



THROMBOSIS AND HEMOSTASIS

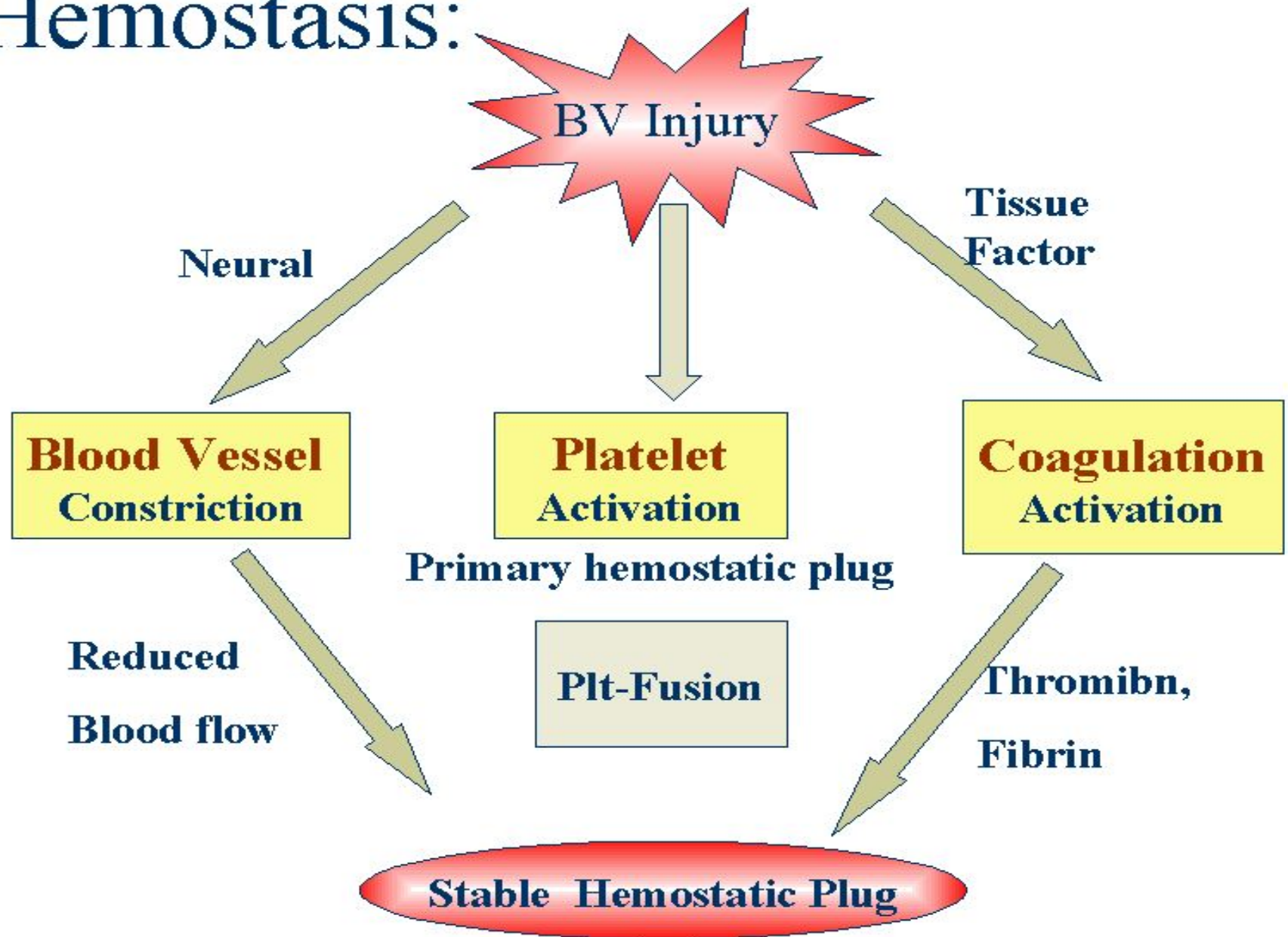
PHYSIOLOGY

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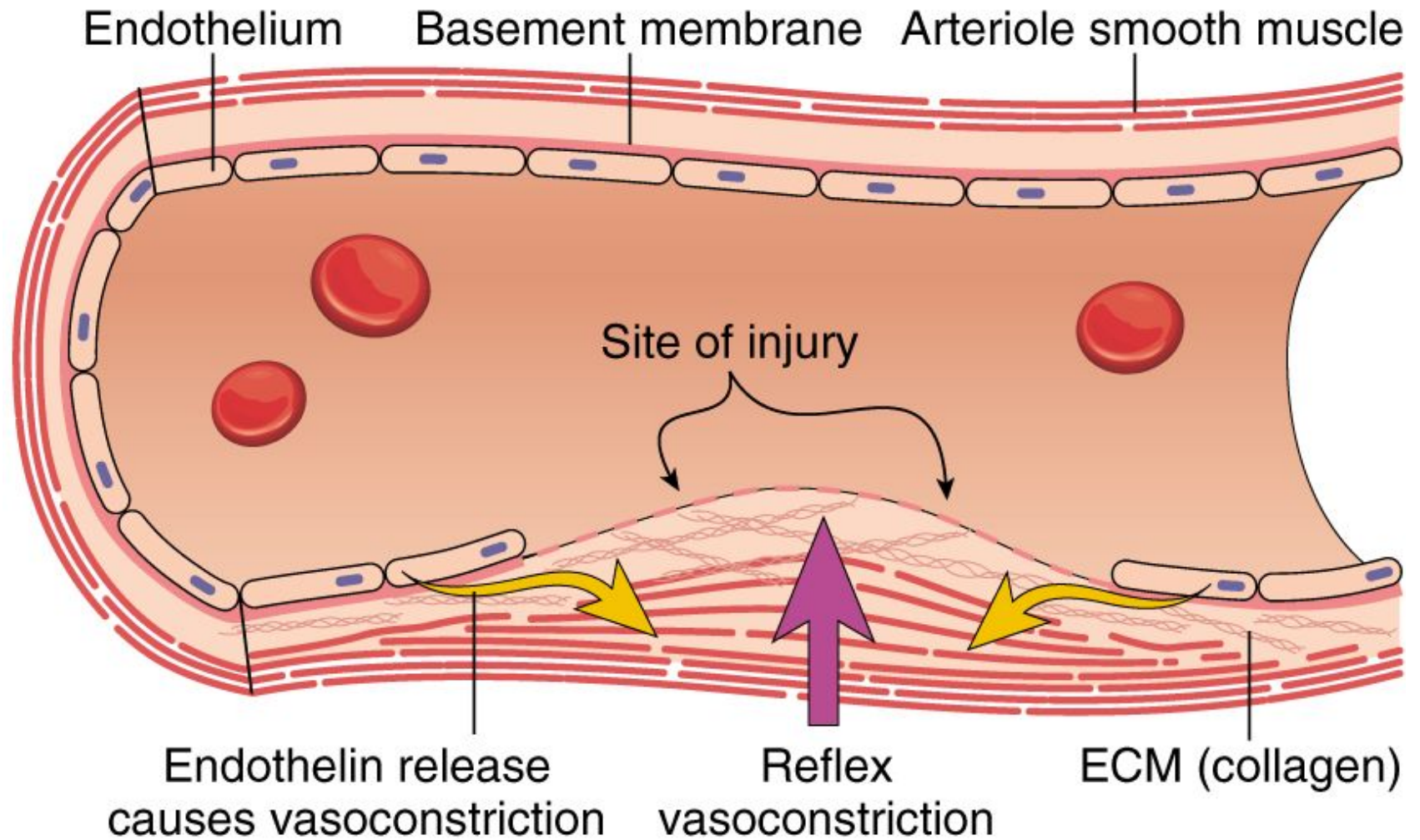
Hemostasis:



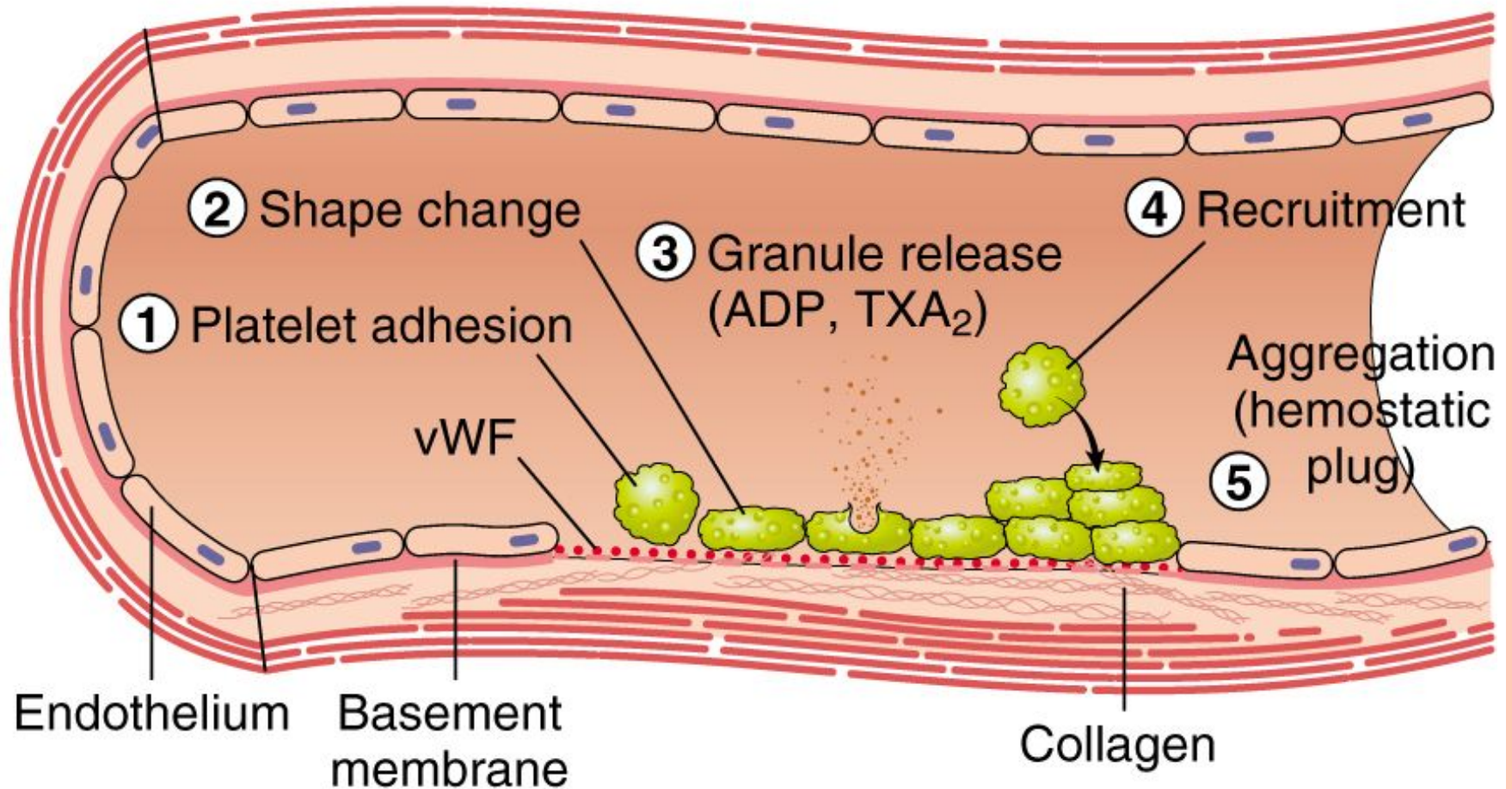
Process- *primary haemostasis*

- ◆ In a normal individual, coagulation is initiated within 20 seconds after an injury occurs to the blood vessel damaging the endothelial cells.
- ◆ Platelets immediately form a haemostatic plug at the site of injury. This is called *primary haemostasis*.

A. VASOCONSTRICTION



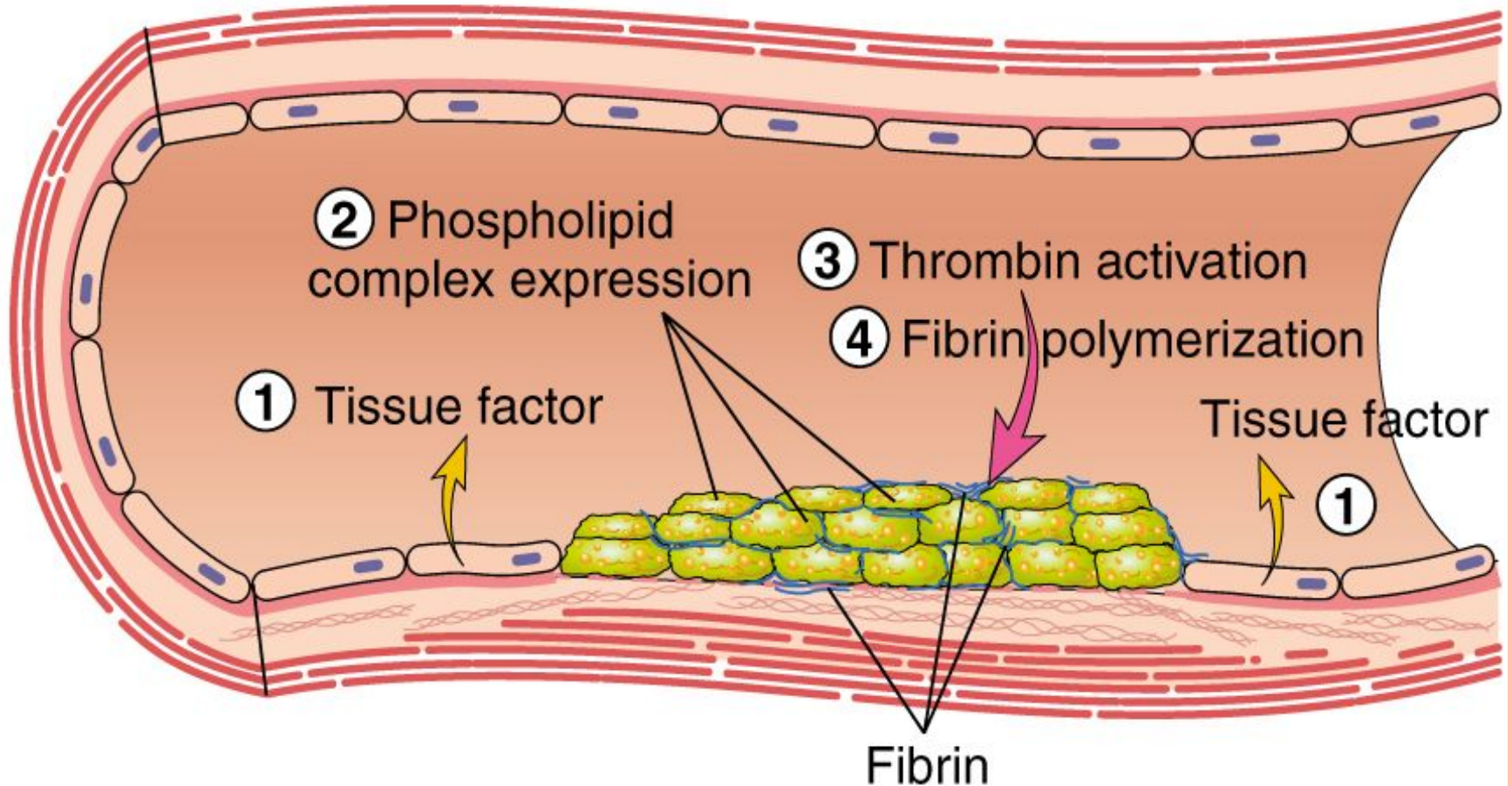
B. PRIMARY HEMOSTASIS



Secondary haemostasis

- ◆ Secondary haemostasis then follows—plasma components called *coagulation factors* respond (in a complex cascade) to form fibrin strands which strengthen the platelet plug.
- ◆ Coagulation from a cut is initiated by platelets adhering to and activated by collagen in the blood vessel endothelium.
- ◆ The activated platelets then release the contents of their granules, these contain a variety of substances that stimulate further platelet activation and enhance the haemostatic process.

