
# TROMBOFILIA E PROFILASSI ANTITROMBOTICA IN GRAVIDANZA

*Ida Martinelli - Milano*

# VTE and pregnancy

- VTE is the leading cause of maternal mortality
- the incidence of VTE in pregnancy is 0.71-1.3 per 1,000 women
- in pregnancy the risk of VTE is increased approximately 10-fold

# Relative distribution of VTE

- not substantially different in the three trimesters
- puerperium (6 weeks after delivery) is a particularly high risk period

# Relative distribution of VTE
## Martinelli et al, T&H 2002

- Duration: pregnancy: 280 days
  puerperium: 42 days

- Relative distribution of 100 VTE:
  pregnancy: 0.15 per day
  puerperium: 1.36 per day

- The probability of puerperium-related VTE is 9 times higher than pregnancy-related VTE

# Thrombophilia and VTE in pregnancy

| | odds ratio (95%CI) | | |
|---|---|---|---|
| | Grandone AJOG 1998 | Gerhardt NEJM 2000 | Martinelli T&H 2002 |
| AT, PC, PS def. | - | 6.0 (3.5-10.3) | 13.1 (5.0-34.2) |
| factor V Leiden | 16.3 (4.8-54.9) | 6.9 (3.3-15.2) | 10.6 (5.6-20.4) |
| PT G20210A | 10.2 (4.0-25.9) | 9.5 (2.1-66.7) | 2.9 (1.0-8.6) |

# Primary prophylaxis

1) Thrombophilia

[2) Positive family history]

# Risk of VTE associated with thrombophilia

| | | |
|---|---|---|
| INHERITED | antithrombin deficiency | ++++ |
| | protein C deficiency | +++ |
| | protein S deficiency | ++ |
| | homoz. factor V Leiden | +++ |
| | homoz. G20210A prothrombin | +++ |
| | **ACQUIRED** | |
| | **antiphospholipid Ab** | **++++** |
| | heteroz. factor V Leiden | + |
| | heteroz. G20210A prothrombin | + |

**severe**

**mild**

# Primary prophylaxis

The risk of VTE during pregnancy in women with thrombophilia calls for a

differentiated approach

# Anticoagulants in pregnancy

- in pregnancy: LMWH instead of UFH

- in puerperium: LMWH or VKA

The 8th ACCP conference, Chest 2012

Grade 1B

# Inherited severe trombophilia

**antithrombin, protein C, protein S deficiency, homozygous factor V Leiden or prothrombin G20210A, combined abnormalities**

- prophylaxis in puerperium
- extended to pregnancy (consider family history, plasma levels, comorbidities, age, obesity)
- particular attention to antithrombin deficiency !

# Acquired severe trombophilia

**antiphospholipid antibodies**

- prophylaxis in puerperium
- extended to pregnancy (LMWH or/and ASA), particularly if previous recurrent miscarriages

# Inherited mild trombophilia

**heterozygous factor V Leiden or prothrombin G20210A**

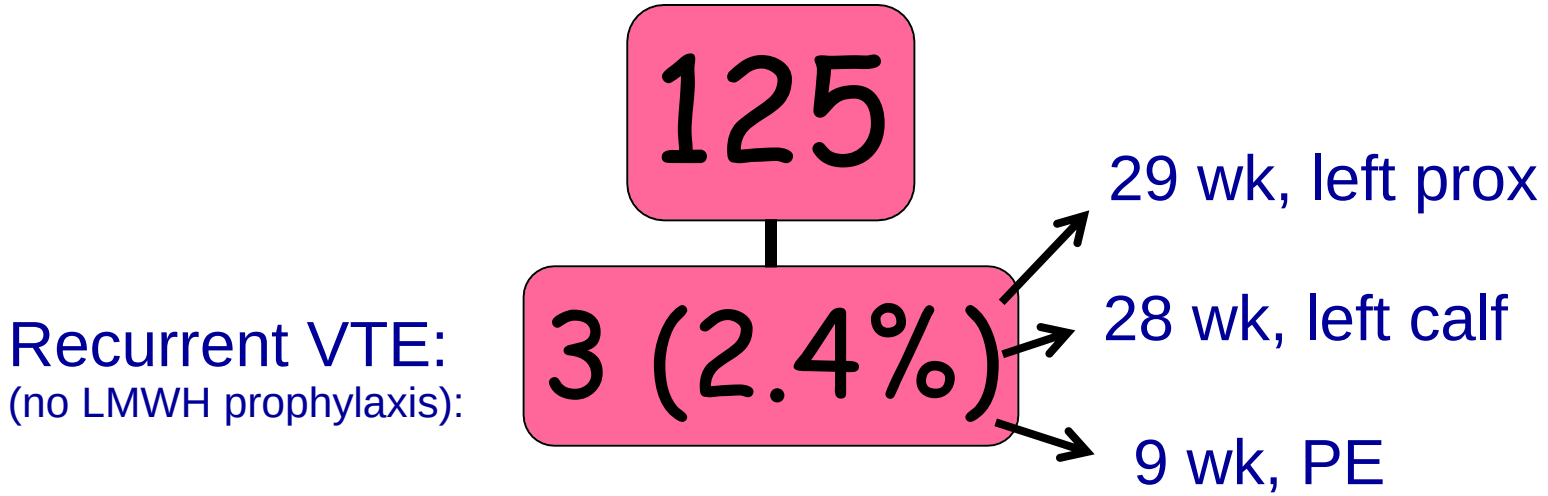
- prophylaxis in puerperium
- watchful waiting during pregnancy
- extended to pregnancy can be considered in some cases (family history, comorbidities, age, obesity)

