



ICT 2023

28th International
Congress on Thrombosis

Venous thromboembolism and pregnancy

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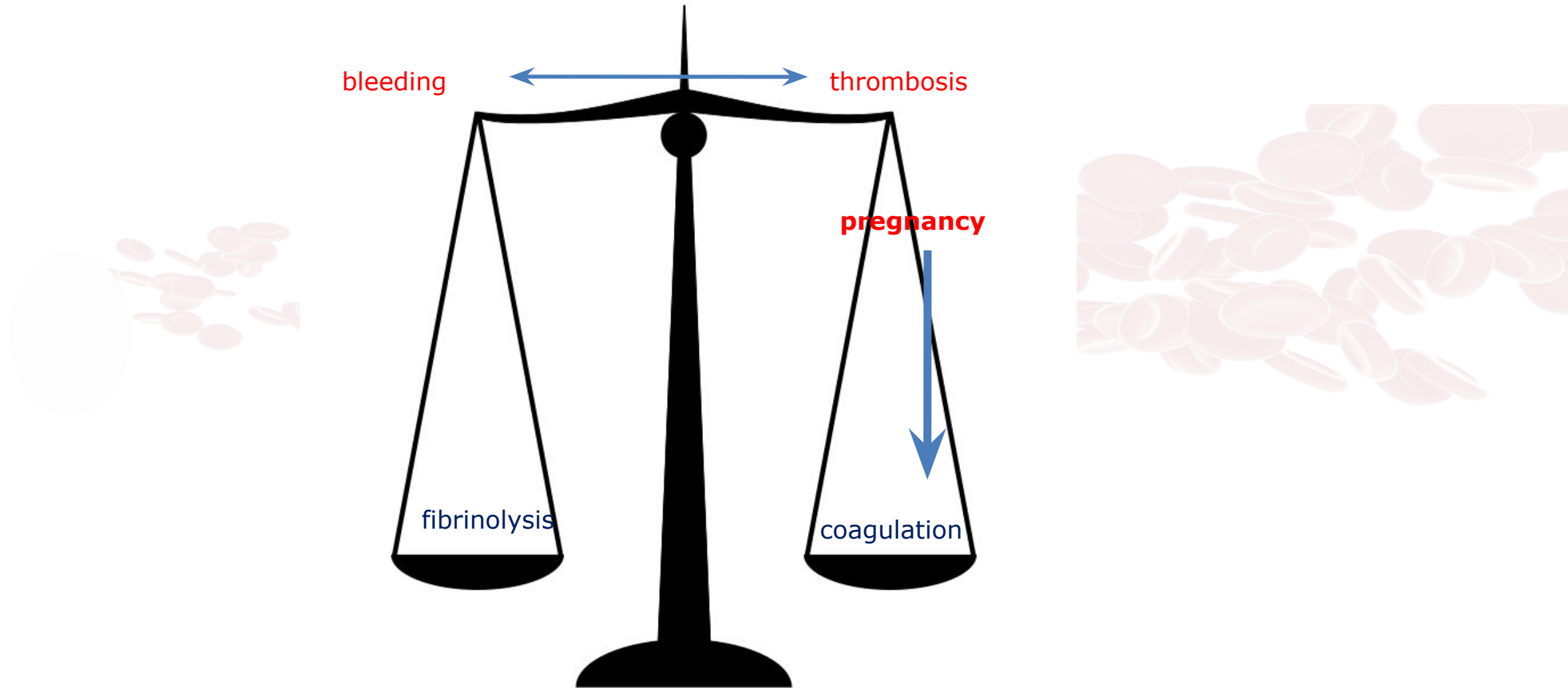
Declaration of Conflict Of Interest



