Thrombosis and Hemostasis Physiology

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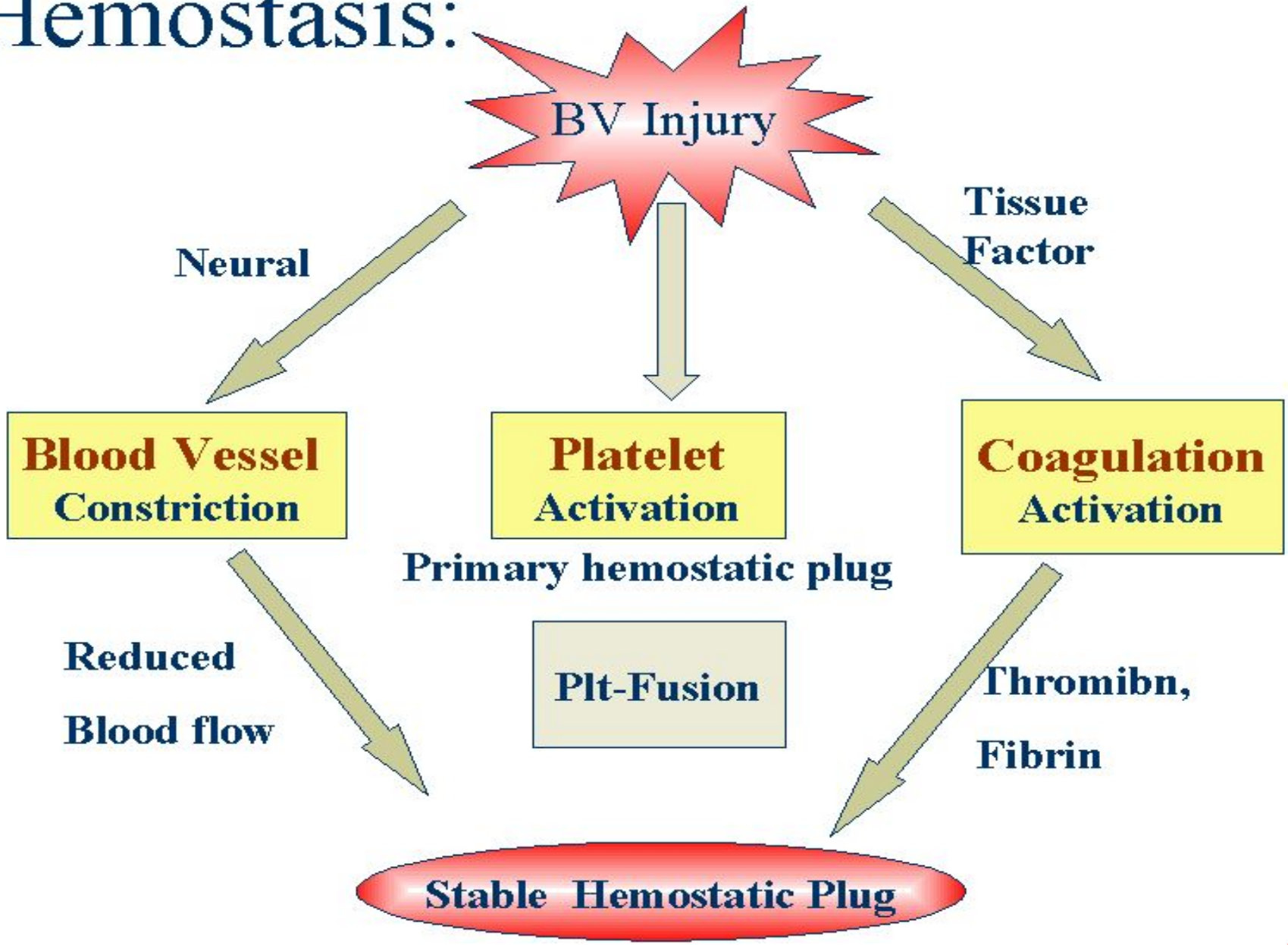
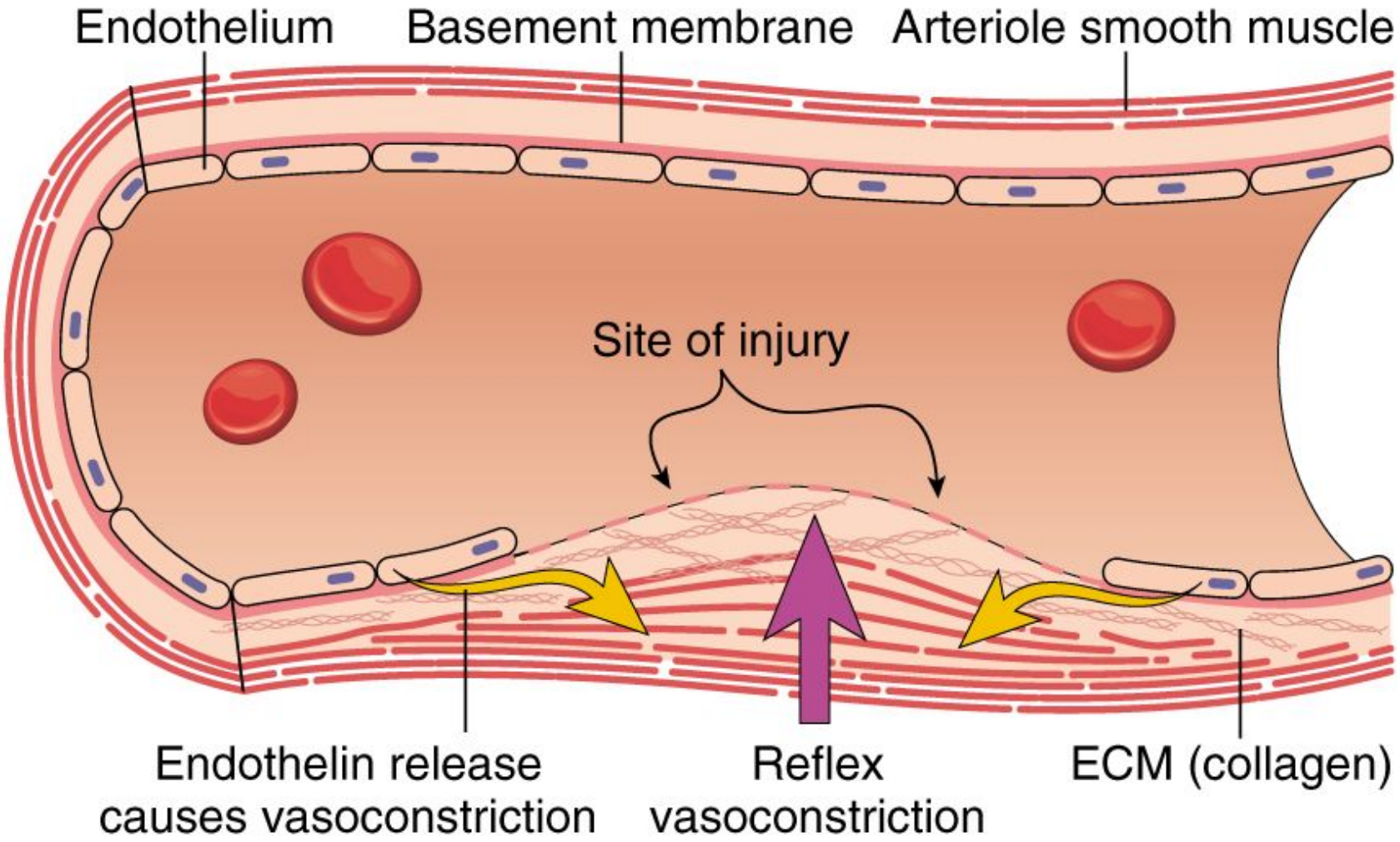
Hemostasis:


