Hypercoagulation Disorders

- Factor V Leiden
- Protein C deficiency/Protein S deficiency
- Prothrombin G20210A mutation
- Antithrombin III deficiency
- Lupus anticoagulant disorder

Coagulation catastrphy

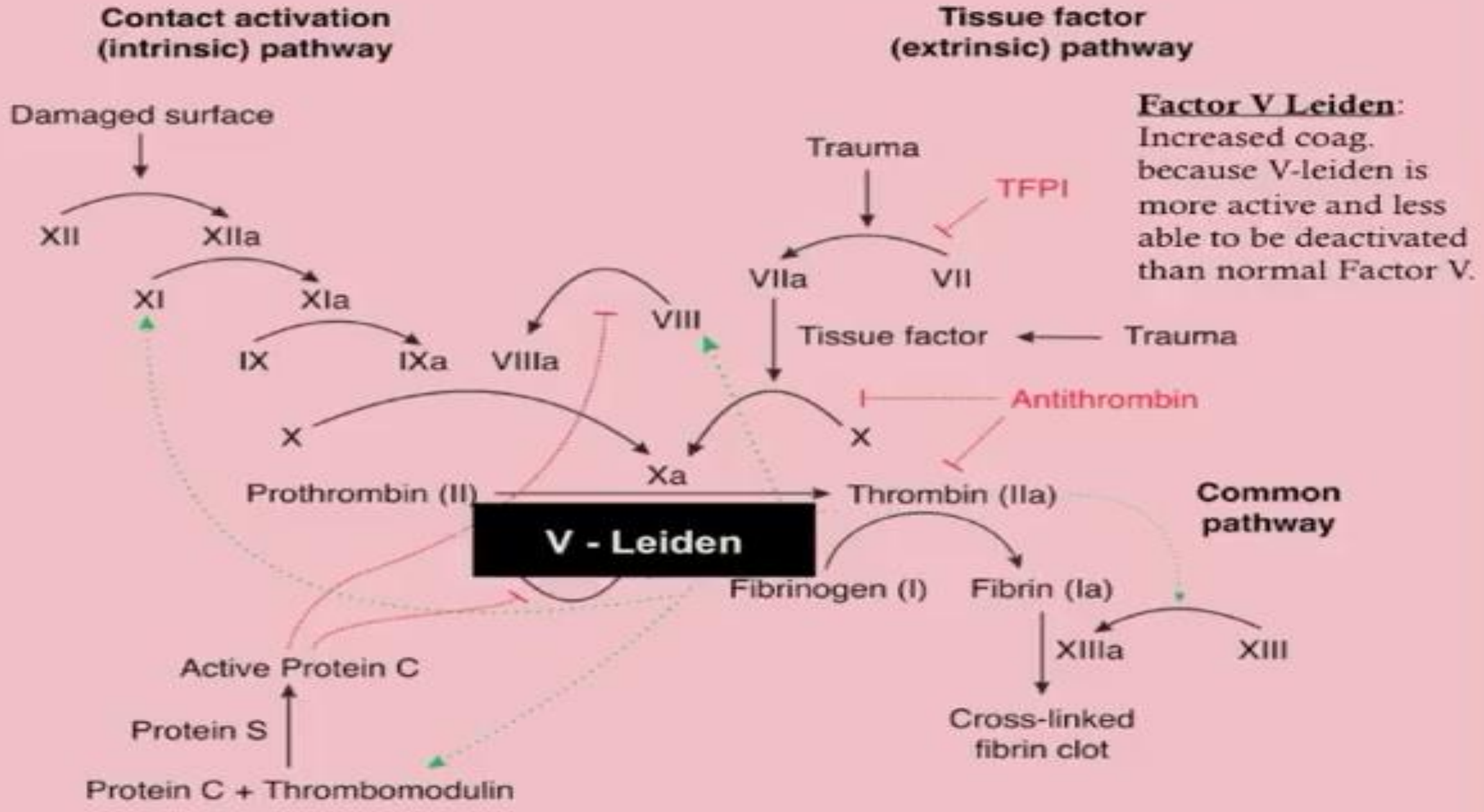
- Pulmonary emobolism
- Deep vein thrombosis
- Myocardial infarction
- Stroke
- Obstetrical complications
  - Abruptio placentae
  - Pre-eclampsia
- Budd-Chiari syndrome
- Purpura fulminans

