm delivery < 36 weeks[22]	2.4	1.6–3.5	pn = 256
Antepartum haemorrhage[23]	2.3	1.8–2.8	
Emergency caesarean section[15]	2.7	1.8–4.1	
Any caesarean section[15,22,23]	3.6[14]	3.0–4.3	
	2.1[22]	1.8–2.4	
	2.0[21]	1.5–2.7	pn = 256
Postpartum haemorrhage > 1 litre[13]	4.1	2.3–7.3	
Postpartum haemorrhage + surgery[13]	12	3.9–36.9	
Obstetric haemorrhage[26]	9	1.1–71	
Postpartum infection[23]	4.1	2.9–5.7	
Postpartum infection + caesarean section[13]	6.2	2.4–16.2	
Transfusion[23]	7.6	6.2–9.4	

Risk assessment for venous thromboembolism (VTE)

Pre-existing risk factors	Tick	Score
Previous recurrent VTE		3
Previous VTE – unprovoked or estrogen related		3
Previous VTE – provoked		2
Family history of VTE		1
Known thrombophilia		2
Medical comorbidities		2
Age (> 35 years)		1
Obesity		1/2[a]
Parity ≥ 3		1
Smoker		1
Gross varicose veins		1
Obstetric risk factors		
Pre-eclampsia		1
Dehydration/hyperemesis/OHSS		1
Multiple pregnancy or ART		1
Caesarean section in labour		2
Elective caesarean section		1
Mid-cavity or rotational forceps		1
Prolonged labour (> 24 hours)		1
PPH (>1 litre or transfusion)		1
Transient risk factors		
Current systemic infection		1
Immobility		1
Surgical procedure in pregnancy or ≤ 6 weeks postpartum		2
TOTAL		

Assessment of Risk Factors

- Before/Early Pregnancy
- Admitted to Hospital
- After Delivery
- Opportunistic

Highest risk periods

- 1- first week postnatal : (53%) VTE occurred in the first week postpartum
- 2- first 6 weeks postnatal: 96% of the postpartum VTEs occurred in the first 6 weeks after delivery, of which (5.7%) were in postnatal week 5 and nine (3%) in postnatal week 6
- 3-antenatal

When to start Antenatal LMWH

- Antenatal thromboprophylaxis should begin as early in pregnancy as practical

When to start Postnatal LMWH

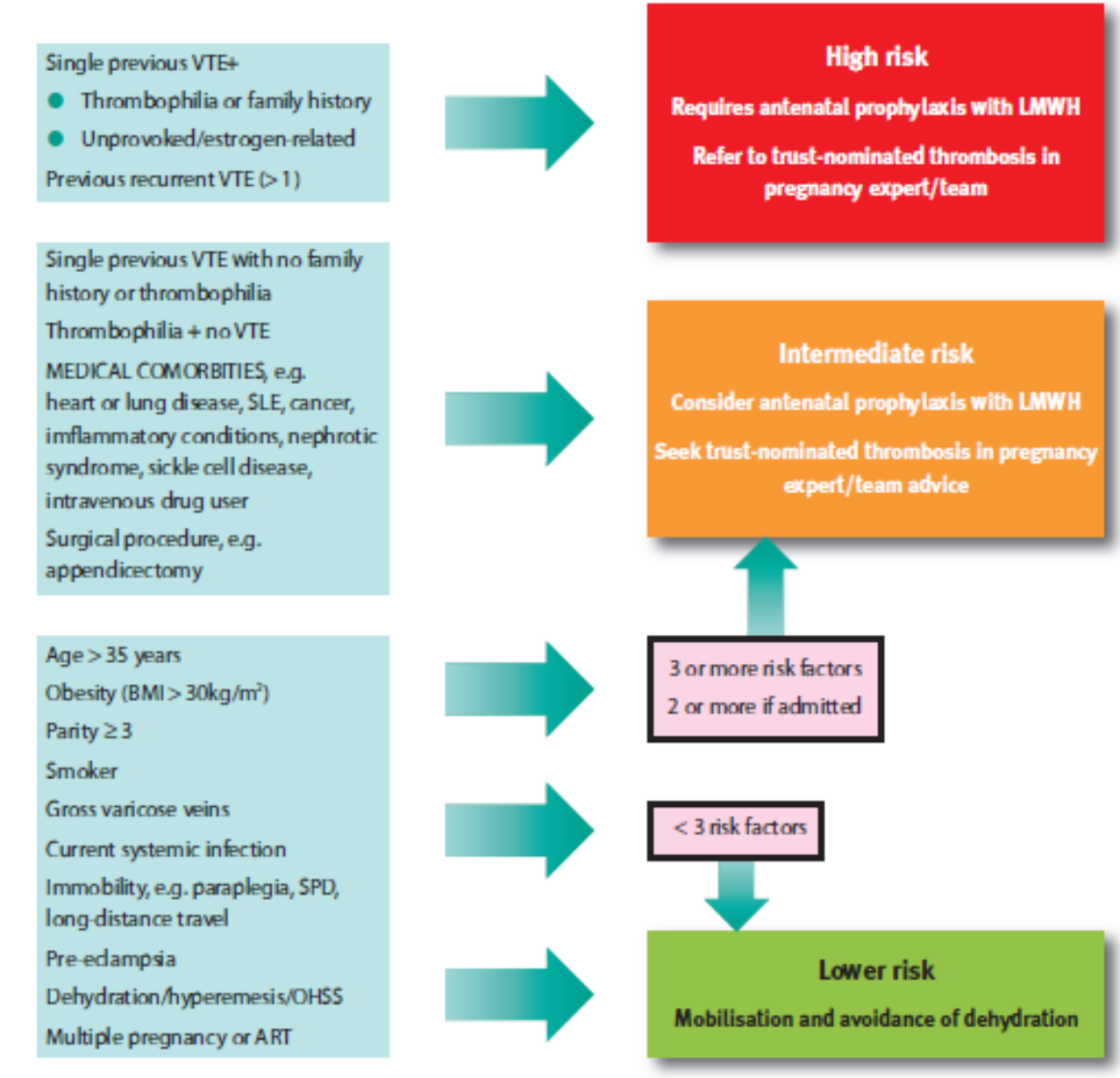
- No postpartum haemorrhage, no HELLP/DIC (Platelet > 75)
- 4 hours after delivery or 4 hours after removal of the epidural catheter