C. SECONDARY HEMOSTASIS



Coagulation cascade

- ◆ The coagulation cascade of secondary hemostasis has two pathways, the *Contact Activation pathway* (formerly known as the Intrinsic Pathway)
- ◆ And the *Tissue Factor pathway* (formerly known as the Extrinsic pathway) that lead to *fibrin* formation.
- ◆ It was previously thought that the coagulation cascade consisted of two pathways of equal importance joined to a common pathway.
- ◆ It is now known that the primary pathway for the initiation of blood coagulation is the *Tissue Factor pathway*. The pathways are a series of reactions, in which a zymogen (inactive enzyme precursor) of a serine protease and its glycoprotein co-factor are activated to become active components that then catalyze the next reaction in the cascade

Prothrombin



Xa

Va



Thrombin

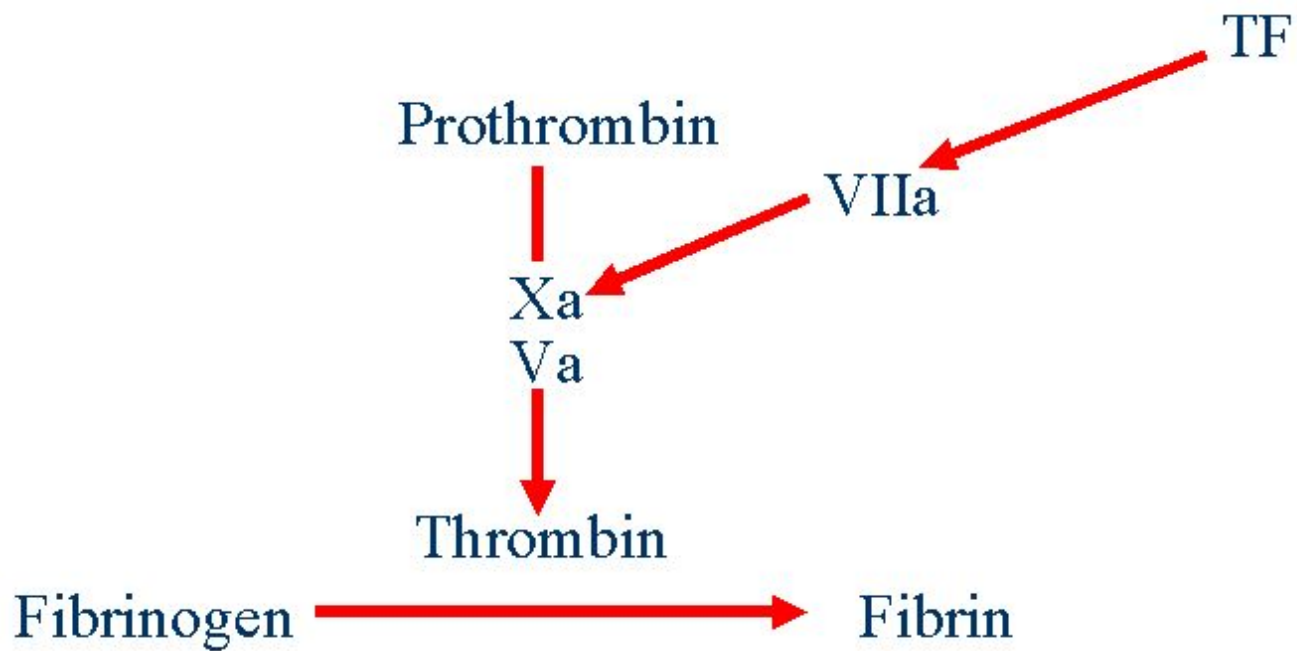
Fibrinogen



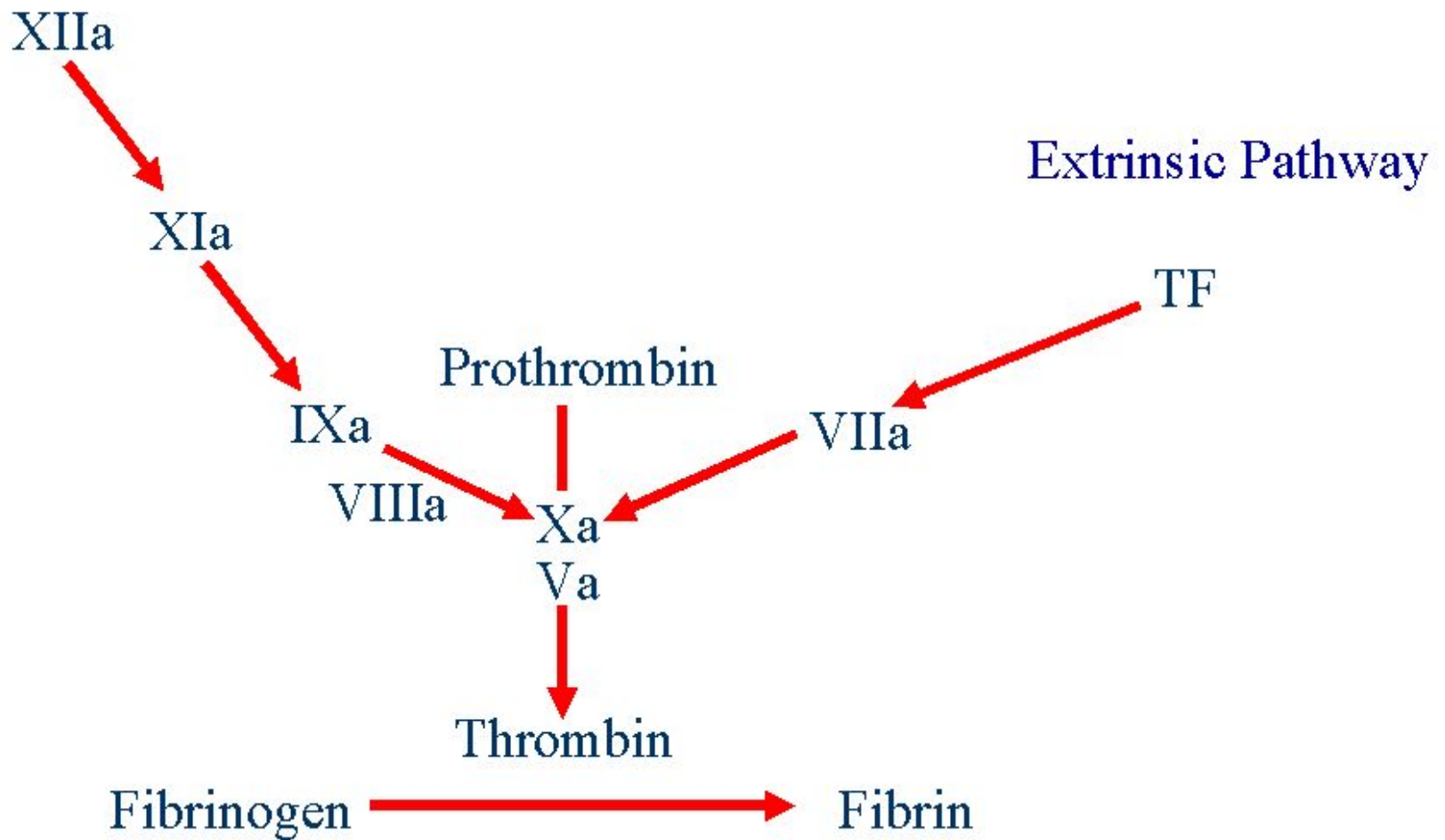
Fibrin



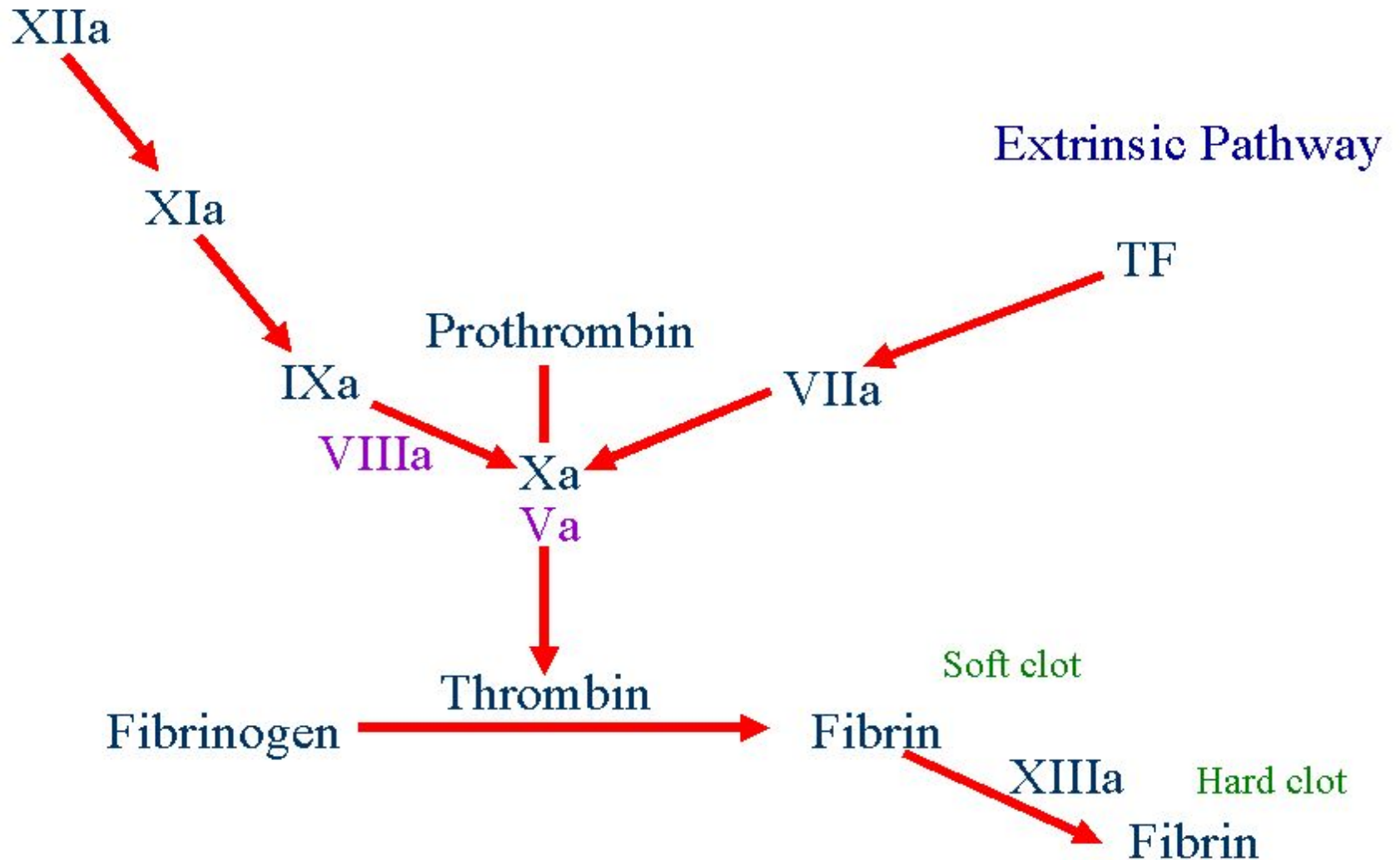
Extrinsic Pathway



Intrinsic pathway



Intrinsic pathway



Platelets:

- ◆ Bone marrow – Megakaryocytes –
- ◆ Life span 7-10d, N.count – $150-400 \times 10^9/l$
- ◆ 36 hours in spleen - 1/3 of plt in spleen
- ◆ Functions:
 - Hemostatic plug formation
 - Coagulation factors - release, synthesis