I have the following potential conflict(s) of interest to report

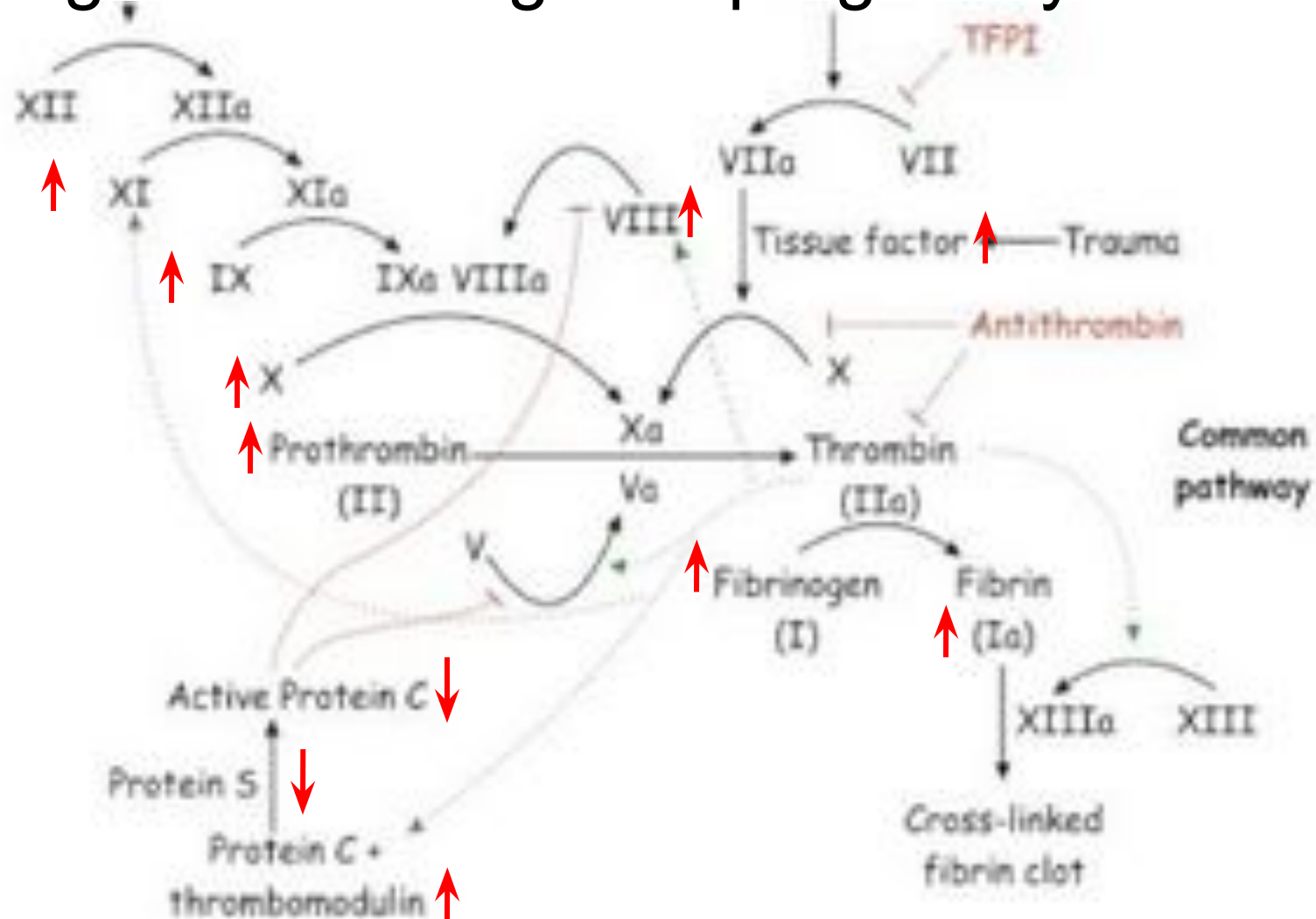
Speaker fees from: Bayer, Boehringer Ingelheim, Pfizer

Advisory board member for: Bayer Slovenia (for peripheral arterial disease)



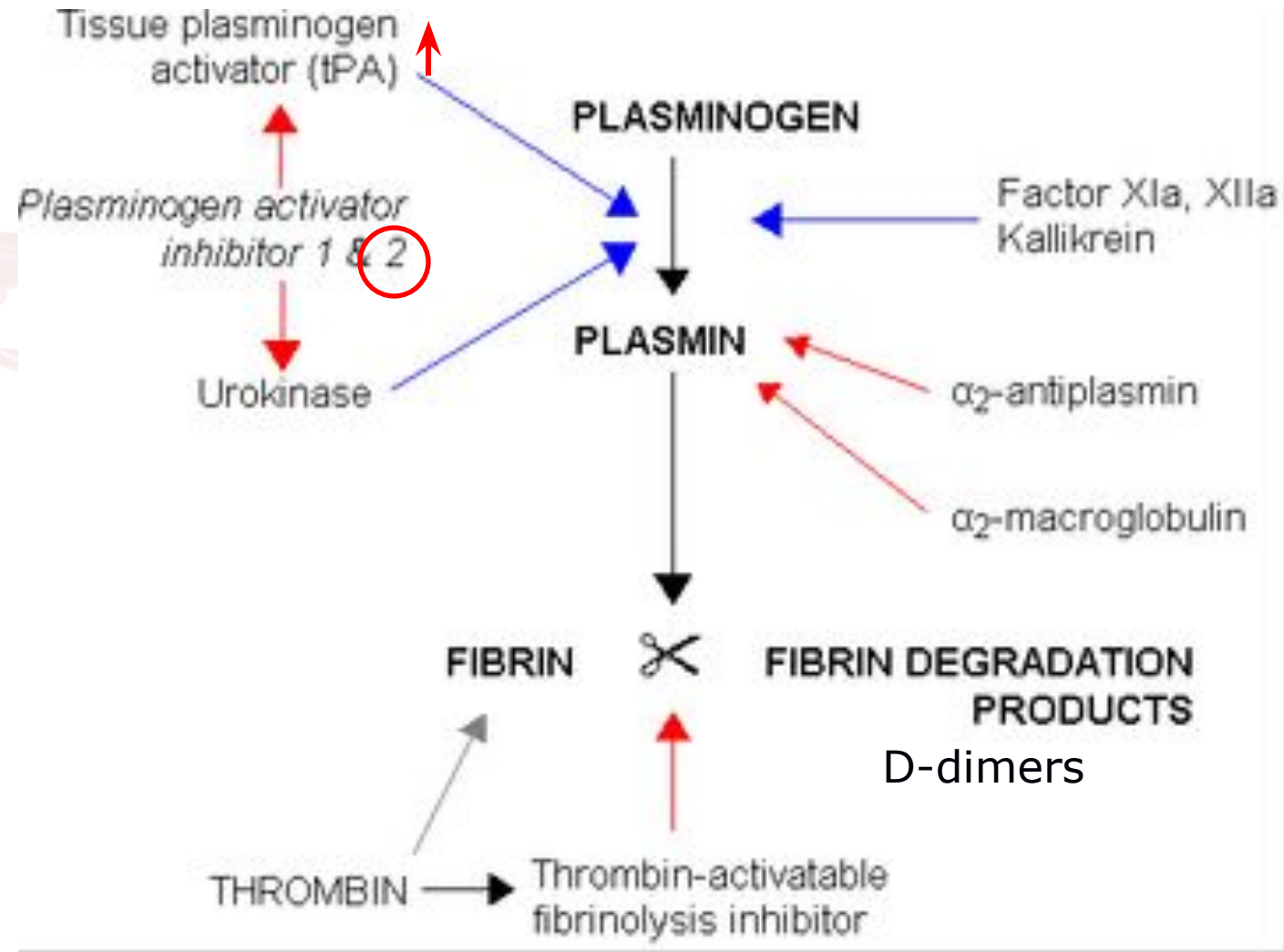
VTE ~ in pregnancy and postpartum 4x more common than in nonpregnant women of the same age