# Secondary prophylaxis

How shall we manage pregnant women with previous VTE?

WHAT IS THE RISK OF RECURRENT VTE DURING PREGNANCY?

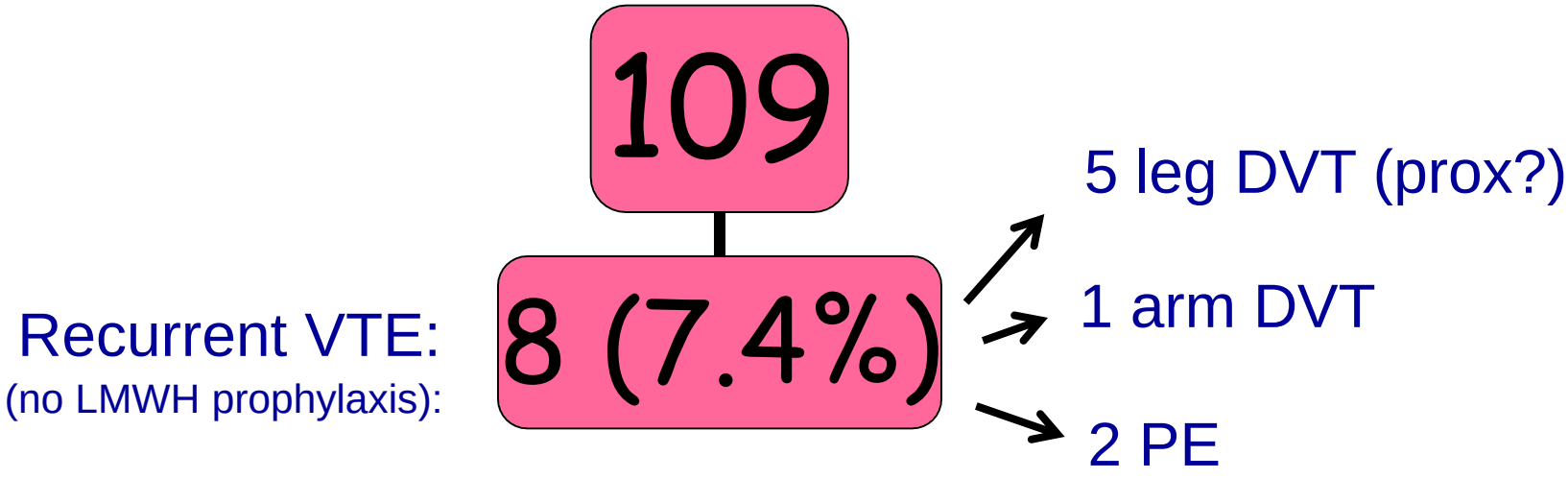
# Brill-Edwards et al, NEJM 2000
# prospective cohort study




- recurrence rate: 4.0 % patient-year
- 2 of the 3 women had inherited thrombophilia
- 1 of the 3 women had a 1st idiopathic VTE

