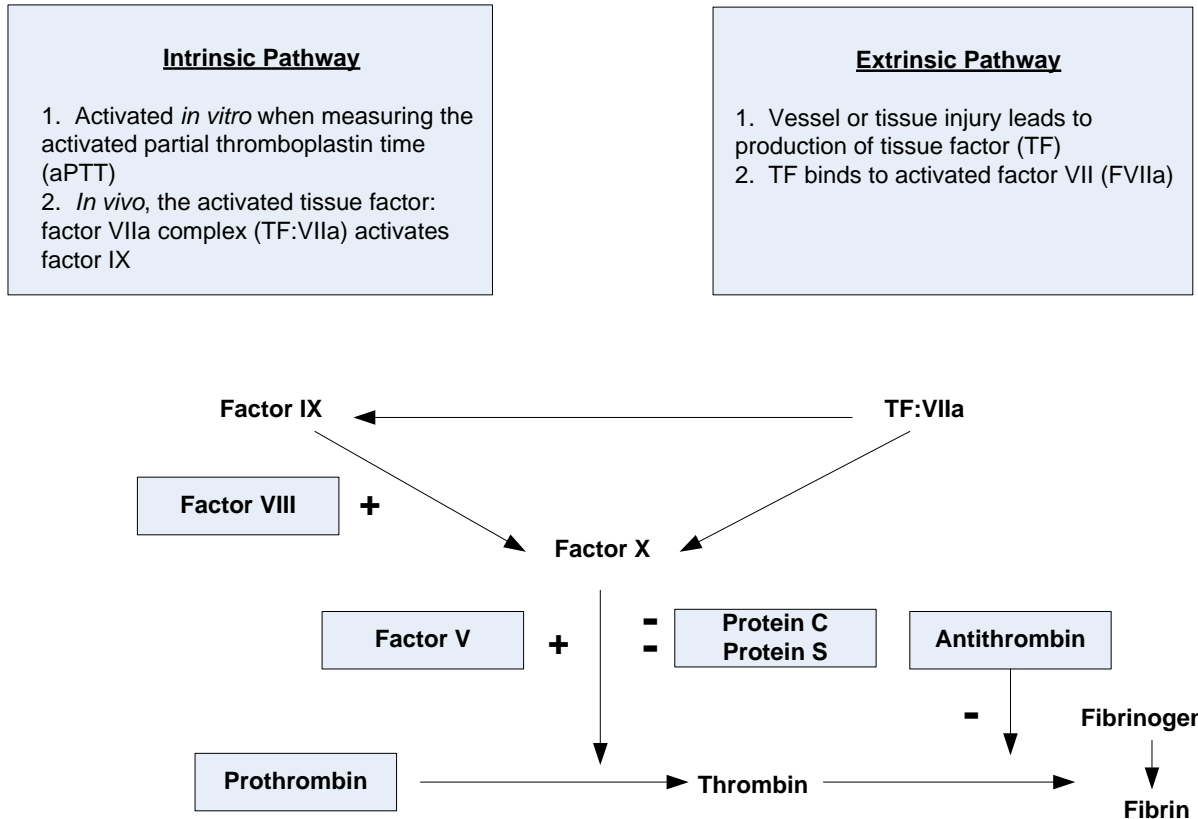


Clotting Cascade with an Emphasis on Inherited Thrombophilias



Overview: Both intrinsic and extrinsic pathways lead to the activation of factor X. Factor X plays a role in converting inactive prothrombin to thrombin. Thrombin converts soluble fibrinogen and fibrin, the major component of blood clots.

The protein C and antithrombin pathways are critical to maintain control of coagulation.

Factor V: Factor V is a procoagulant protein that helps promote the conversion of prothrombin to thrombin. Activated factor V is typically inactivated by a complex that forms between activated protein C and S. When factor V Leiden mutation is present, the protein C/S complex cannot break down activated factor V (Va) as efficiently, leading to a hypercoagulable state.

Prothrombin: The G20210A polymorphism results in increased production of prothrombin. This creates a hypercoagulable state since more thrombin is generated.

Antithrombin: Typically inactivates thrombin, leading to less conversion of fibrinogen to fibrin. Antithrombin deficiency reduces this inhibitory effect, creating a hypercoagulable state. Antithrombin also inactivates factors Xa, IXa and XIa.

Protein C/S: Deficiencies of either protein C or S result in decreased inhibition of activated factor V and increased thrombin generation, leading to a hypercoagulable state.

Activated protein C (ACP) resistance: Leads to a hypercoagulable state since factor Va (normally inactivated by ACP) is not inactivated as quickly. APC also inactivates factor VIIIa.