Coagulation changes in pregnancy

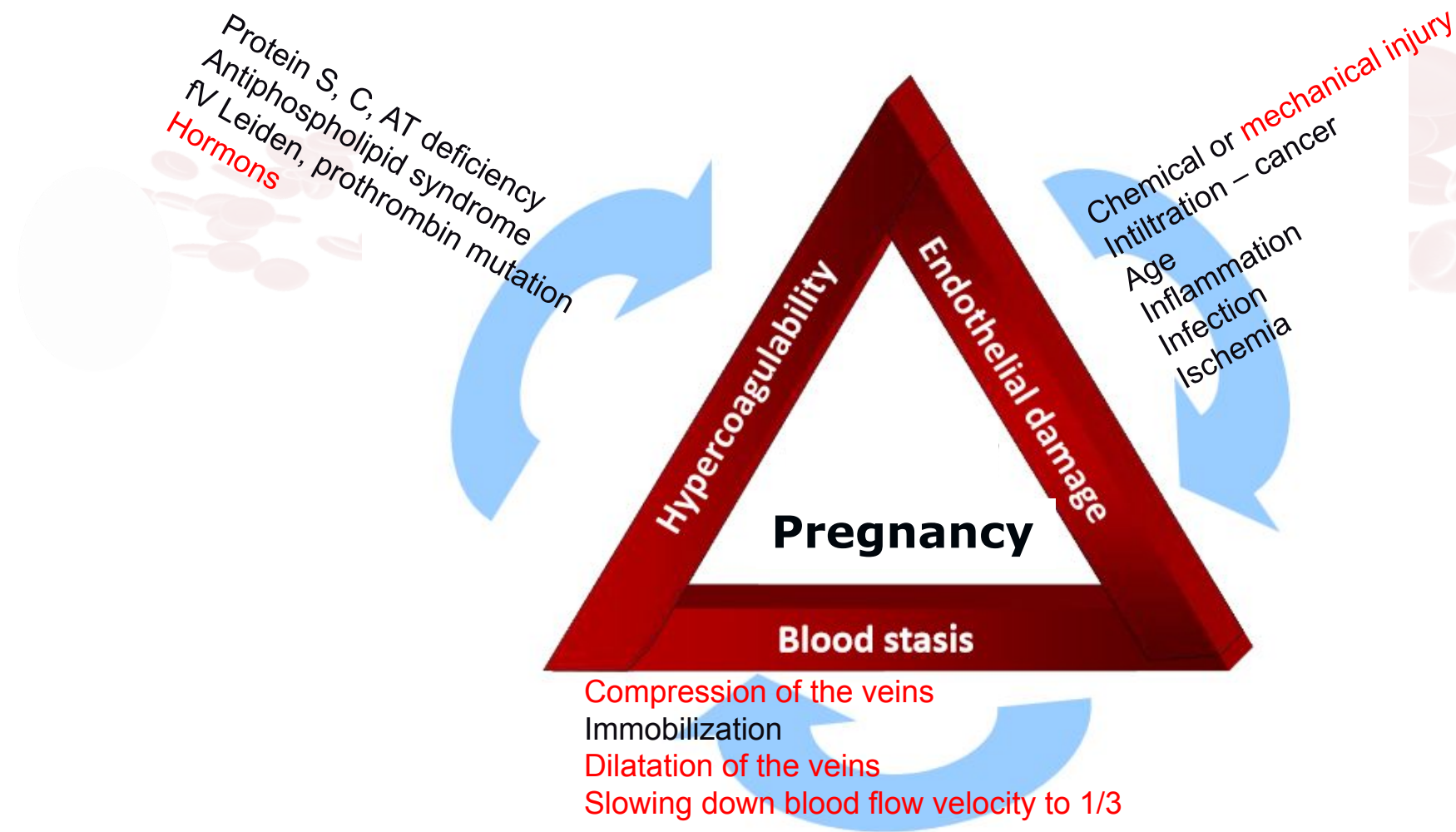


Normalisation: several weeks after postpartum

Changes of fibrinolysis in pregnancy



Patophysiology



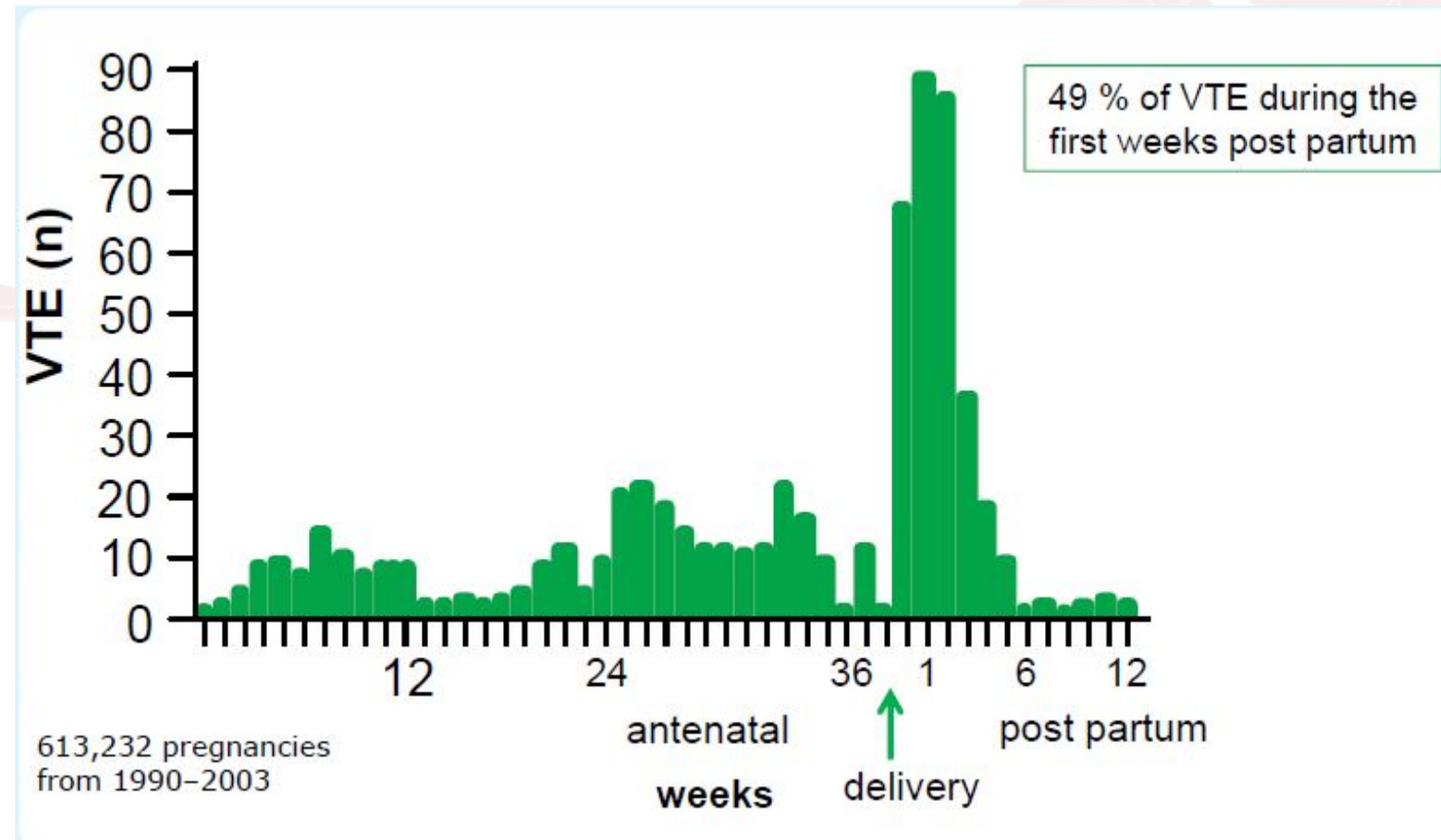
Epidemiology and the time course

VTE ~ 4x more common than in the nonpregnant women of the same age

Absolut risk 199 VTE/100 000 years
Heit et al. Ann Intern Med. 2005;143:697-706.

Incidence 0.06–0.13 %
Kourlaba et al. Int J Gynaecol Obstet . 2016 ;132:4-10.

We do not know how preventive measures influence the above data.