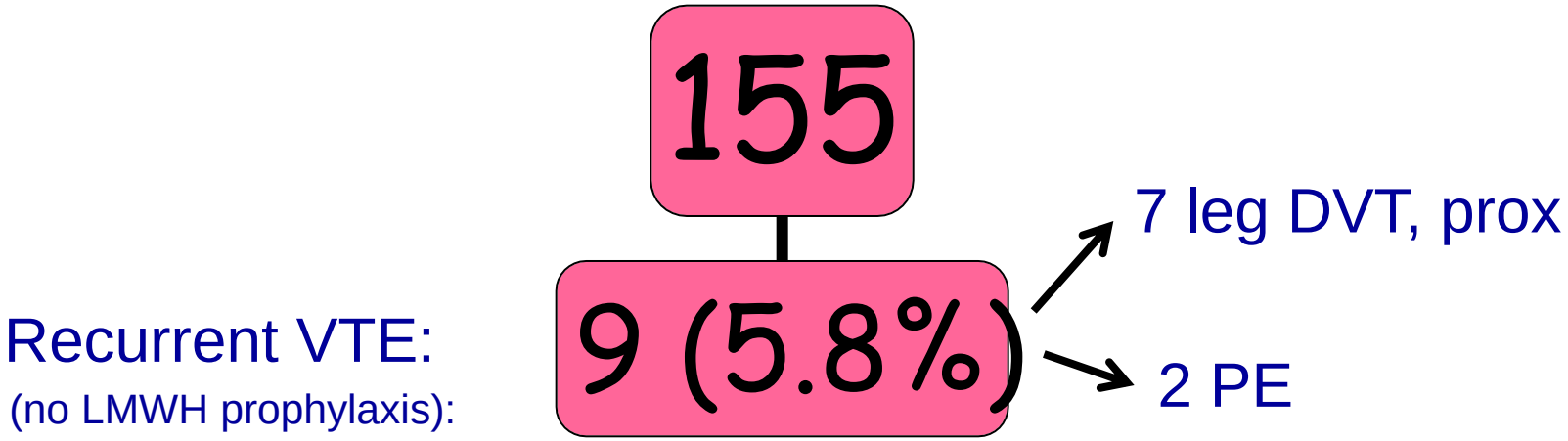
**Conclusions: routine LMWH during pregnancy is not warranted;** ***"… we recommend offering the choice of antepartum heparin or regular follow-up examinations."***

# Pabinger et al, Blood 2002
# retrospective cohort study




- 5 events in the 1st, 2 in the 2nd, 1 in the 3rd trimester
- recurrence rate: 10.9 % patient-year
- 4 of the 8 women had inherited thrombophilia
- 7 of the 8 women had 1st VTE on OC

# De Stefano et al, BJH 2006
# retrospective cohort study




- 4 events in the 1st, 2 in the 2nd, 3 in the 3rd trimester
- recurrence rate: 7.5 % patient-year
- 5 of the 9 women had inherited thrombophilia
- 5 of the 9 women had the 1st VTE during pregnancy and 2 on OC

# White et al, T&H 2008
# hospital discharge data, State of California

| | Recurrent VTE (6 months to 5 years) | |
|---|---|---|
| | overall | during pregnancy |
| Pregnancy-VTE n=1085 | 5.8% | 35% |
| | *p=0.02* | *p<0.001* |
| Unprovoked VTE n=7625 | 10.4% | 8.7% |
| | | |

Limitations: only admitted patients, no data on VKA duration after 1st VTE, non data on LMWH prohylaxis…

# Secondary prophylaxis

- prophylaxis in puerperium and pregnancy
  - if previous VTE was idiopathic, pill- or pregnancy-related