- ◆ Surface binding sites for fibrinogen, VWF
- ◆ Surface platelet antigens, HPA1

- ◆ I (fibrinogen)
- ◆ II (prothrombin)
- ◆ Tissue factor
- ◆ Calcium
- ◆ V (proaccelerin, labile factor)
- ◆ VI
- ◆ VII (stable factor)
- ◆ VIII (antihemophilic factor)
- ◆ IX (Christmas factor)
- ◆ X (Stuart-Prower factor)
- ◆ XI (plasma thromboplastin antecedent)
- ◆ XII (Hageman factor)
- ◆ XIII (fibrin-stabilizing factor)
- ◆ von Willebrand factor

Tests of Hemostasis:

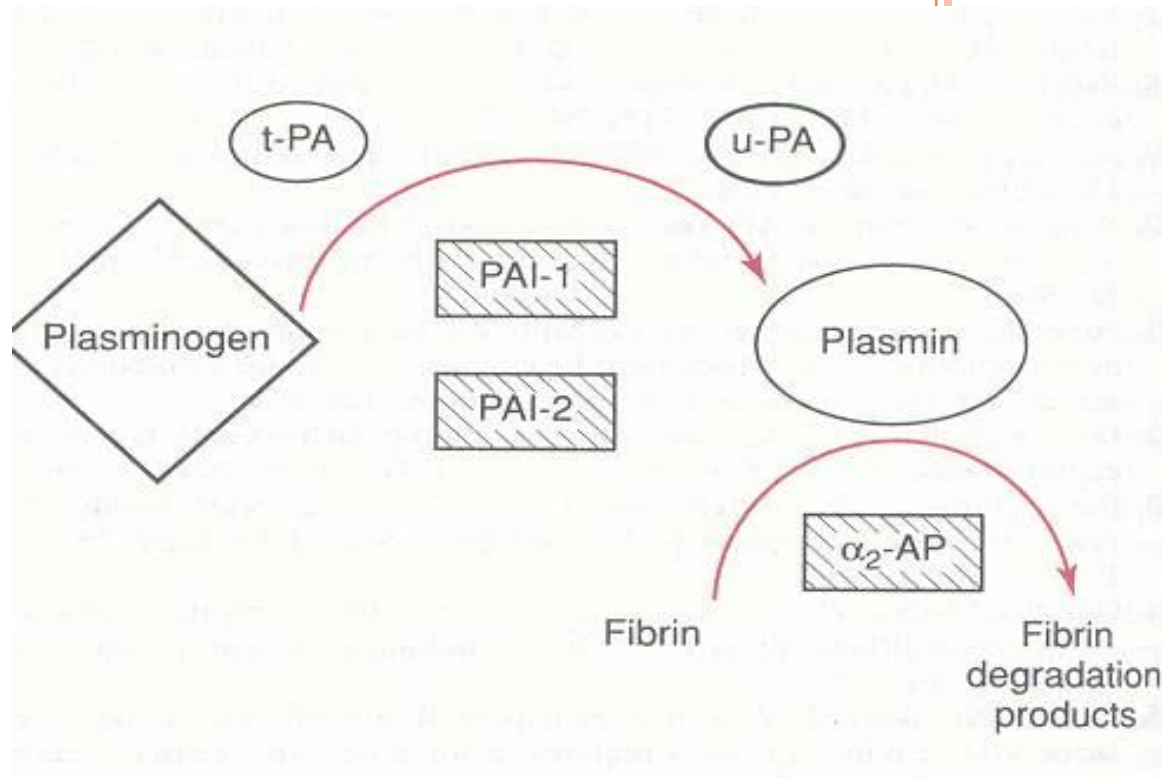
◆ **Screening tests:**

- Bleeding.T - To test Platelet & BV function
- Prothrombin.T – Extrinsic, aPTT – Intrinsic
- Thrombin.T – Both paths. (DIC)