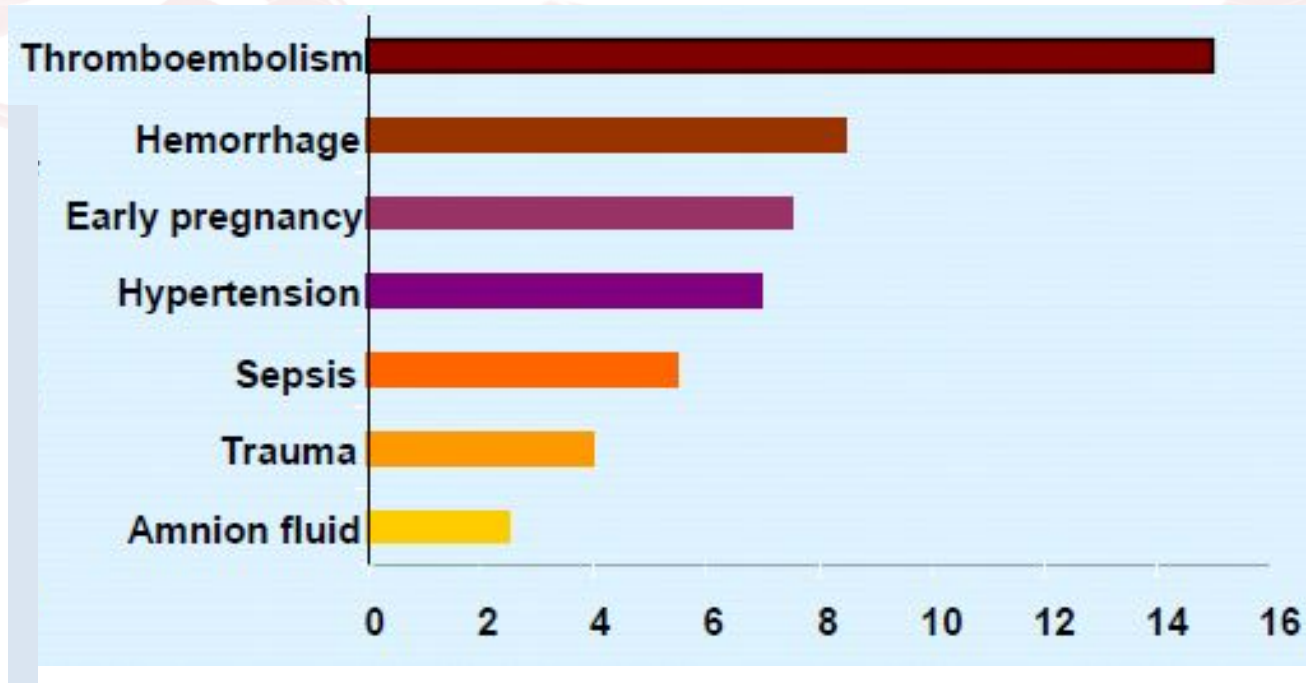


Jacobsen et al. AJOG 2008; 198 (2): 233.e1–7.

VTE in real life

- One death due to VTE on 100 000 deliveries
- (in developed countries ~ around 10 % of all deaths)
- - more than sepsis, preeclampsia, bleedings together

Deaths on 1 000 000 deliveries



CEMACH: The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer, 2003-5. The Seventh Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. London; 2007:

Greer IA, *Lancet* 1999;353:1258-65. Stein PD, et al. *Am J Med* 2004;117:121-5.

Risk assessment - risk factors

Many; lifestyle, related to the previous diseases, pregnancy, pregnancy related pathology

Additive effect of different risk factors

Assessment is sometimes difficult and unreliable.

Differences among different professional associations.

McLintock et al. Aust N Z J Obstet Gynec. 2012 Feb;52(1):14-22.

Bates et al. Chest. 2012; 141 (2 Suppl): e691S–736S. Thromboembolic Disease in Pregnancy and the Puerperium: Acute Management Green-top Guideline No. 37b;<https://www.rcog.org.uk/media/wj2lpc05/gtg-37b-1.pdf>

Risk factors

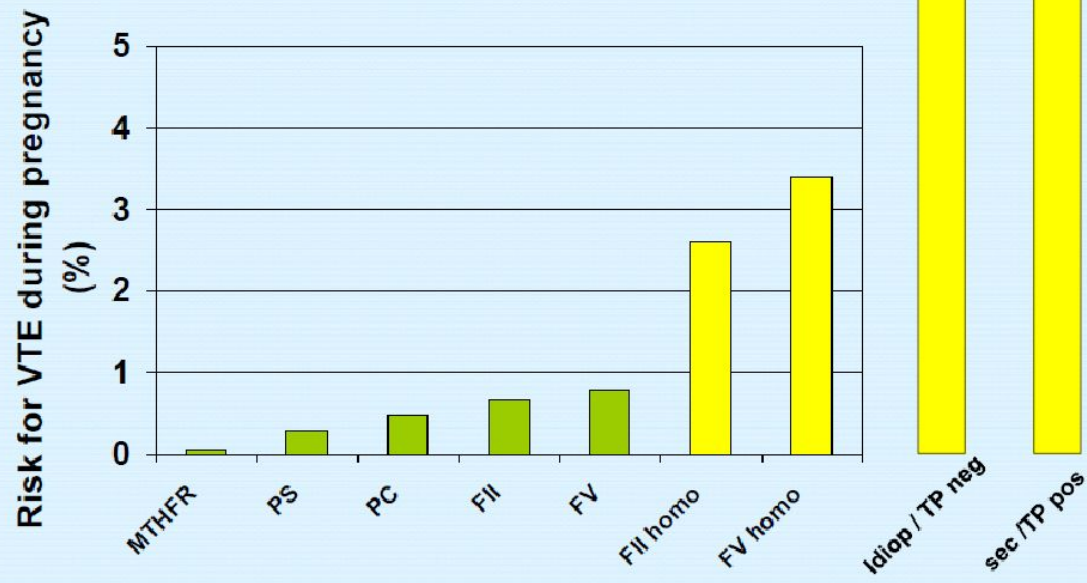
Adjusted Odds Ratios for Risk of VTE in pregnancy and / or postpartum with different risk factors