- prophylaxis in puerperium
  - if previous VTE occurred after surgery or trauma

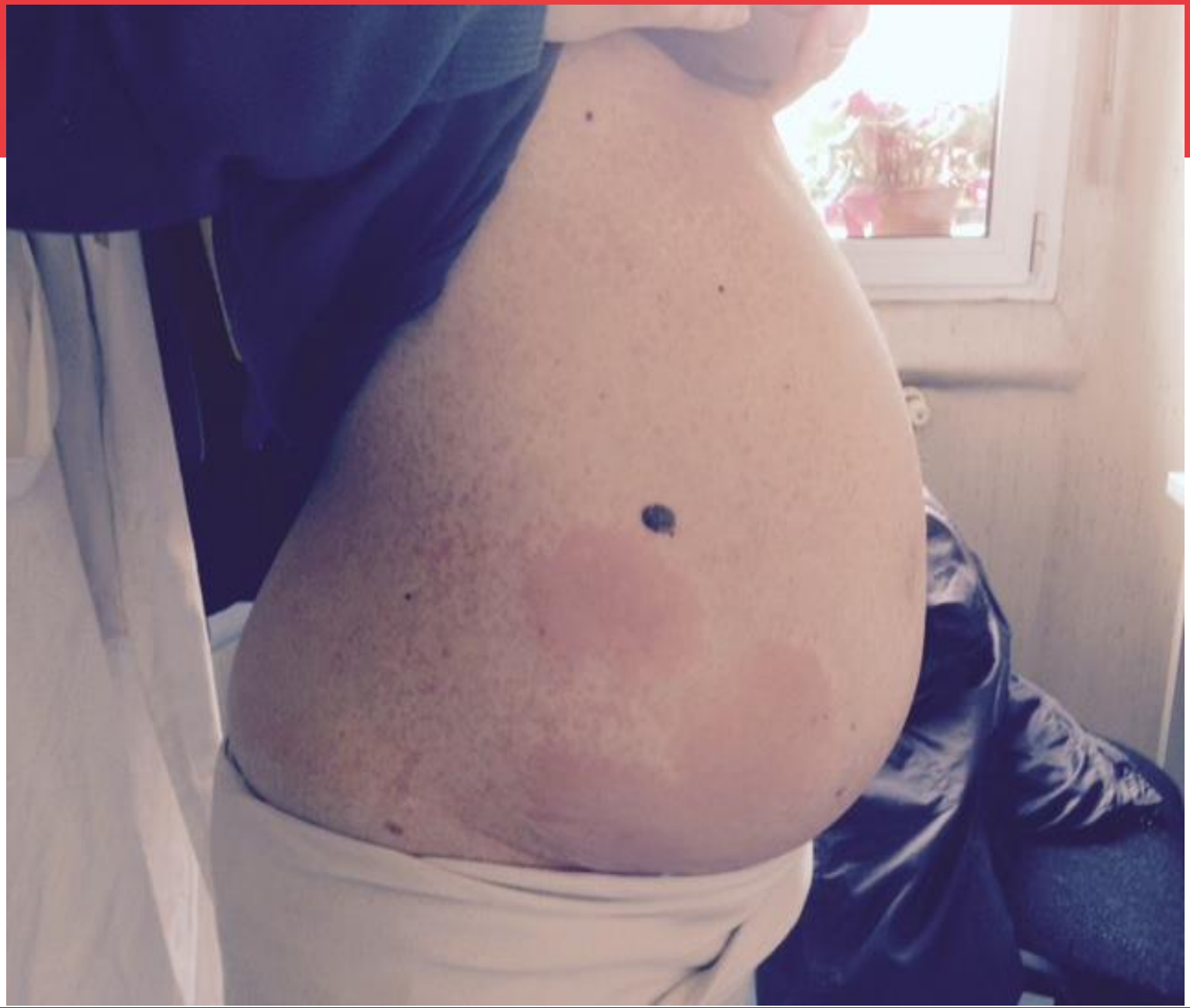
REGARDLESS OF THROMBOPHILIA ABNORMALITIES

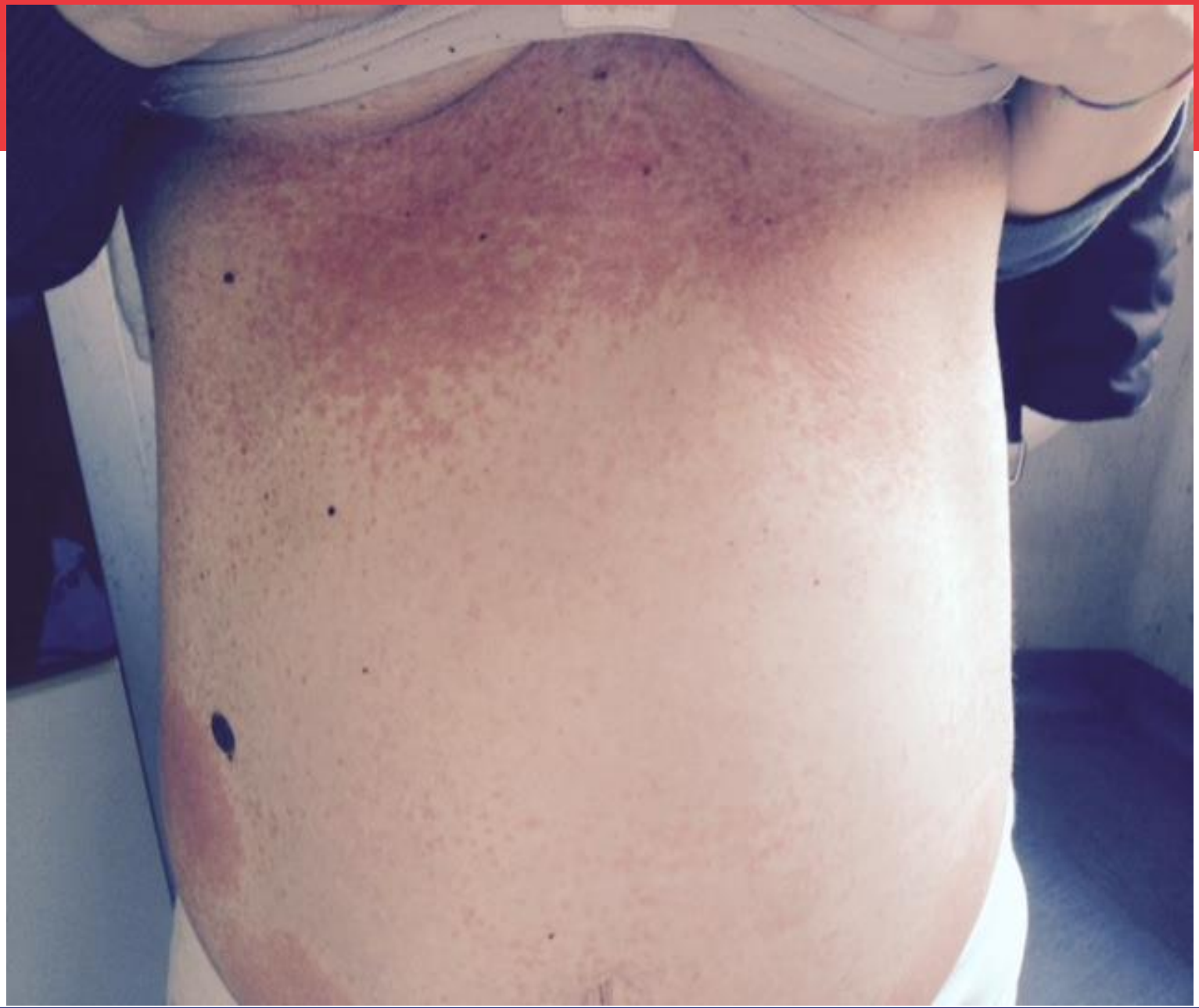
# LMWH prophylaxis in pregnancy (1)

