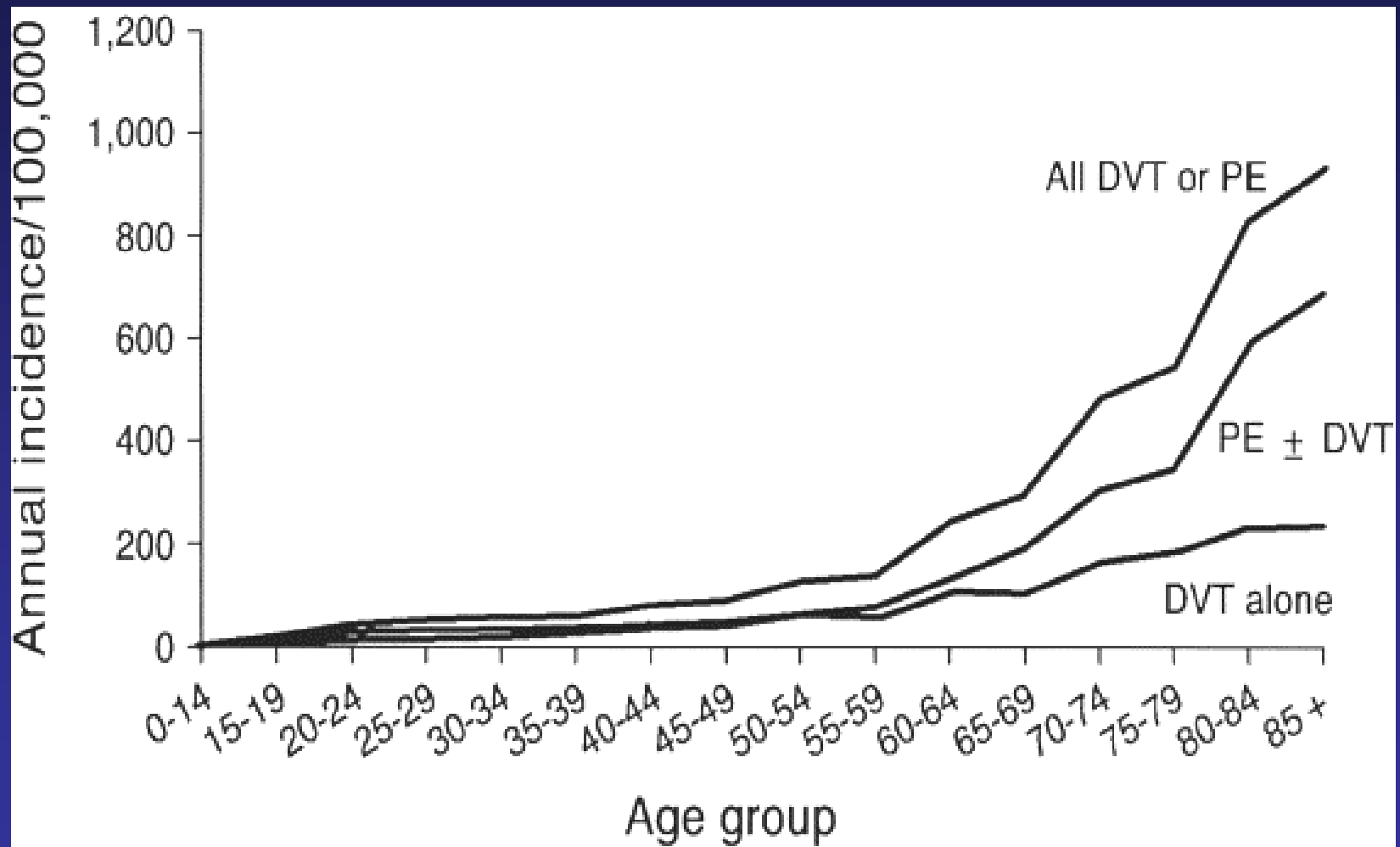


VTE Risk: A Problem of Genes or the Environment?