BV Injury
Neural
Tissue Factor
Blood Vessel Constriction
Platelet Activation
Coagulation Activation
Primary hemostatic plug
Reduced Blood flow
Plt-Fusion
Thromibn, Fibrin
Stable Hemostatic Plug

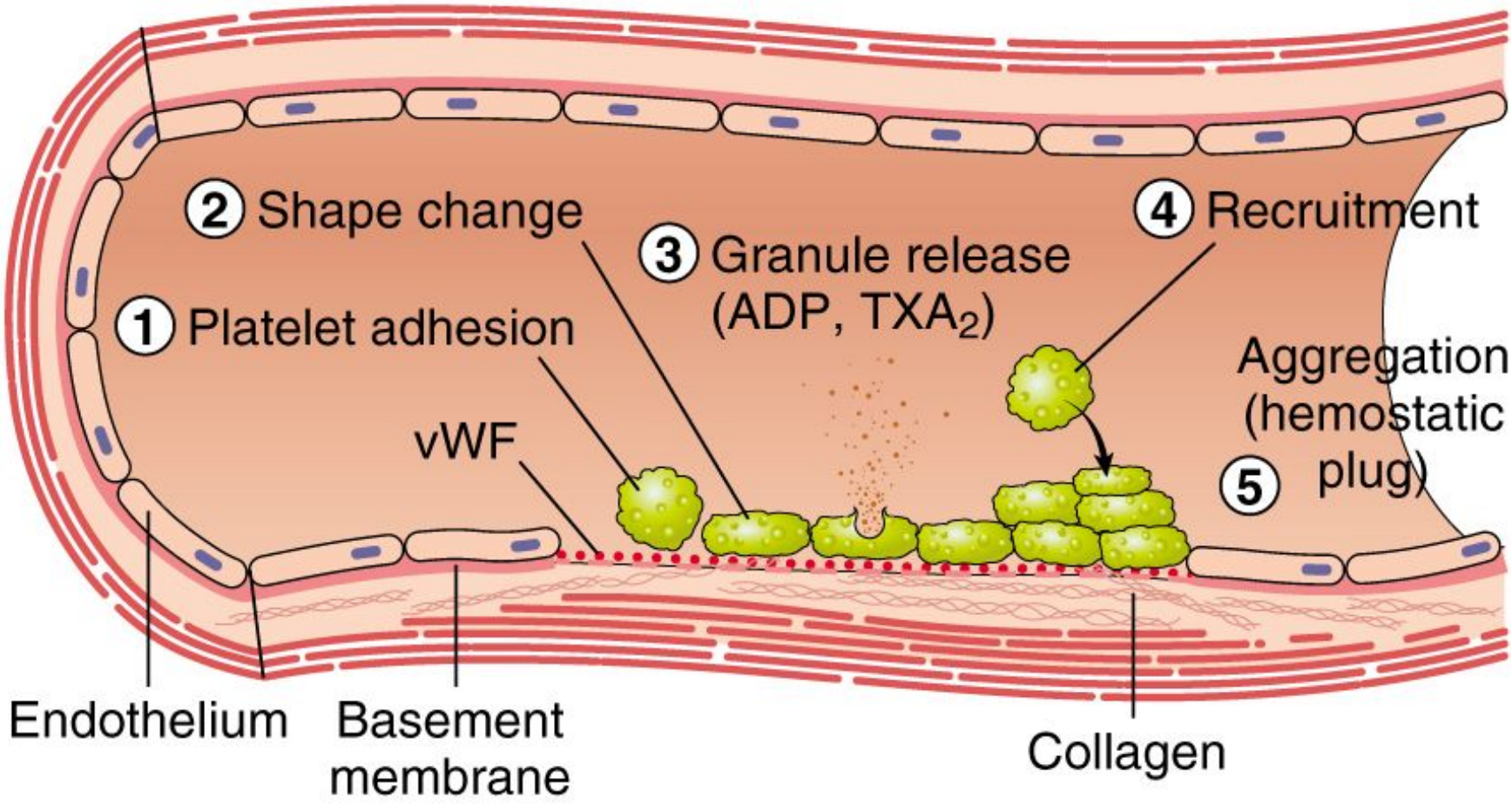
Process- *primary haemostasis*

- 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



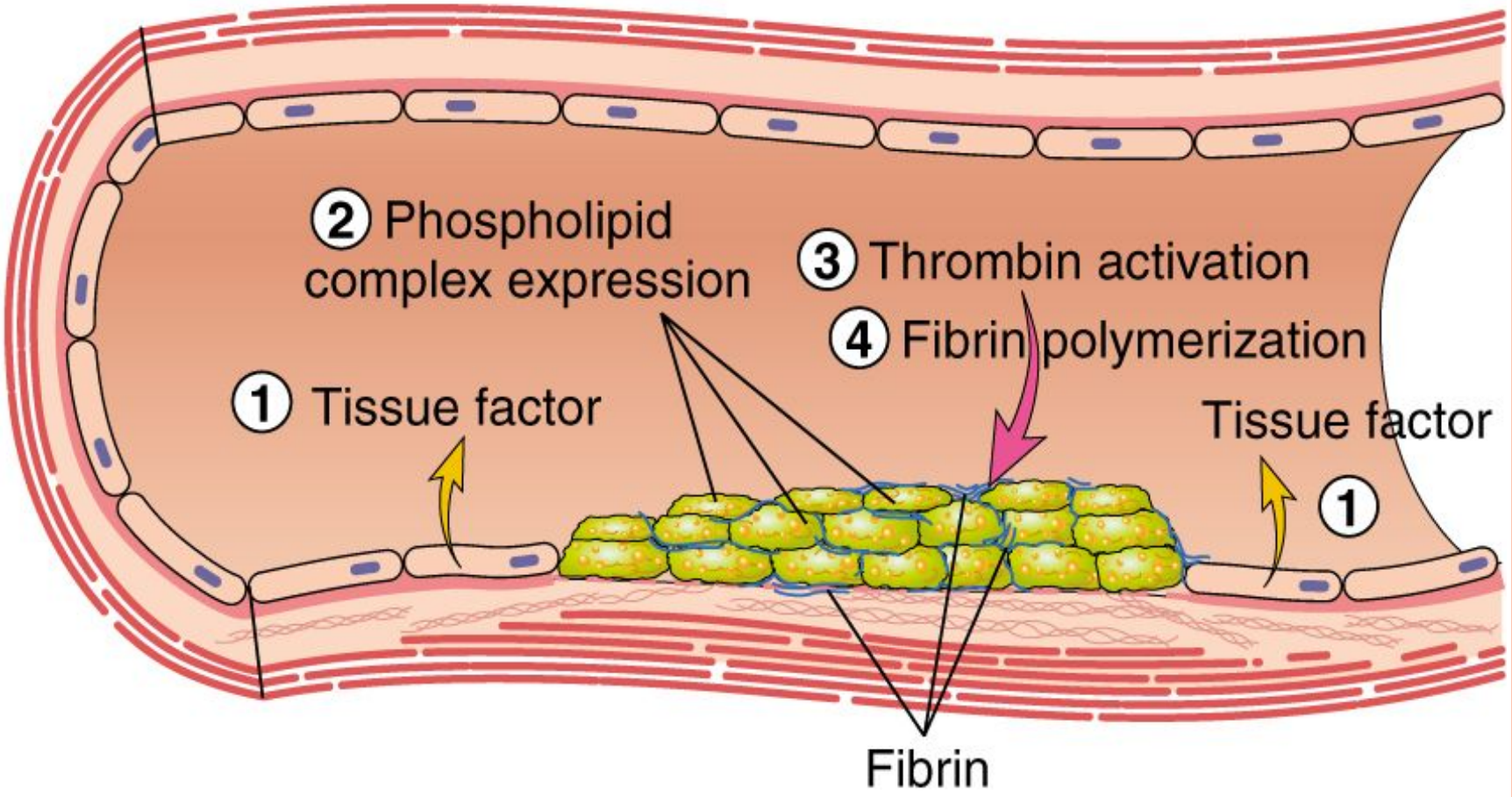
B. PRIMARY HEMOSTASIS



Secondary haemostasis