Data from various case-control studies

Risk factor	Adjusted OR	95% CI
BMI > 30	4.4	3.4-5.7
Smoking	2.1	1.3-3.4
Varicose veins	2.4	1.04-5.4
Hyperemesis gravidarum	2.5	2-3.2
ART	4.3	2.0-9.4
Preterm delivery <36 week	2.4	1.6-3.5
Cesarean section	3.6	3.0-4.3
Postpartum infection	4.1	2.9-5.7
Postpartum hemorrhage	9	1.1-71
Transfusion	7.6	6.2-9.4
Immobilization	7.7	3.2-19
Systemic lupus erythematosus	8.7	5.8-13
Prior VTE	24.8	17.1-36

Risk factors- thrombophilia

Thrombophilia and VTE risk in pregnancy Risk for women without prior VTE / with prior VTE



Diagnosis

Clinical picture of VTE (deep venous thrombosis (DVT) and pulmonary embolism (PE))

Symptoms and signs of VTE are the same as in nonpregnant women.

DVT leg swelling and pain is a frequent complaint or finding also in normal pregnant women.

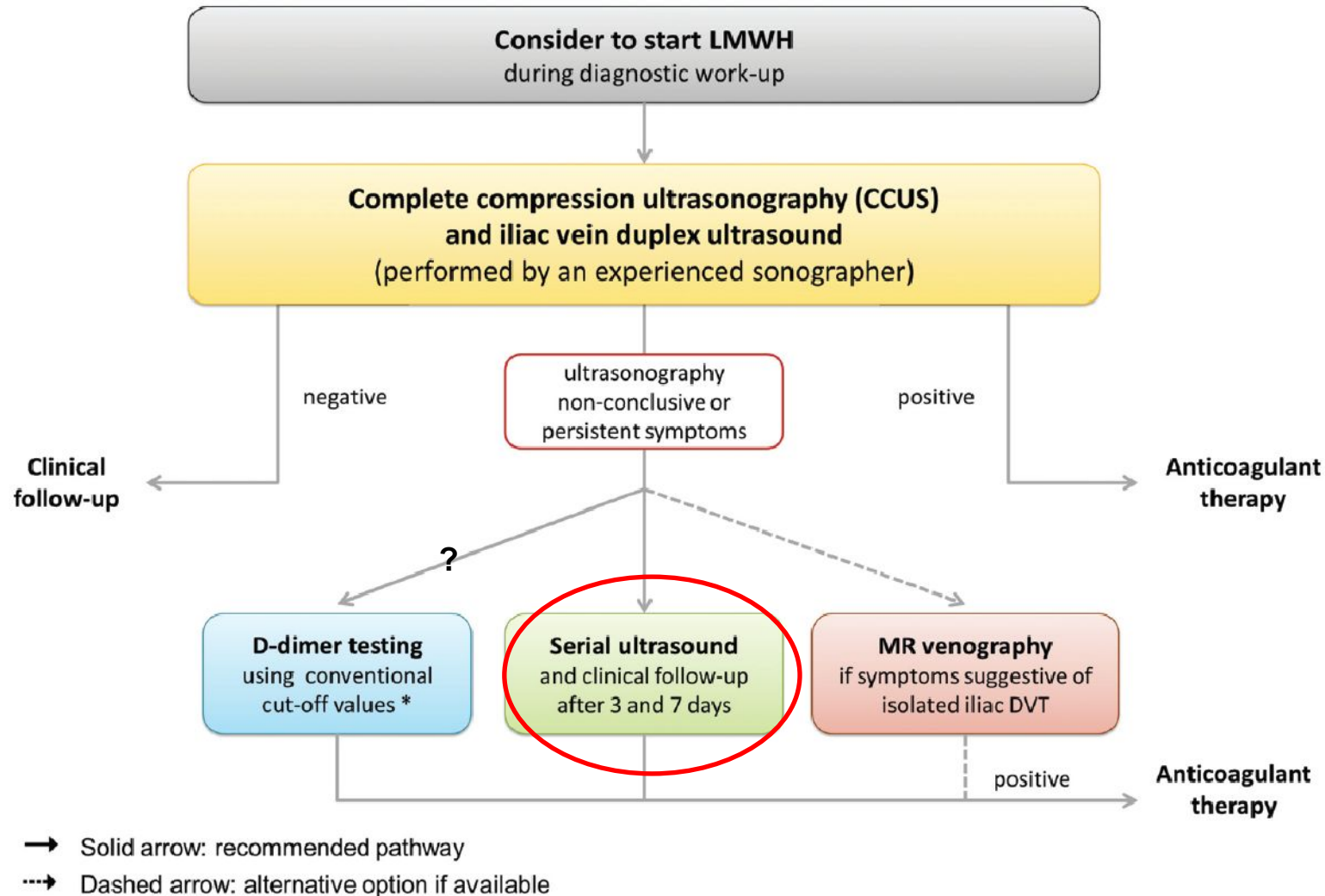
PE dyspnea (cardinal symptom?) is quite common complaint in healthy pregnant women.