Thomas L. Ortel, M.D., Ph.D.
Duke University Medical Center
15 September 2008

Incidence of VTE increases with age



Risk Factor Model for VTE

Inherited Risk Factors



Intrinsic

Thrombotic Risk

Thrombosis Threshold

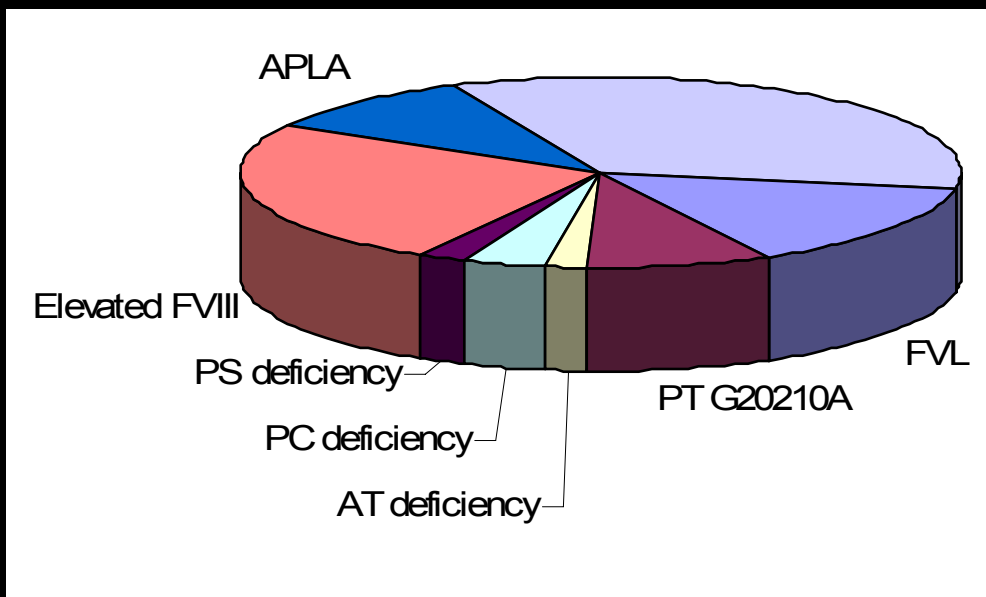
Venous Thromboembolism

Inherited thrombophilic disorders

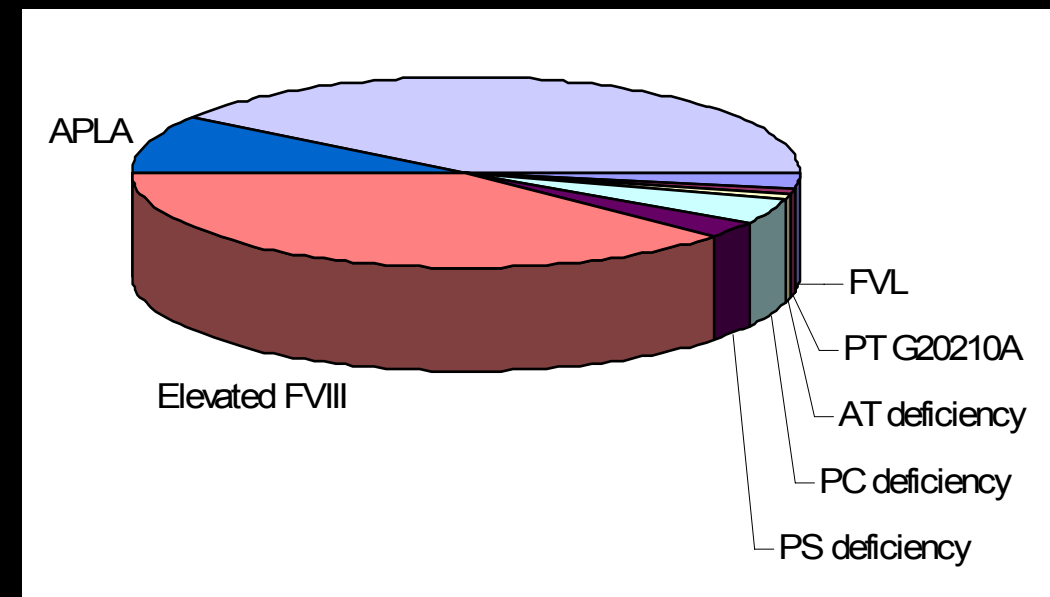
Disorder	Frequency in VTE patients	RR for first VTE
Factor V Leiden (RQ)	18.8%	7
Prothrombin G20210A	7.1%	2.8
Protein C deficiency	3.7%	6.5
Protein S deficiency	2.3%	5.0
Antithrombin deficiency	1.9%	20
Elevated factor VIII level	25%	4.8