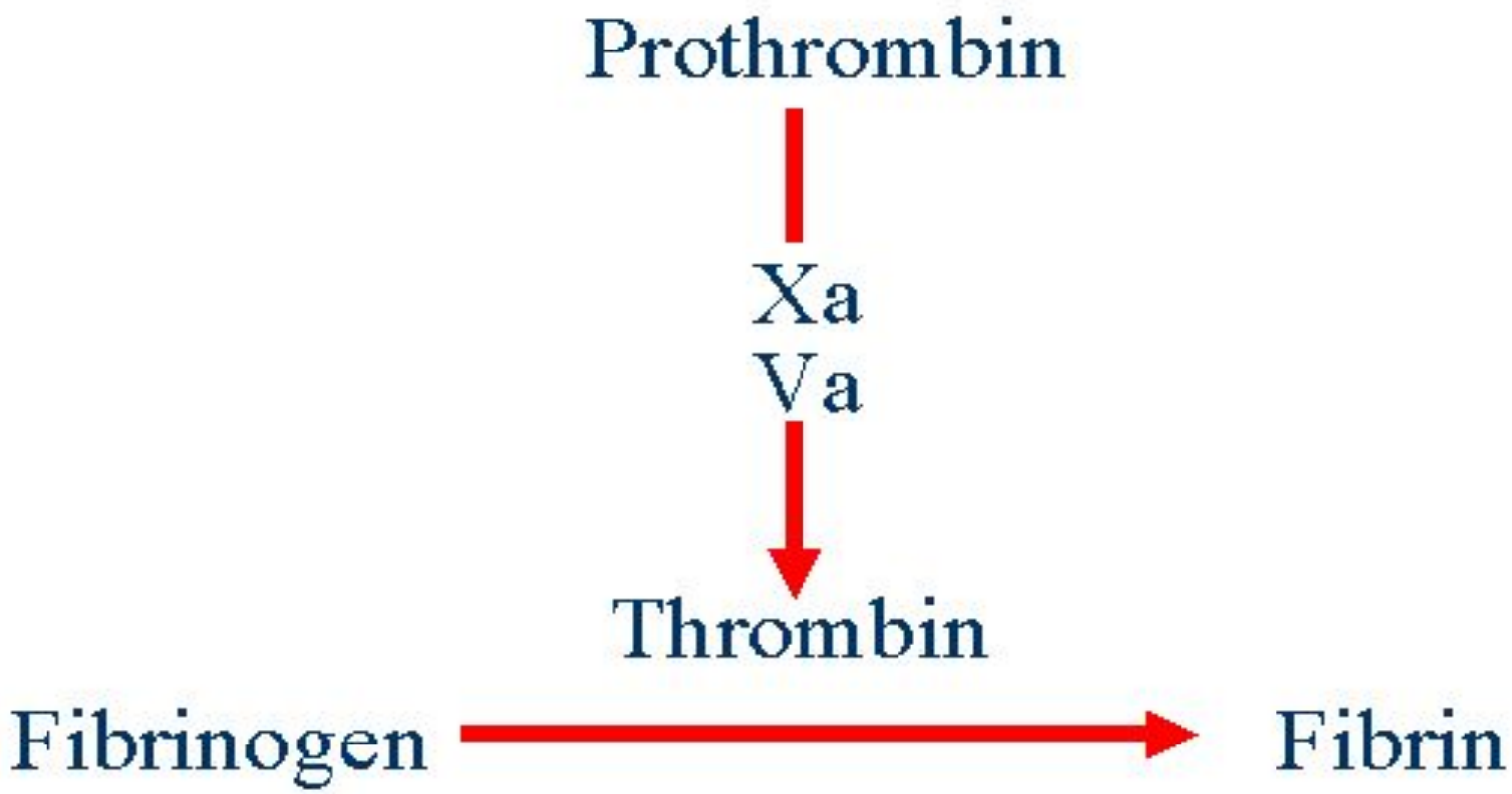
- Secondary haemostasis then follows—plasma components called *coagulation factors* respond (in a complex cascade) to form fibrin strands which strengthen the platelet plug.
- Coagulation from a cut is initiated by platelets adhering to and activated by collagen in the blood vessel endothelium.
- The 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.