◆ **Specific tests:**

- Factor assays –
- Tests of thrombosis – TT, FDP, DDA,
- Platelet function studies:
 - Adhesion, Aggregation, Release & PG pathway tests.
- Bone Marrow study





T-PA (TISSUE PLASMINOGEN ACTIVATOR)

U-PA (UROKINASE PLASMINOGEN ACTIVATOR)

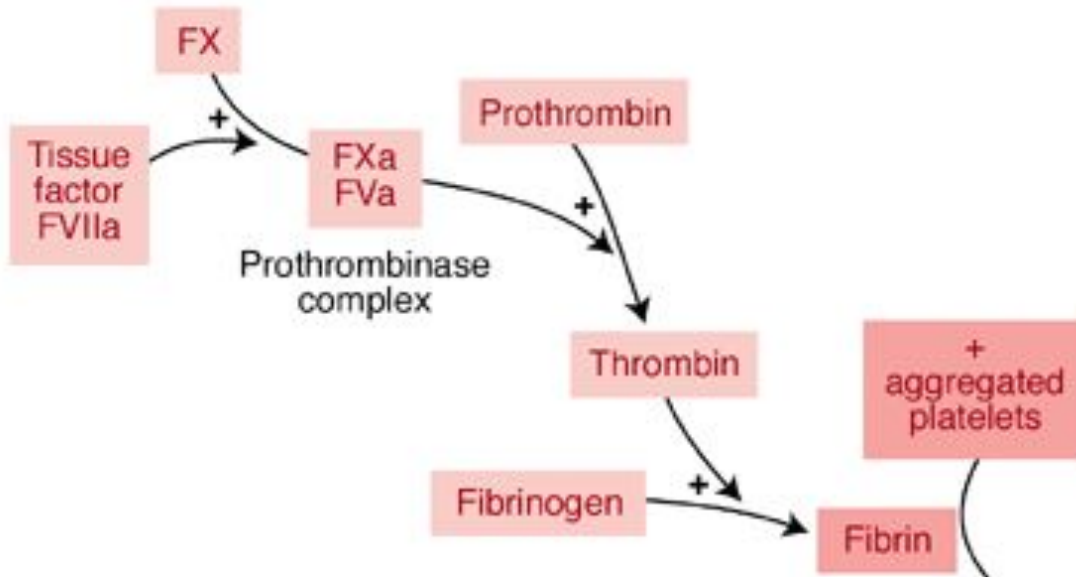
PAI-1 (PLASMINOGEN ACTIVATOR INHIBITOR 1)

PAI-2 (PLASMINOGEN ACTIVATOR INHIBITOR 2)

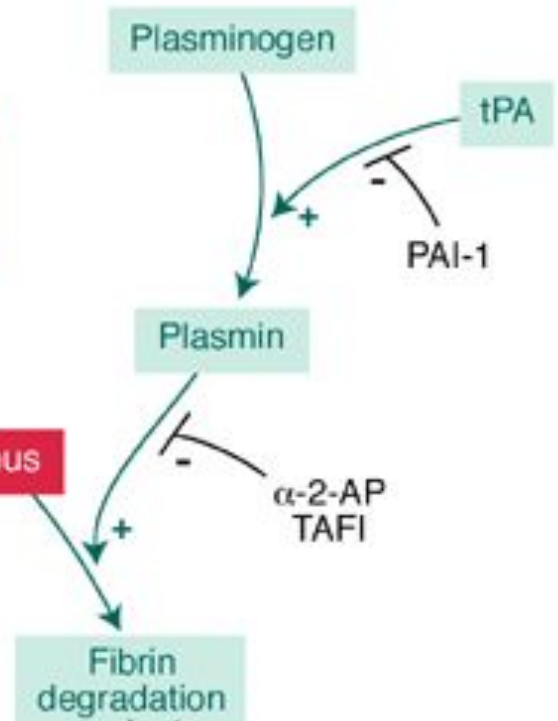
α_2 -AP (α_2 -ANTI PLASMIN)