Thrombophilic states and race

Caucasian



African-American

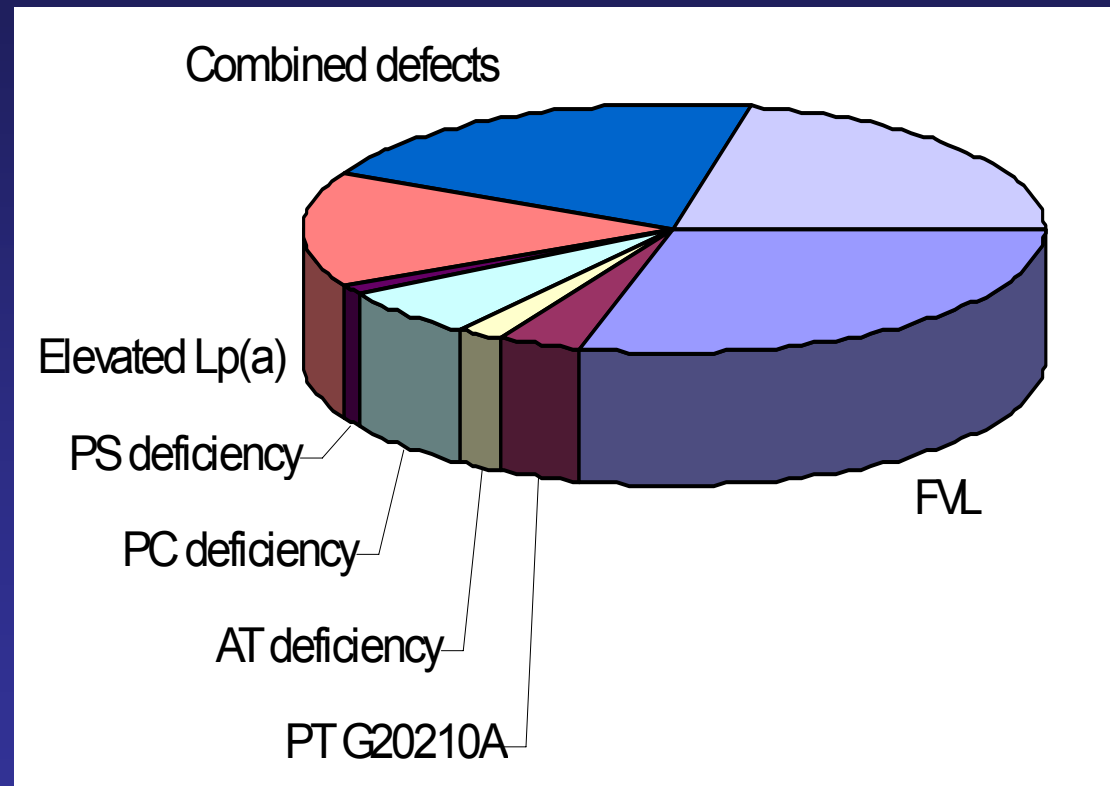


VTE Risk and Sickle Cell Trait

Event	Hb AS	Hb AA	OR	95% CI
Controls	35 (6.3%)	520	1.0	-
DVT only	23 (7%)	307	1.1	0.65-1.9
PE only	24 (21.9%)	91	3.9	2.2-6.9
DVT/PE	9 (14.5%)	53	2.5	1.2-5.5