- does not cross the placenta
- subcutaneous injection, od
- monitoring not needed
- prophylaxis dose uncertain!
- avoid epidural/spinal anesthesia < 12h since the last injection

# LMWH prophylaxis in pregnancy (2)

- less HIT and osteoporosis than UH
- allergic skin reactions are common





# LMWH/VKA prophylaxis in puerperium

- LMWH given to nursing mothers are not secreted into breast milk and can be safely administered
- VKA given to nursing mothers do not induce anticoagulant effect in the breast-fed infant

# Patient 1: DP, 10.7.1980

***- Storia familliare negativa per trombosi.***

***- 2000 TVP popliteo-femoro-iliaca sx + EP non massiva dopo 3 mesi di estroprogestinico (Mercilon, prima utilizzatrice). VKA per circa un anno.***

***- Screening → fattore V Leiden omozigote mutato.***

***- G2, P2. 2008 parto vaginale a termine, F 3280g. Clexane 4000 UI/die in gravidanza e puerperio.***

***- 2009 recidiva di TVP femoro-iliaca dx alla 9na settimana di gestazione nonostante Clexane 4000 UI/die.***

***- Peso 63 kg, altezza 168 cm, BMI 22.6***

# Patient 2: TE, 5.5.1963

*-Madre con tfs ricorrenti, safenectomizzata.*

*- Mai estroprogestinici, interventi chirurgici, fratture. BMI 22.1*

*-G5, P4. 1990 F 3100 g. 1994 M 2900 g. 1998 M 3500 g. 2000 aborto spontaneo precoce. 2001 M 3200 g.*

*- 2010 varicoflebite dorso del piede e VGS al III distale di gamba dopo camminata con scarponi, trattata con LMWH per 2 settimane con risoluzione.*

*- Screening: AT 99%, PC 95%, PS funz 17%, PEG 14%, FVL e PT G20210A wild type, APA assenti, omo 12 µmol/ml, FVIII 105%*

# Patient 3: MN, 21.1.1988

***- Storia familiare dubbia (padre?).***

***- 2008 TVP popliteo-femorale dx dopo 20 giorni di estroprogestinico (Yasmin, prima utilizzatrice). TAO x circa un anno.***

***- Screening → nella norma.***

***- G2, TC2. 2010 parto a termine, M 3200g. Clexane 2000 IUx2/die iniziato alla 16ma w e proseguito fino al puerperio.***

***- 2014 recidiva di TVP femoro-iliaca sx alla 10ma w di gestazione, non ancora in profilassi.***

***- Peso 51 kg, altezza 165 cm, BMI 18.7***


Thank you !

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