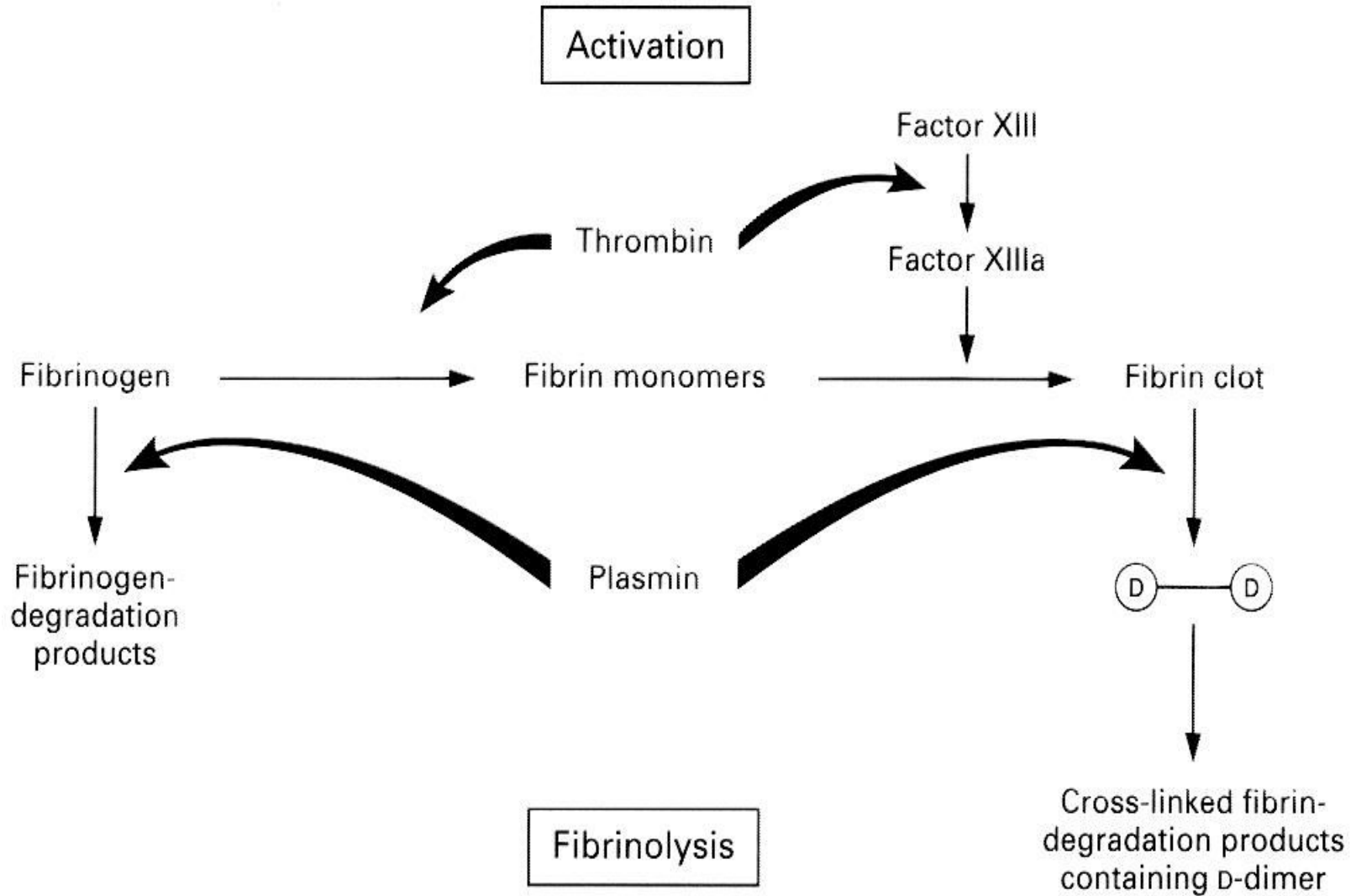


TAFI (thrombin
activatable
fibrinolysis
inhibitor)



b Plasmin-mediated fibrinolysis

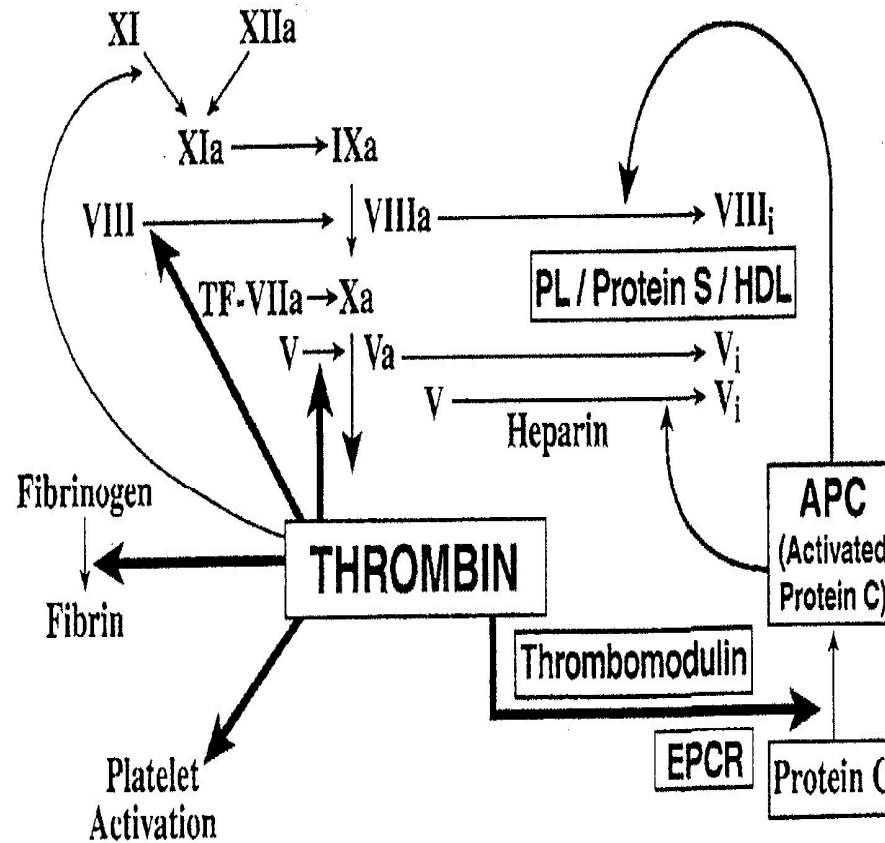




COAGULATION INHIBITORS

Blood Coagulation Pathways

Protein C Pathway



- Anti Thrombin inhibitor
- Inhibition of Factor VIIa by TFPI