VTE in pregnancy confirmed in about 10 % of suspected women.

Clinical prediction rules inconclusive

D-dimer - to exclude VTE; useful? (Bellesini et al. JTH. 2021;19:2454-67.)

Diagnostic procedure in suspected DVT in pregnancy



Linnemann et al. *Vasa* (2016), 45 (2), 87 – 101.

American Society of Hematology 2018 Guidelines for Management of Venous Thromboembolism

Diagnostic procedure in suspected PE in pregnancy

Recommendations	Class ^a	Level ^b
Diagnosis		
Formal diagnostic assessment with validated methods is recommended if PE is suspected during pregnancy or in the post-partum period. ^{388,391}	I	B
D-dimer measurement and clinical prediction rules should be considered to rule out PE during pregnancy or the post-partum period. ^{388,391}	IIa	B
In a pregnant patient with suspected PE (particularly if she has symptoms of DVT), venous CUS should be considered to avoid unnecessary irradiation. ³⁸⁸	IIa	B



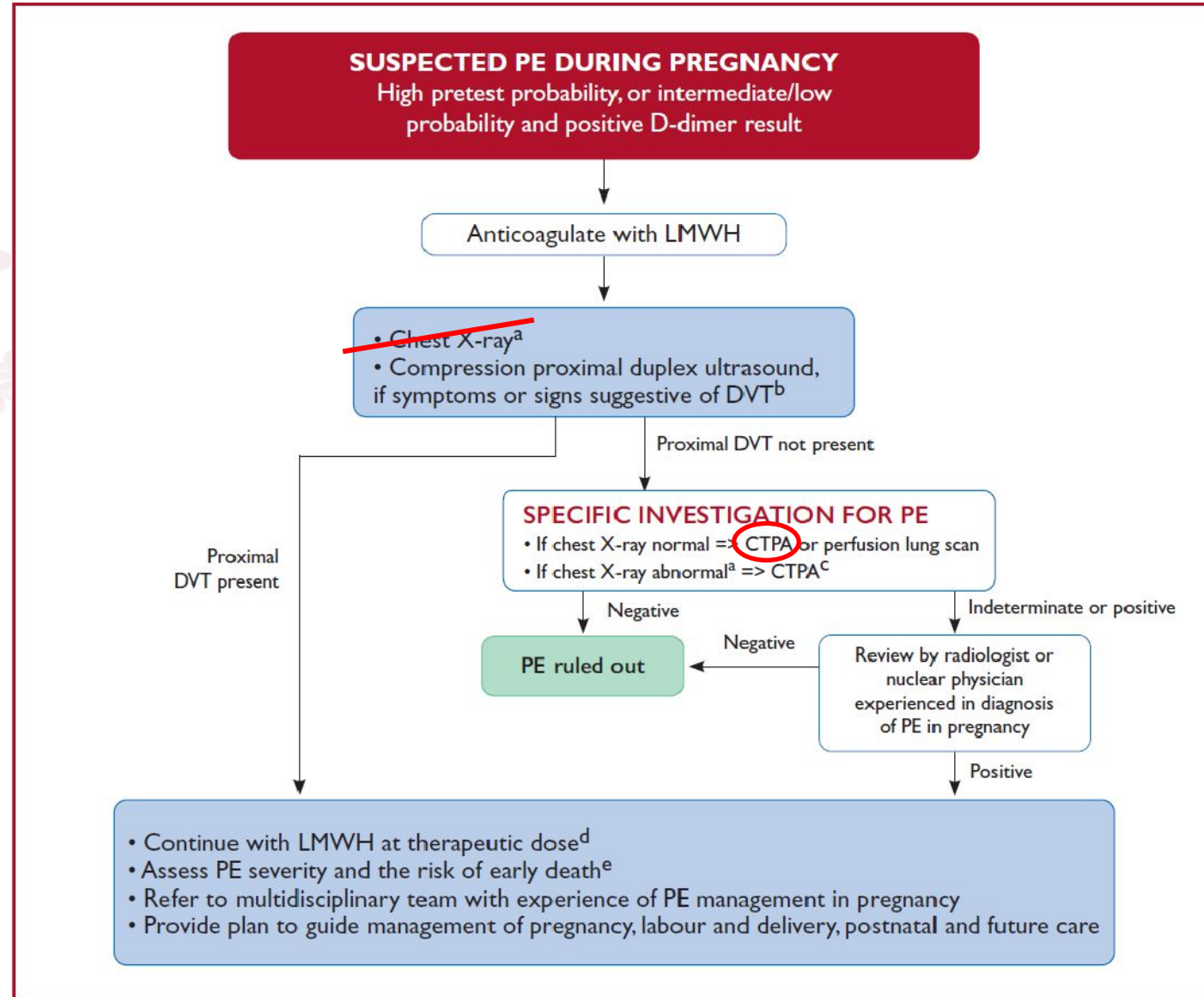
893 PE suspected pregnant patients
In 241 radiologic investigation was avoided

Righini M et al. Ann Intern Med. 2018;169(11):766-773.