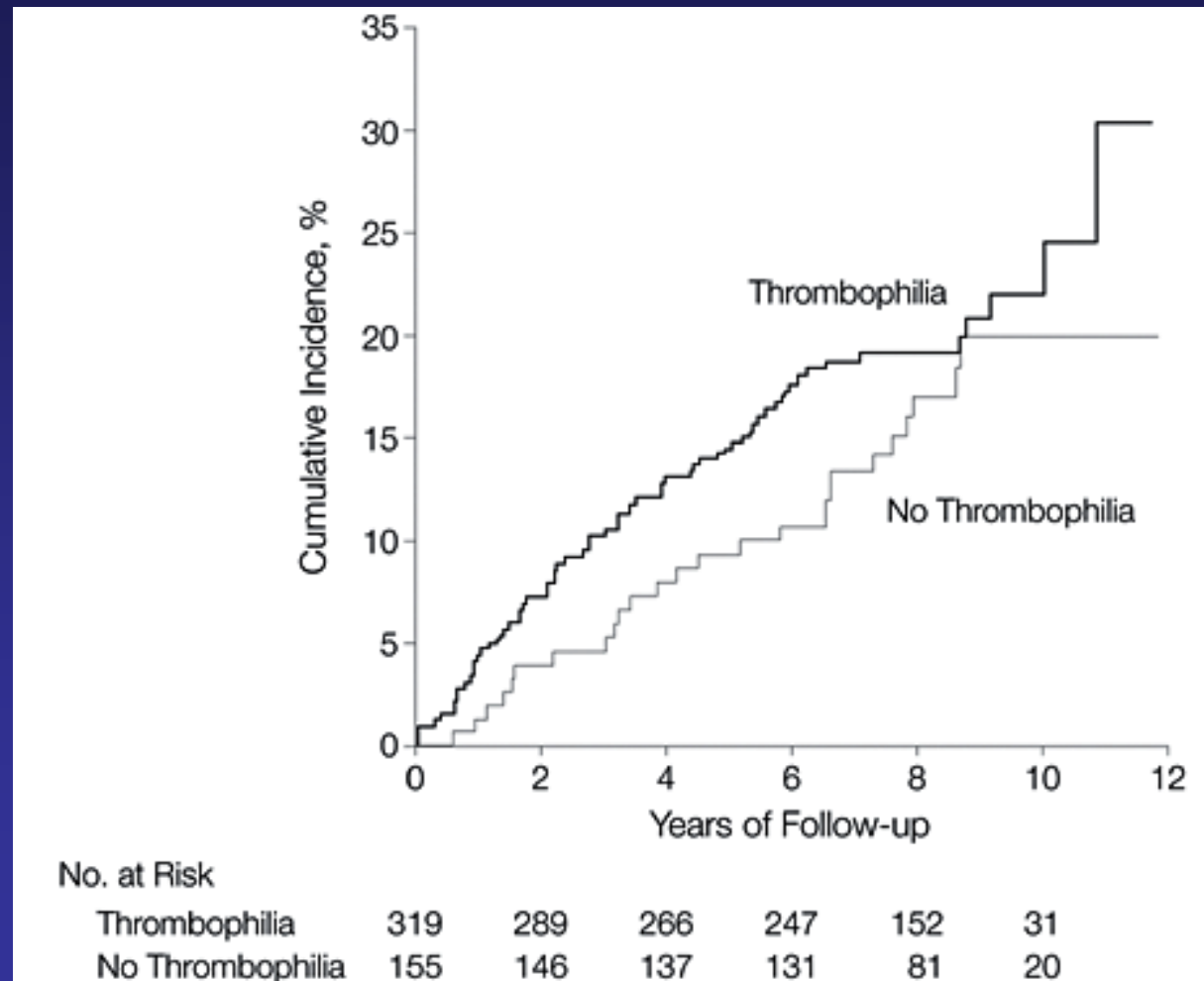
Thrombophilia in the pediatric patient

- Many studies include children with central venous lines and other acquired disorders.
- Elevated factor VIII and D-dimer is also associated with recurrent thrombosis