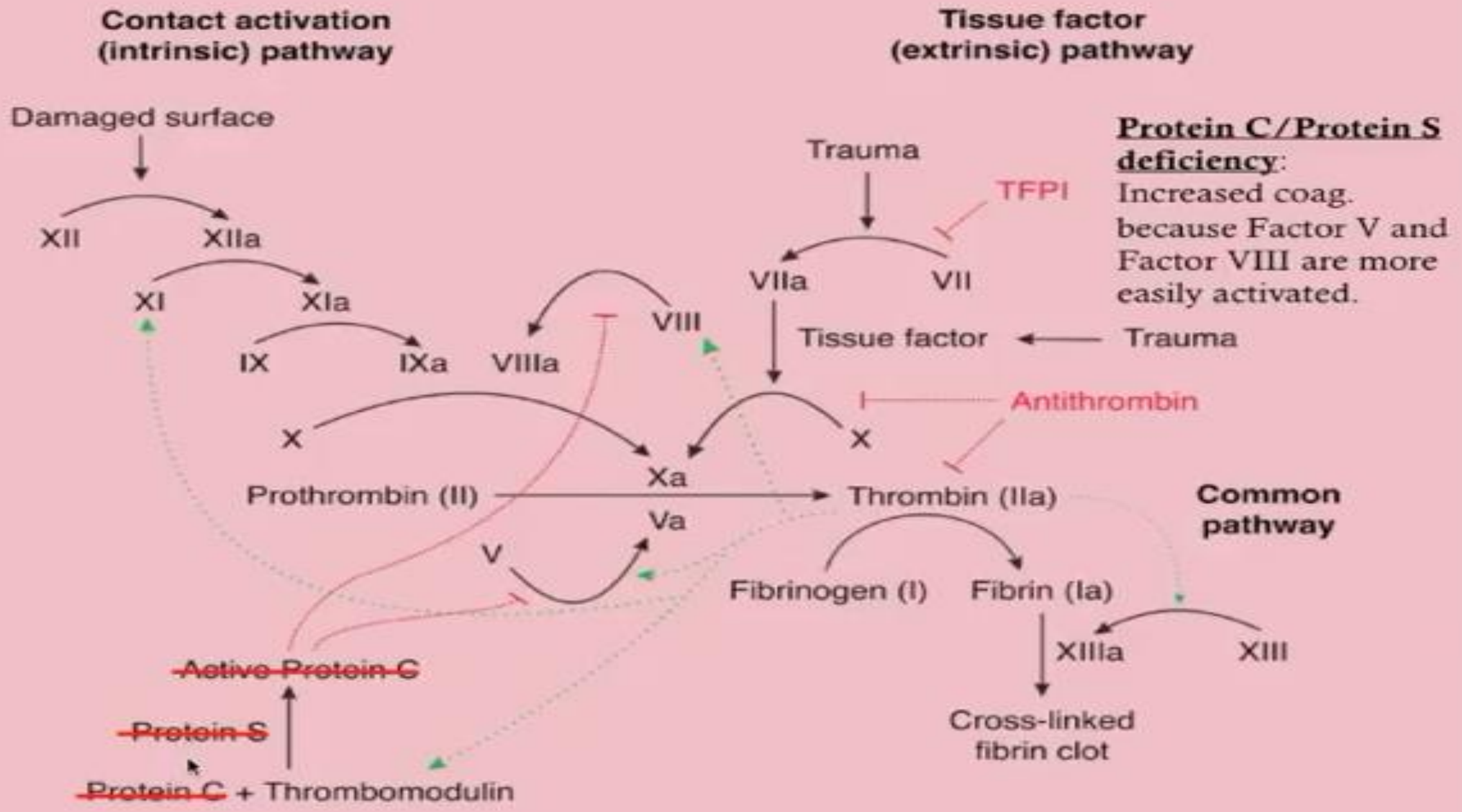
Hypercoagulability

- In general: It doesn't matter which exact hypercoagulation disorder the pt has (FVL, Protein C def., etc.), the result and outward expression is an increased risk of thrombosis.
  - This may be at a *younger* age (20s-40s), or at an older age (50s) despite anticoagulation
- "Hypercoagulation panels" are laboratory tests performed frequently today, so in many cases a hypercoagulation disorder may be a coincidental diagnosis.
- The main implication is that any kind of hypercoagulation disorder **significantly increases the risk of thrombosis** compared to the general population.
- The problem is rarely the disease itself, but rather when other risk factors for thrombosis comingle (OCPs/estrogen, pregnancy/puerperium, prolonged travel, bed rest, trauma, surgery, renal disease, age, etc.)

Hypercoagulability

	Incidence	Relative risk VTE	
Factor V Leiden	3 – 7%	4.3	
Protein C def.	0.02 – 0.05%	11.3	
Protein S def.	0.01 – 1%	32.4	
AT-III def.	0.02 – 0.04%	17.5	
PT G20210A mut.	1 – 3%	1.9	
Lupus anticoag.	2 – 4%*	4.6	


Contact activation
(intrinsic) pathway
Tissue factor
(extrinsic) pathway
Factor V Leiden:
Increased coag. because V-leiden is more active and less able to be deactivated than normal Factor V.
Damaged surface
XII
XIIa
XI
XIa
IX
IXa
VIIIa
VIII
Trauma
TFPI
VIIa
VII
Tissue factor
Trauma
Antithrombin
X
X
Xa
Prothrombin (II)
Thrombin (IIa)
V - Leiden
Common pathway
Fibrinogen (I)
Fibrin (Ia)
XIIIa
XIII
Cross-linked fibrin clot
Active Protein C
Protein S
Protein C + Thrombomodulin


Contact activation (intrinsic) pathway
Tissue factor (extrinsic) pathway
Damaged surface
XII
XIIa
XI
XIa
IX
IXa
VIIIa
VIII
X
Xa
Prothrombin (II)
Thrombin (IIa)
V
Va
Fibrinogen (I)
Fibrin (Ia)
XIIIa
XIII
Cross-linked fibrin clot
Trauma
TFPI
VIIa
VII
Tissue factor
Trauma
Antithrombin
X
Common pathway
Protein C/Protein S deficiency: Increased coag. because Factor V and Factor VIII are more easily activated.
Active Protein C
Protein S
Protein C + Thrombomodulin

When should I suspect an inherited hypercoagulability disorder?

- Thrombosis is something that ***many*** people get, and most of them do not have an inherited hypercoagulability disorder.
- However, when people with no or few risk factors (the young, the healthy, good cholesterol levels, not on OCPs/estrogen, not pregnant, etc.), *this raises suspicions*.
- In pts w/ inherited hypercoagulability disorders, personal hx may include recurrent pregnancy loss or miscarriages. Family hx may include premature MIs, strokes (< 50 years).
- Clinical suspicion is reason enough to order a hypercoagulation panel, which will assess for the major causes of hypercoagulation.
- In the United States, the most common inherited hypercoagulation disorder is **Factor V Leiden** (3 – 7% incidence).