Van der Pol et al. N Engl J Med 2019; 380:1139-1149

Konstantinides SV, et al. Eur Heart J. 2019

Diagnostic procedure in suspected PE in pregnancy



Radiation exposure

Test	Estimated foetal radiation exposure (mGy)	Estimated maternal radiation exposure to breast tissue (mGy)
Chest X-ray	<0.01	<0.1
Perfusion lung scan with technetium-99m labelled albumin		
Low dose: ~40 MBq	0.02–0.20	0.16–0.5
High dose: ~200 MBq	0.20–0.60	1.2
Ventilation lung scan	0.10–0.30	<0.01
CTPA	0.05–0.5	3–10

CTPA = computed tomography pulmonary angiography.

Treatment of VTE in pregnancy

Anticoagulant	Acceptability in Pregnancy	Comments
LMWH	Yes	<ul style="list-style-type: none"> Does not cross the placenta LMWH preferred over UFH due to maternal safety profile (likely lower risk of HIT, reduced bone mineral density)
UFH	Yes	<ul style="list-style-type: none"> Does not cross the placenta
Fondaparinux	Not preferred	<ul style="list-style-type: none"> Reported to cross placenta in small amounts Clinical experience with fondaparinux very limited
Vitamin K Antagonist (VKA)	No	<ul style="list-style-type: none"> Crosses the placenta Potential for teratogenicity, pregnancy loss, fetal bleeding, neurodevelopmental deficits
Direct Oral Anticoagulants	No	<ul style="list-style-type: none"> Dabigatran and Xa inhibitors likely cross the placenta Reproductive effects in humans are unknown

Bates et al. Chest. 2012; 141 (2 Suppl): e691S–736S. Thromboembolic Disease in Pregnancy and the Puerperium: Acute Management Green-top Guideline No. 37b; <https://www.rcog.org.uk/media/wj2lpc05/gtg-37b-1>. American Society of Hematology 2018 Guidelines for Management of Venous Thromboembolism. *Blood Adv* (2018) 2 (22): 3198–3225.

Treatment of VTE in pregnancy

UFH

Short half life (1-2h)

APTT as control test

rarely used - when quick normalisation of coagulation needed due to expected problems (around the delivery date?)

LMWH

dosage according to the body weight, once or twice daily (in the last months twice?)

Anti-Xa test (specific for LMWH used)

Routine measurement of peak anti-Xa activity for patients on LMWH for treatment of acute VTE in pregnancy or postpartum **is not recommended** except in women at extremes of body weight (< 50 kg, or > 90 kg) or with other complicating factors (for example, with renal impairment or recurrent VTE).

Bates et al. Chest. 2012; 141 (2 Suppl): e691S–736S.

Green-top Guideline No. 37b;<https://www.rcog.org.uk/media/wj2lpc05/gtg-37b-1>.

Treatment in special situations

Hemodynamic instable PE

systemic thrombolysis, catheter procedures, ECMO could be used

Anticoagulation not possible or is ineffective

consider filter insertion

Konstantinides SV, et al. Eur Heart J. 2019.
Green-top Guideline No. 37b;<https://www.rcog.org.uk/media/wj2lpc05/gtg-37b-1>

Treatment of VTE at term

Labor seems to start – no anticoagulation (advice for the woman);

If no obstetric indication for a planned delivery, wait for spontaneous delivery

Vaginal delivery is preferred

Elective c.s. or induction - stop LMWH 24 h before

When neuraxial anesthesia stop 24 hours before, and anticoagulate not before 4 h after removal of the catheter

Anticoagulation after labor

Should be restarted after delivery as soon as possible, depending on the amount of estimated vaginal blood loss and the type of delivery; (6-8)12 to 24 hours, longer if bleeding

Further on - once every 24 hours.

When VTE happens in the last days before labor – UFH could be used – stop it 4 h before, consider retrievable filter.

Treatment of VTE postpartum

Duration

Till the end of the 6th week, at least 3 months

LMWH (breast feeding possible)

VKA (breast feeding possible)

DOACs contraindicated in breast feeding, possible, when no breast feeding

Side effects of anticoagulation (LMWH)

- Injections
- Allergic reactions (20 %?),
- HIT (very low incidence),
- Osteoporosis?,
- Bleeding - during treatment 1-2% (mainly minor); at labor probably not more than „normal“
- Recurrency VTE (PE 1.3 %) 1.9%

Schindewolf et al. J Allergy Clin Immunol. 2013;132(1):131-9.

Romualdi et al. JTH. 2013;11:270-81.

Roshani et al. BMJ. 2011;1:e000257

Bates et al. Chest. 2012; 141 (2 Suppl): e691S–736S.

Green-top Guideline No. 37b;<https://www.rcog.org.uk/media/wj2lpco5/gtg-37b-1.pdf>

Bates et al. J Thromb Thrombolysis 2016;41:92-128

Conclusions

VTE in pregnancy is more common due to physiological changes and some additional risk factors

Clinical presentation of VTE is less reliable than in non pregnant women

Objective diagnostics should be performed

LMWH is used as a drug of choice for the whole pregnancy and 6 weeks postpartum

Treatment is safe and effective with rare side effects

Thank you for your attention

Questions?