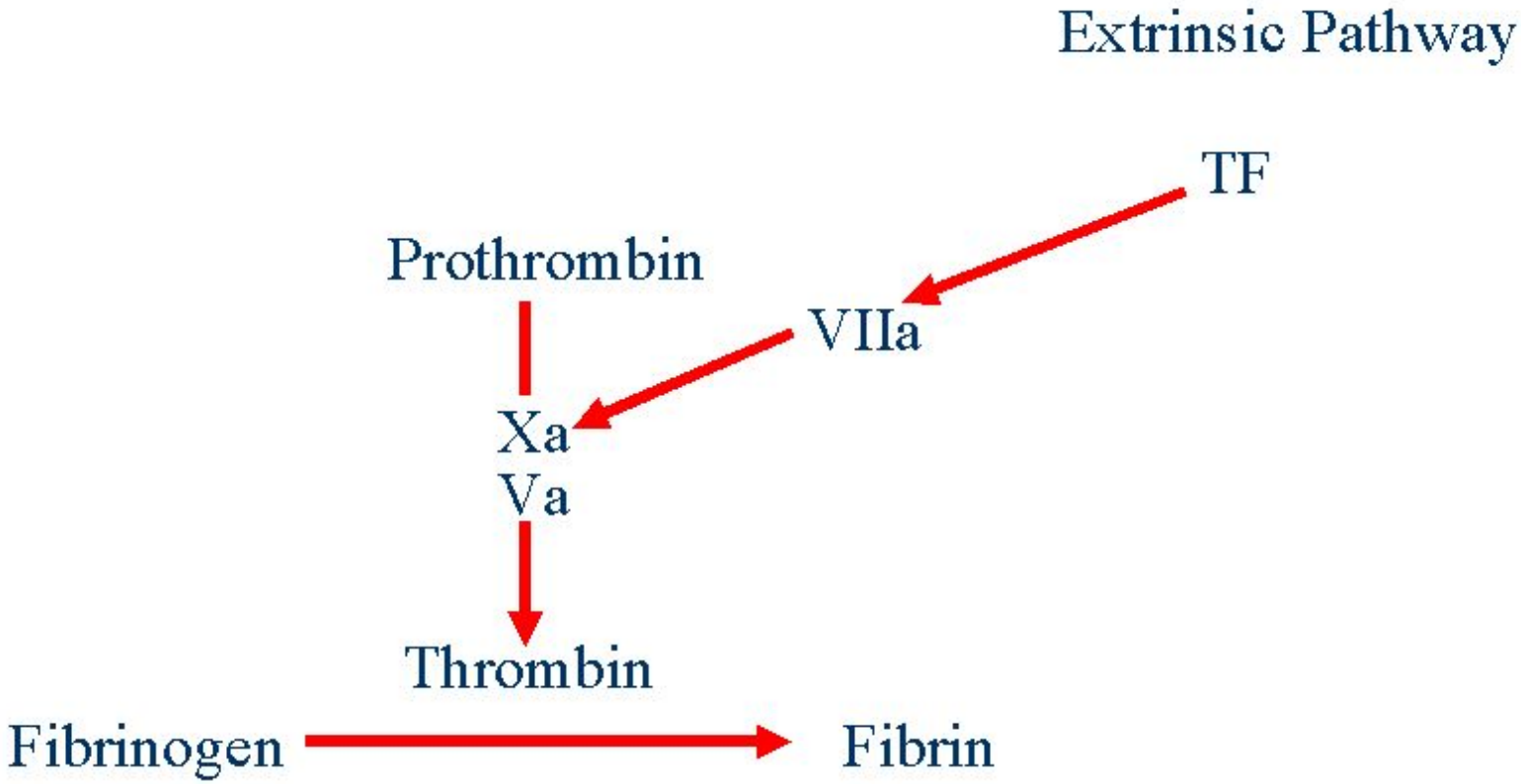
C. SECONDARY HEMOSTASIS

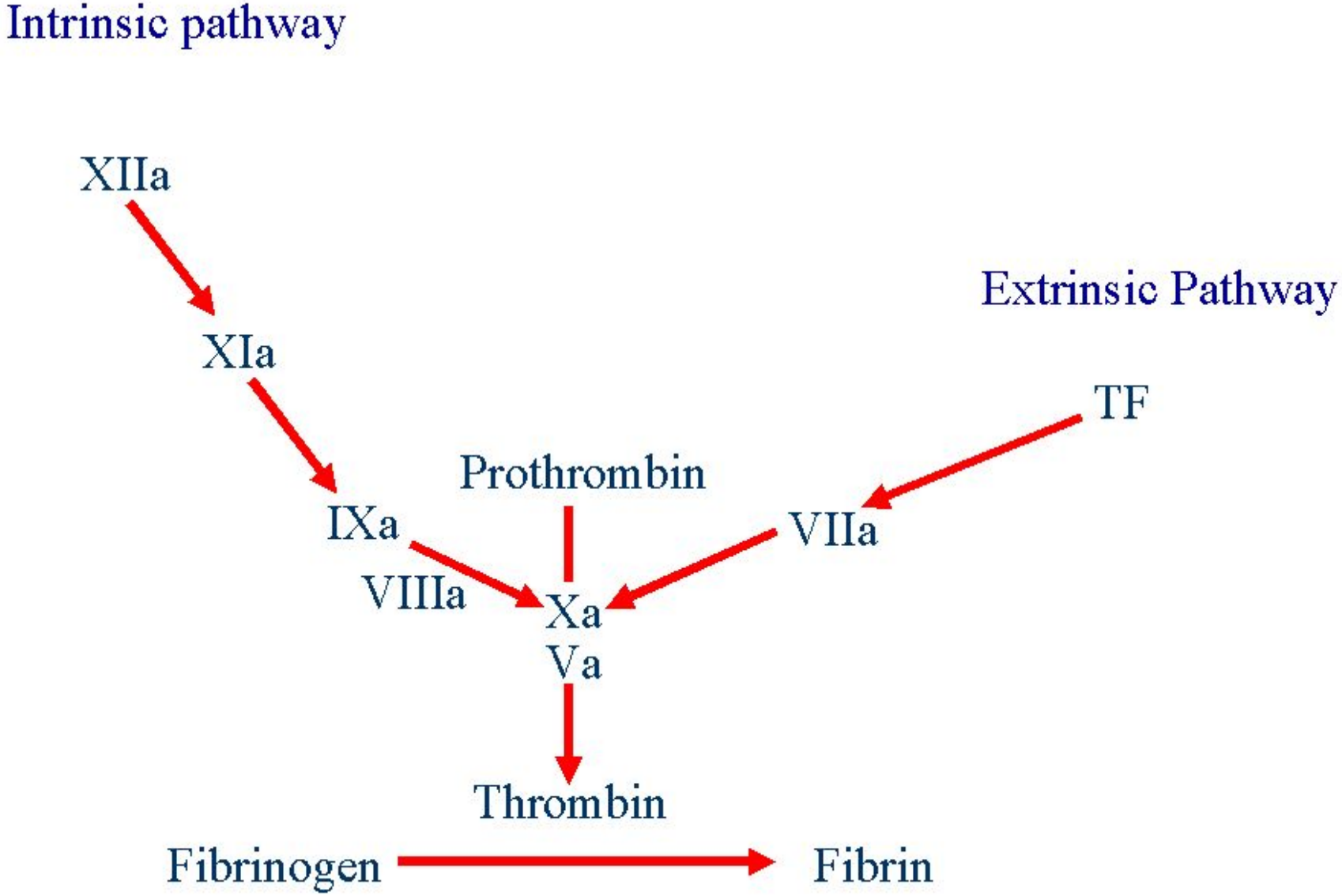


Coagulation cascade

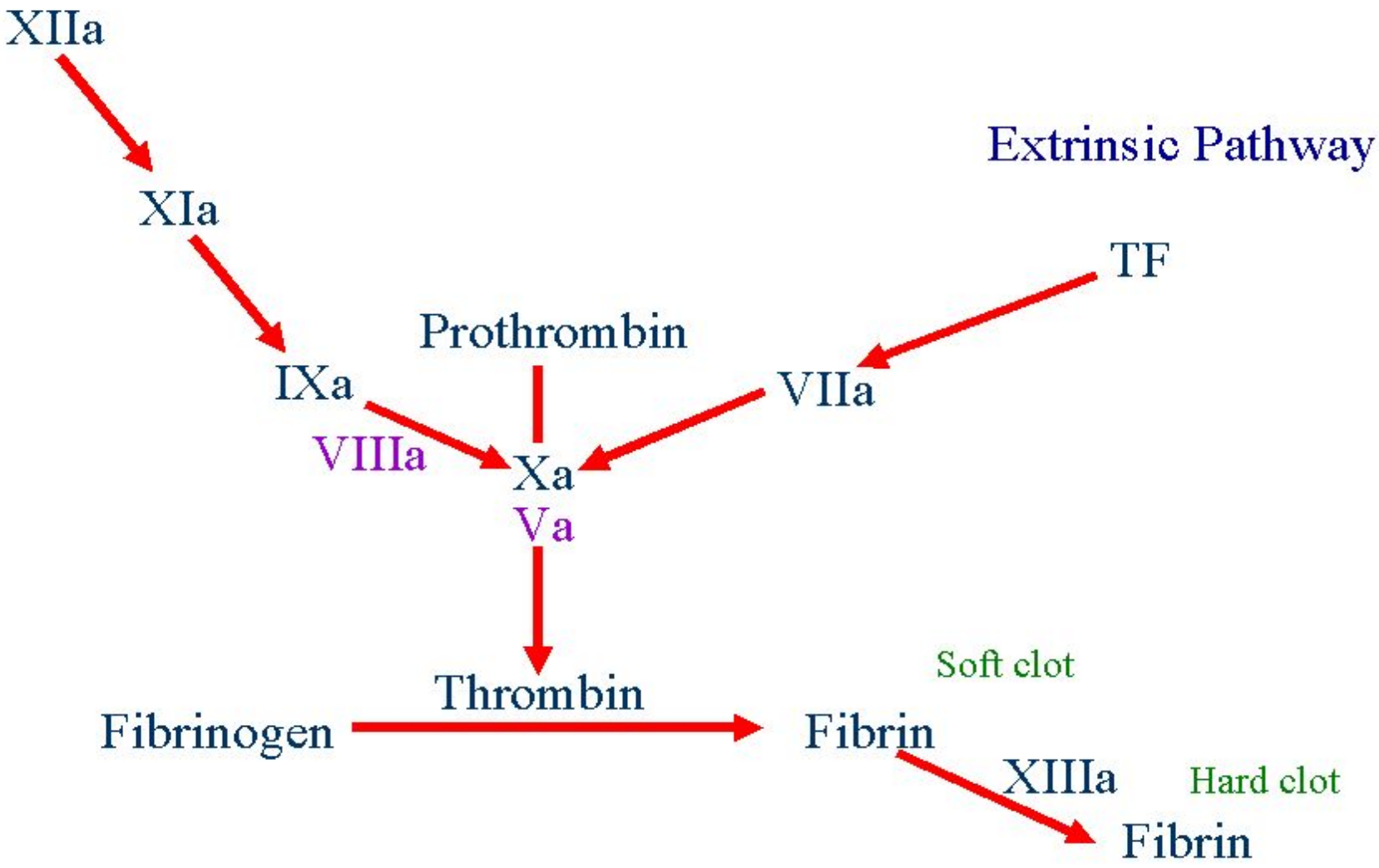
- The coagulation cascade of secondary hemostasis has two pathways, the *Contact