Age: neonate to 18 yrs

Thrombophilia and Recurrent VTE



ACCP Guidelines: 2008

- “The presence of hereditary thrombophilia has not been used as a major factor to guide duration of anticoagulation for VTE in these guidelines because evidence from prospective studies suggests that these factors are not major determinants in the risk of recurrence.”

Risk Factor Model for VTE

Inherited Risk Factors:

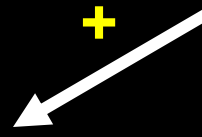
- AT, PC, PS deficiency.
- Factor V Leiden.
- Prothrombin G20210A.



Intrinsic

Thrombotic Risk

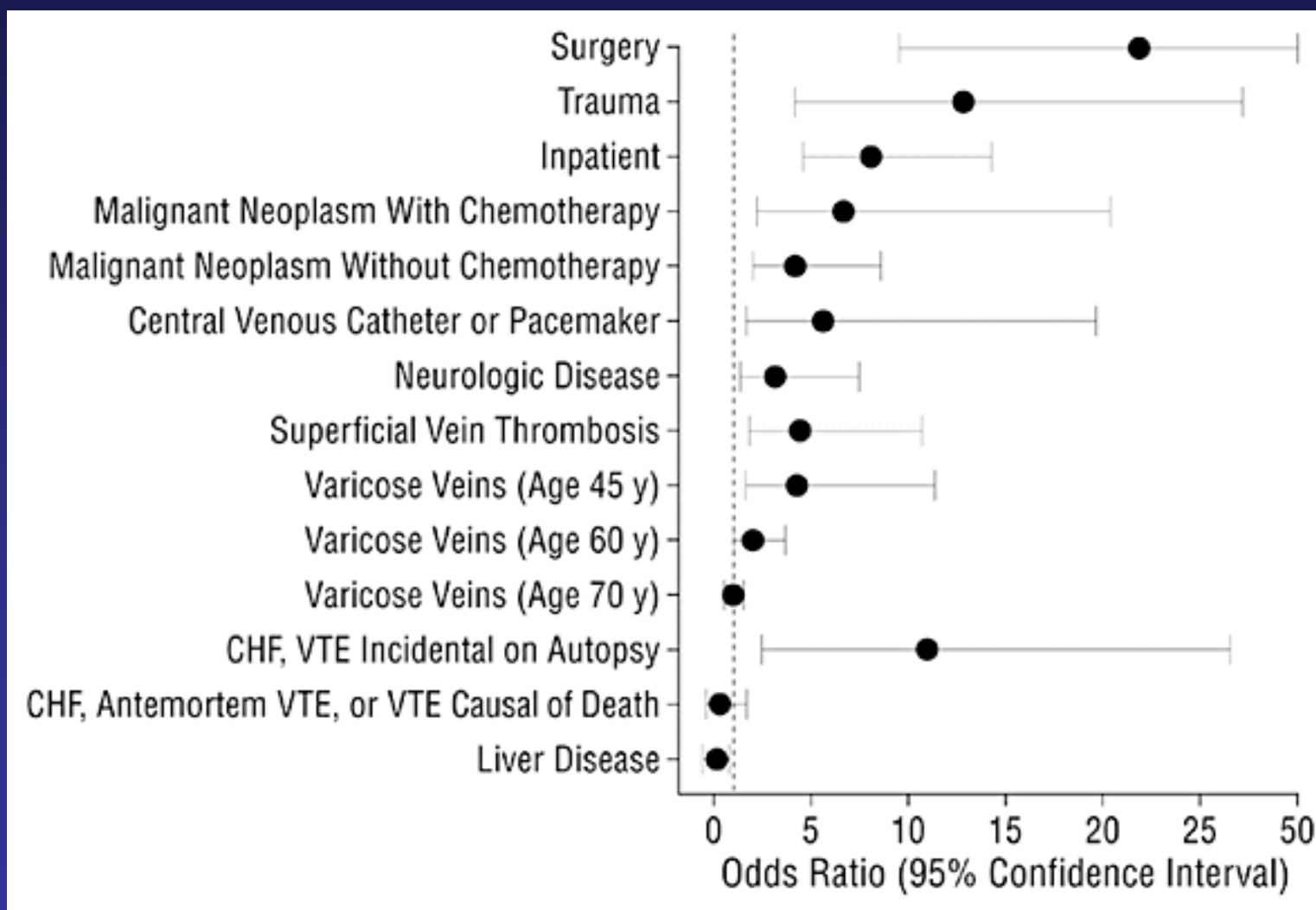
Acquired Risk Factors



Thrombosis Threshold

Venous Thromboembolism

Risk Factors for VTE



Obesity and Venous Thromboembolism

Parameter	Odds Ratio	95% CI
BMI \geq 30 kg/M ² ⁽¹⁾	2.26	1.49-3.41
BMI \geq 30 kg/M ² + OC use ⁽¹⁾	9.8	3.0-31.8
BMI \geq 30 kg/M ² + prior VTE ⁽²⁾	1.6	1.0-2.4

⁽¹⁾ Abdollahi M, et al. Thromb Haemost 2003;89:493-8; ⁽²⁾ Eichinger S, et al. Arch Intern Med 2008;168: 1678-83.

Risk Factor Model for VTE

Inherited Risk Factors:

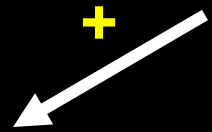
- AT, PC, PS deficiency.
- Factor V Leiden.
- Prothrombin G20210A.



Intrinsic