General advice

- Good Hydration
  - Be aware of Pre-eclamptic patients
- Early Ambulation
  - Minimizing thrombosis & expediting recovery
- Anti-Embolism Stockings
  - Effective, needs to be appropriate size and appropriately worn

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

Obstetric thromboprophylaxis risk assessment and management



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

Obstetric thromboprophylaxis risk assessment and management

Any previous VTE+

Anyone requiring antenatal LMWH

→ **High risk**

At least 6 weeks postnatal prophylactic LMWH

Caesarean section in labour

Asymptomatic thrombophilia (inherited or acquired)

BMI > 40 kg/m²

Prolonged hospital admission

MEDICAL COMORBIDITIES, e.g. heart or lung disease, SLE, cancer, imflammatory conditions, nephrotic syndrome, sickle cell disease, intravenous drug user

→ **Intermediate risk**

At least 7 days postnatal prophylatic LMWH

Note: if persisting or > 3 risk factors, consider extending thromboprophylaxis with LMWH

Age > 35 years

Obesity (BMI > 30kg/m²)

Parity ≥ 3

Smoker

Elective caesarian section

Any surgical procedure in the puerperium

Gross varicose veins

Current systemic infection

Immobility, e.g. paraplegia, SPD, long distance travel

Pre-eclampsia

Mid-cavity rotational operative delivery

Prolonged labour (> 24 hours)

PPH > 1 litre or blood transfusion

→ 2 or more risk factors

→ < 2 risk factors

→ **Lower risk**

Mobilisation and avoidance of dehydration

Prophylactic dose of LMWH

Table 3: Suggested thromboprophylactic doses for antenatal and postnatal LMWH

Weight (kg)	Enoxaparin	Dalteparin	Tinzaparin (75u/kg/day)
< 50	20 mg daily	2500 units daily	3500 units daily
50–90	40 mg daily	5000 units daily	4500 units daily
91–130	60 mg daily*	7500 units daily*	7000 units daily*
131–170	80 mg daily*	10 000 units daily*	9000 units daily*
> 170	0.6 mg/kg/day*	75 units/kg/day*	75 u/kg/day*
High prophylactic (intermediate) dose for women weighing 50–90 kg	40 mg 12-hourly	5000 units 12-hourly	4500 units 12-hourly
Treatment dose	1 mg/kg/12 hourly antenatal; 1.5 mg/kg/daily postnatal	100 units/kg/12 hourly or 200 units/kg/daily postnatal	175 u/kg/daily (antenatal and postnatal)

* may be given in two divided doses

Duration of Thrombo-prophlyaxis Postpartum

- High Risk Group : 6 weeks

- Intermediate risk : 7 days
  - In women at intermediate risk of VTE, there has been much debate as to the optimal duration of thromboprophylaxis. There is little evidence to support recommendations regarding duration of thromboprophylaxis in such women and research in this area is needed.
  - In an American population-based study,11 34 of the 64 (53%) VTE occurred in the first week postpartum. Thus, a minimum of 7 days of thromboprophylaxis is recommended.