Activation pathway* (formerly known as the Intrinsic Pathway)
- And the *Tissue Factor pathway* (formerly known as the Extrinsic pathway) that lead to *fibrin* formation.
- It was previously thought that the coagulation 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
TF
Prothrombin
VIIa
Xa
Va
Thrombin
Fibrinogen
Fibrin


Intrinsic pathway
XIIa
XIa
IXa
VIIIa
Prothrombin
Xa
Va
Thrombin
Fibrinogen
Fibrin
Extrinsic Pathway
TF
VIIa

Intrinsic pathway



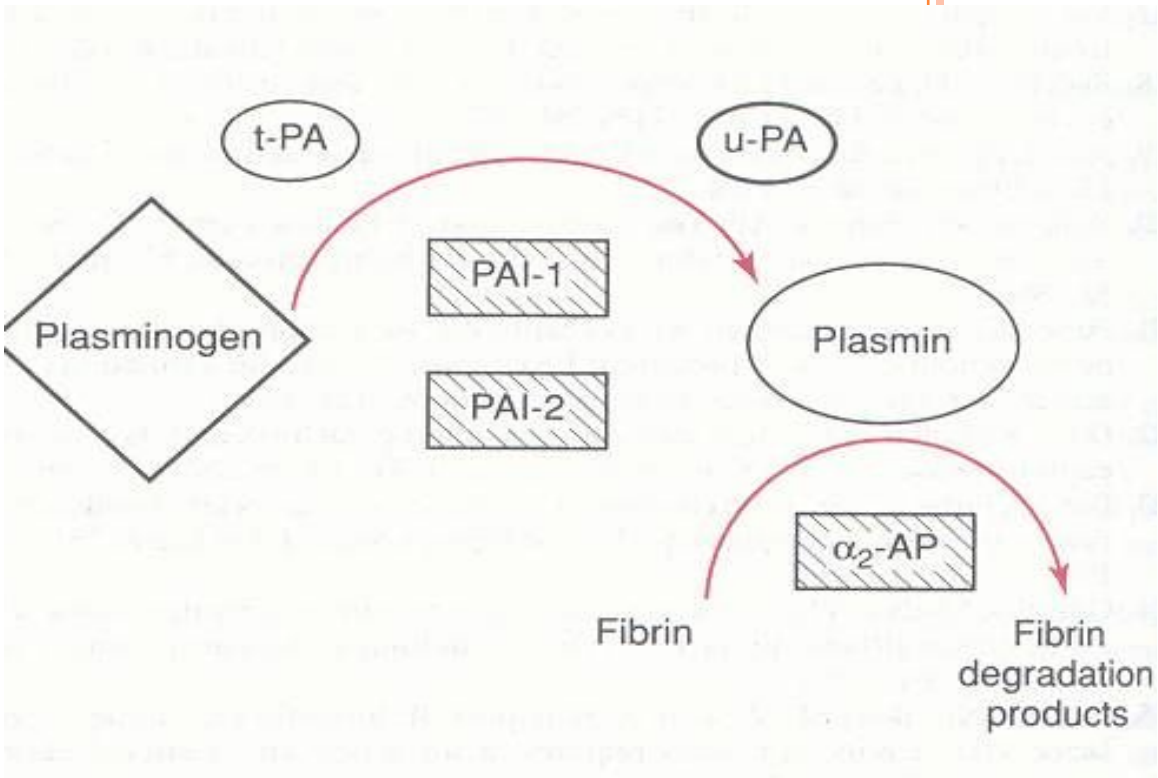
Platelets:

- Bone marrow – Megakaryocytes –
- Life span 7-10d, N.count – 150-400x10^9/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 – Instrinsic
  - 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

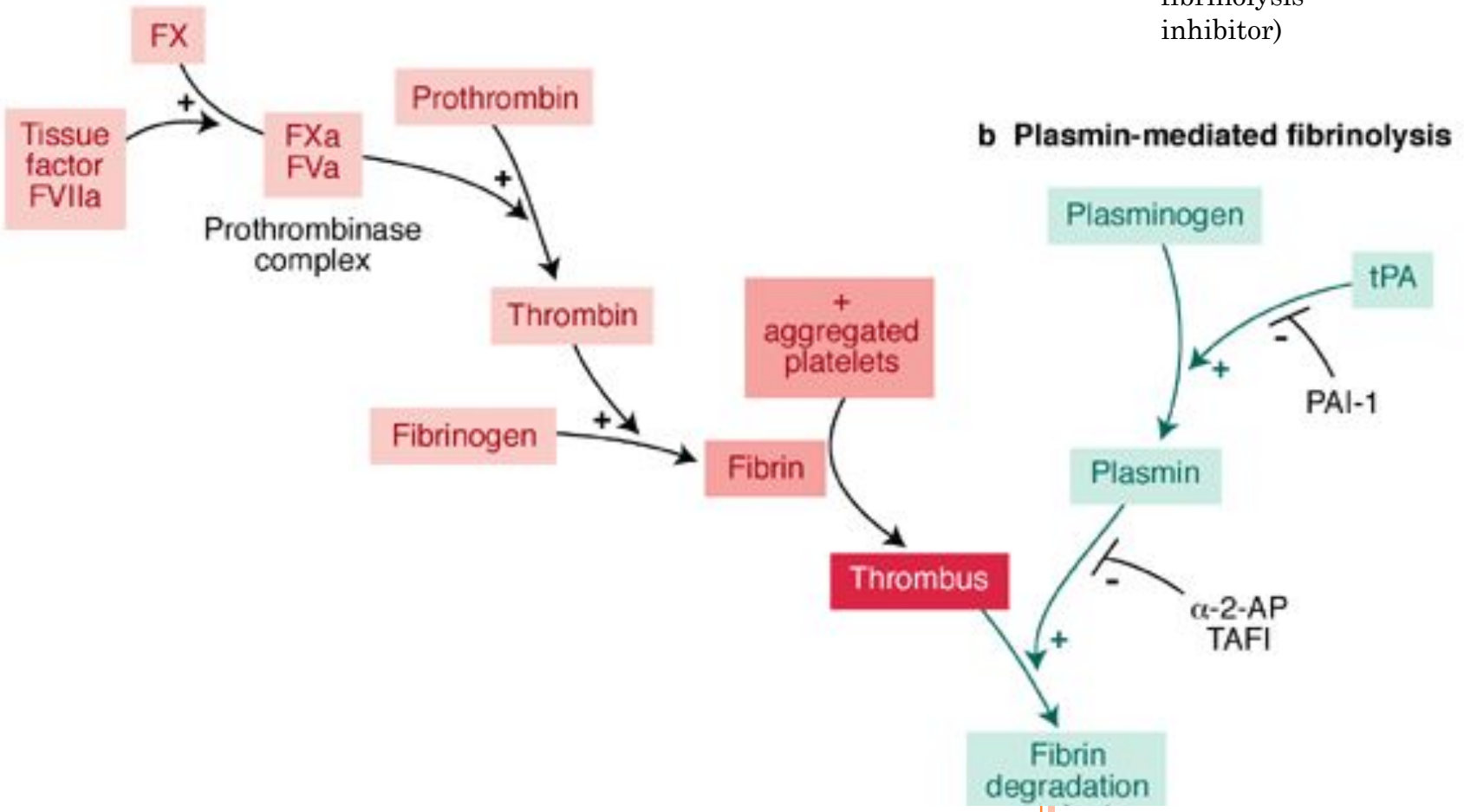


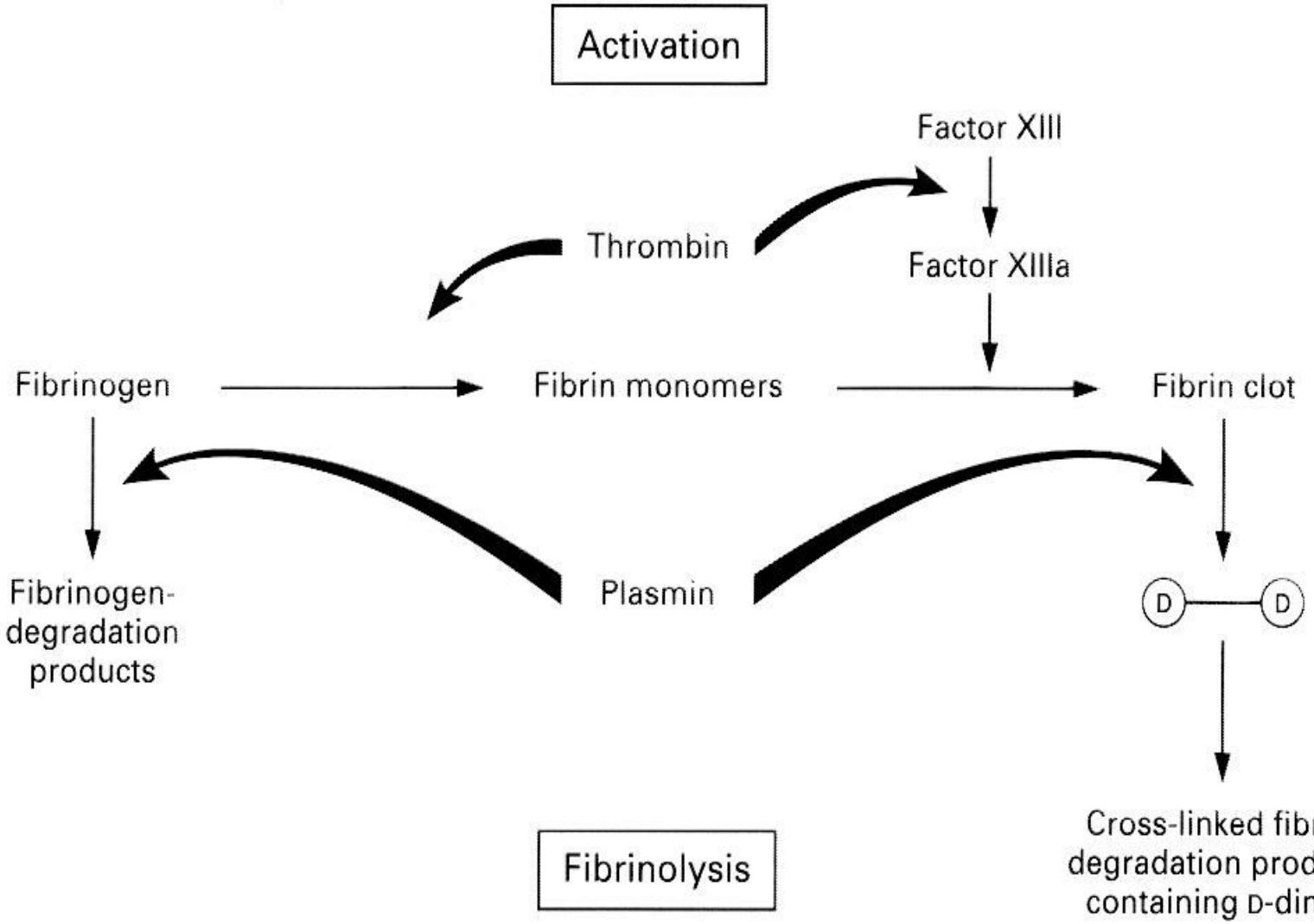
t-PA (tissue plasminogen activator)
u-PA (urokinase plasminogen activator)

PAI-1 (plasminogen activator inhibitor 1)
PAI-2 (plasminogen activator inhibitor 2)