Thrombotic Risk

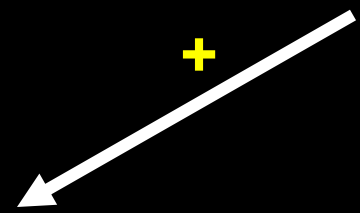
Acquired Risk Factors:

- Age.
- Previous VTE.
- Cancer.
- Obesity.
- OC's, HRT.



Prothrombotic Triggers:

- Surgery.
- Pregnancy.
- Trauma.



Thrombosis Threshold



Venous Thromboembolism

Risk Factor Model for VTE

Inherited Risk Factors:

- AT, PC, PS deficiency.
- Factor V Leiden.
- Prothrombin G20210A.



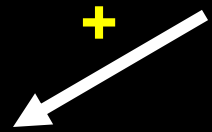
+

Intrinsic
Thrombotic Risk

+

Acquired Risk Factors:

- Age.
- Previous VTE.
- Cancer.
- Obesity.
- OC's, HRT.



Decreasing thrombotic risk:

- Modify acquired risk factors.
- Appropriate thromboprophylaxis.

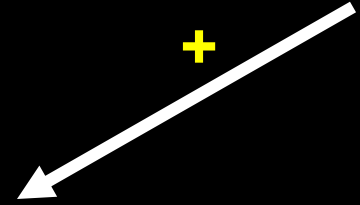


-

+

Prothrombotic Triggers:

- Surgery.
- Pregnancy.
- Trauma.



Thrombosis Threshold



Venous Thromboembolism

VTE Risk: *Genes and Environment*

- Genetic risk factors contribute to increased thrombotic risk, but unclear how this information can best be used to determine optimal treatment strategies for the individual patient.
- Modify acquired risk factors that can be altered (e.g., obesity, OC/HRT use).
- Thromboprophylaxis at times of highest risk (environmental triggers).