Contraindications to LMWH

- **women with active antenatal or postpartum bleeding**
- **women considered at increased risk of major haemorrhage (such as placenta previa)**
- women with a bleeding diathesis, such as von Willebrand's disease, haemophilia or acquired coagulopathy
- **women with thrombocytopenia (platelet count less than 75 x 109)**
- acute stroke in the last 4 weeks (ischaemic or haemorrhagic)
- severe renal disease (glomerular filtration rate less than 30 ml/minute/1.73 m2)
- severe liver disease (prothrombin time above normal range or known varices)
- **uncontrolled hypertension (blood pressure greater than 200 mmHg systolic or greater than 120 mmHg diastolic).**

Which agents should be used for thromboprophylaxis?

- **LMWHs are the agents of choice for antenatal thromboprophylaxis. They are at least as effective as and safer than unfractionated heparin.**
  - **Safer : risk of thromboytopenia & osteoporosis : nil to very minimal**
- *Unfractionated heparin*
  - Unfractionated heparin has a shorter half-life than LMWH and there is more complete reversal of its activity by protamine sulphate.
- The required interval between a prophylactic dose of unfractionated heparin and regional anaesthesia is less (4 hours) than with LMWH (12 hours) and there is less concern regarding neuraxial haematomas with unfractionated heparin

Caesarean section

- **emergency caesarean section (category 1–3)**
  - **LMWH for 7 days after delivery**

- **elective caesarean section (category 4)**
  - **+ 1 further risk = LMWH for 7 days after delivery**
    - **Risks: age > 35 , BMI> 30, smoking, gross varicose vein, immobility**

Antiphospholipid syndrome

- *Only positive Antiphospholipid Antibodies : 6 weeks P/N*
- *Antiphospholipid syndrome (previous VTE) : very high risk, A/N : High Dose Prophylactic, 6 weeks P/N*
- *Antiphospholipid syndrome (Recurrent Miscarriage, IUGR/Pre-eclampsia) : A/N Prophylactic + Aspirin , P/N: 6 weeks*

Summary of guideline for thromboprophylaxis in women with previous venous thromboembolism (VTE) and/or thrombophilia (prophylactic doses are given in Table 3; see also Figure 1)

Risk	History	Prophylaxis
Very high	Previous VTE on long-term warfarin Antithrombin deficiency Antiphospholipid syndrome with previous VTE	Recommend antenatal high-dose LMWH and at least 6 weeks postnatal LMWH/warfarin Requires specialist management by experts in haemostasis and pregnancy
High	Previous recurrent or unprovoked VTE Previous estrogen-provoked (pill or pregnancy) VTE Previous VTE + thrombophilia Previous VTE + family history of VTE Asymptomatic thrombophilia (combined defects, homozygous FVL)	Recommend antenatal and 6 weeks postnatal prophylactic LMWH
Intermediate	Single previous VTE associated with transient risk factor no longer present without thrombophilia, family history or other risk factors Asymptomatic thrombophilia (except antithrombin deficiency, combined defects, homozygous FVL)	Consider antenatal LMWH (but not routinely recommended) Recommend 6 weeks postnatal prophylactic LMWH Recommend 7 days (or 6 weeks if family history or other risk factors) postnatal prophylactic LMWH

Thrombophilia

- **Heritable or Acquired thrombophilia**
  - **7 days following delivery, even if they were not receiving antenatal thromboprophylaxis. This could be extended to 6 weeks if there is a family history or other risk factors present.**

Previous VTE

- **Thromboprophylaxis with LMWH or warfarin for 6 weeks postpartum, regardless of the mode of delivery**

Examples:

- BMI 41 , NVD
- Homozygous factor V leiden
- Pre-eclamptic , admitted to hospital
- 20/40 weeks had an appendicectomy
- Factor V Leiden heterozygote , NVD
- Antiphospholipid syndrome with previous stillbirth(IUGR)
- Antiphospholipid syndrome with previous PE
- Hyperemsis , admitted with 4+ ketone
- Placenta previa admitted with bleeding
- 28/40 weeks, admitted with pyelonephritis
- Post c/section readmitted with wound infection

Take Home Message

- Follow the guideline to protect your patients and yourself
- If you don’t remember , look it up
- If it is not there , ask haematologist (with the appropriate expertise)
- If in doubt : hydration, TEDS, ambulation and LMWH (esp. first week P/N)

Thank You