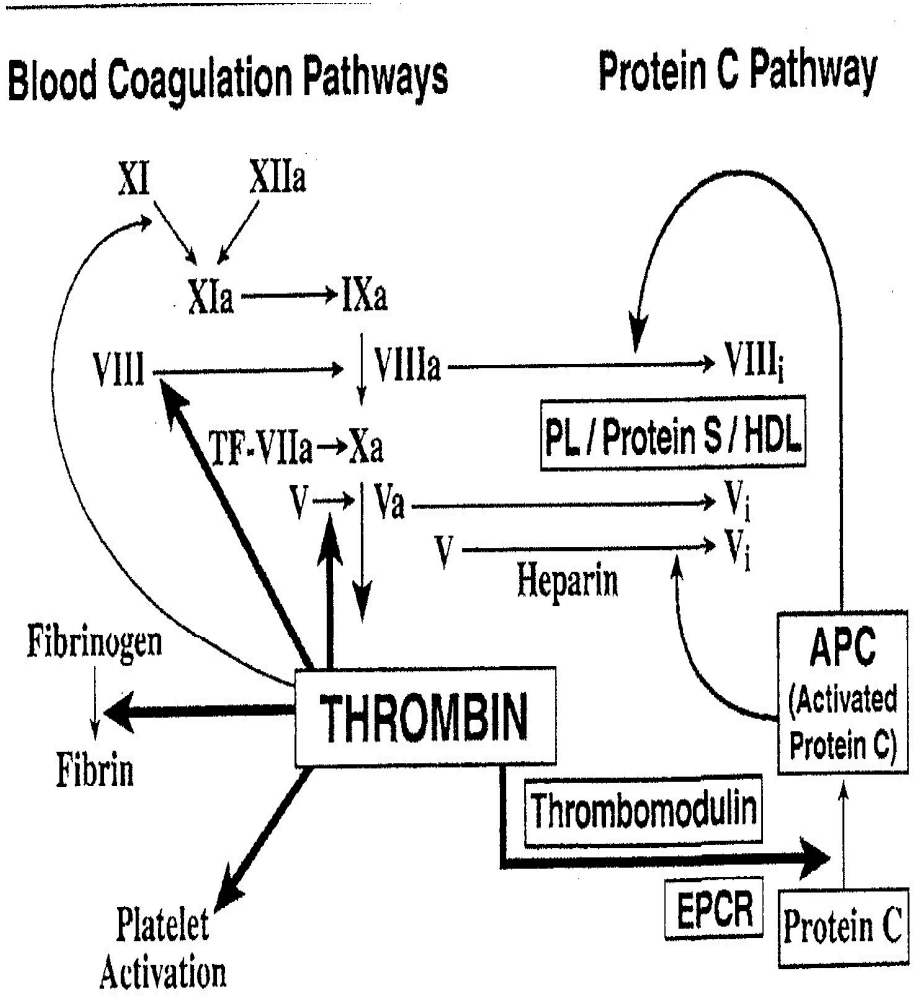
A_2-AP (A_2-anti plasmin

TAFI (thrombin activatable fibrinolysis inhibitor)




Activation
Factor XIII
Thrombin
Factor XIIIa
Fibrinogen
Fibrin monomers
Fibrin clot
Fibrinogen-degradation products
Plasmin
D
D
Fibrinolysis
Cross-linked fibrin-degradation products containing D-dimer

Coagulation inhibitors



- Anti Thrombin inhibitor
- Inhibition of Factor VIIa by TFPI