



# **THROMBOSIS AND HEMOSTASIS**

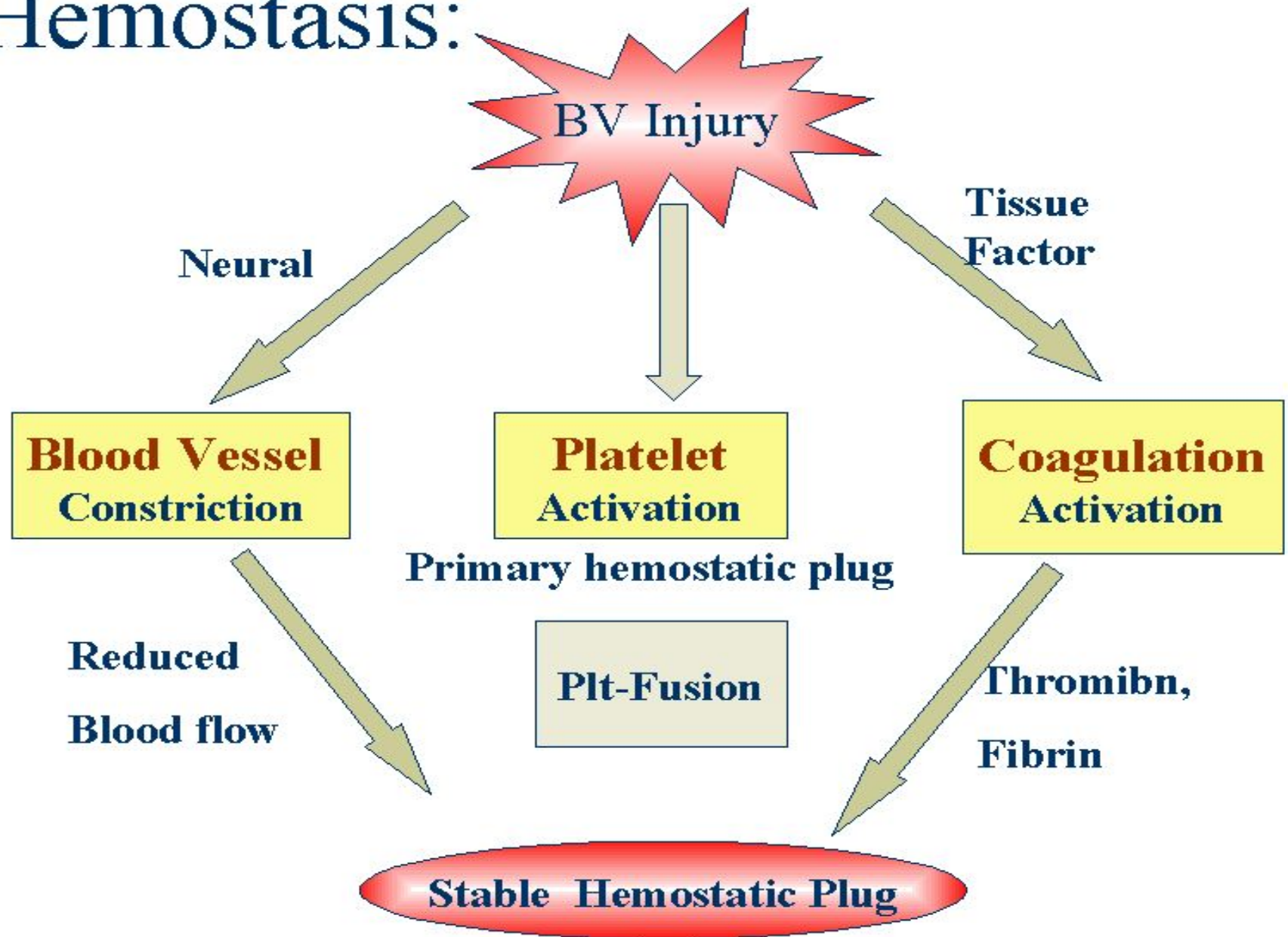
## **PHYSIOLOGY**

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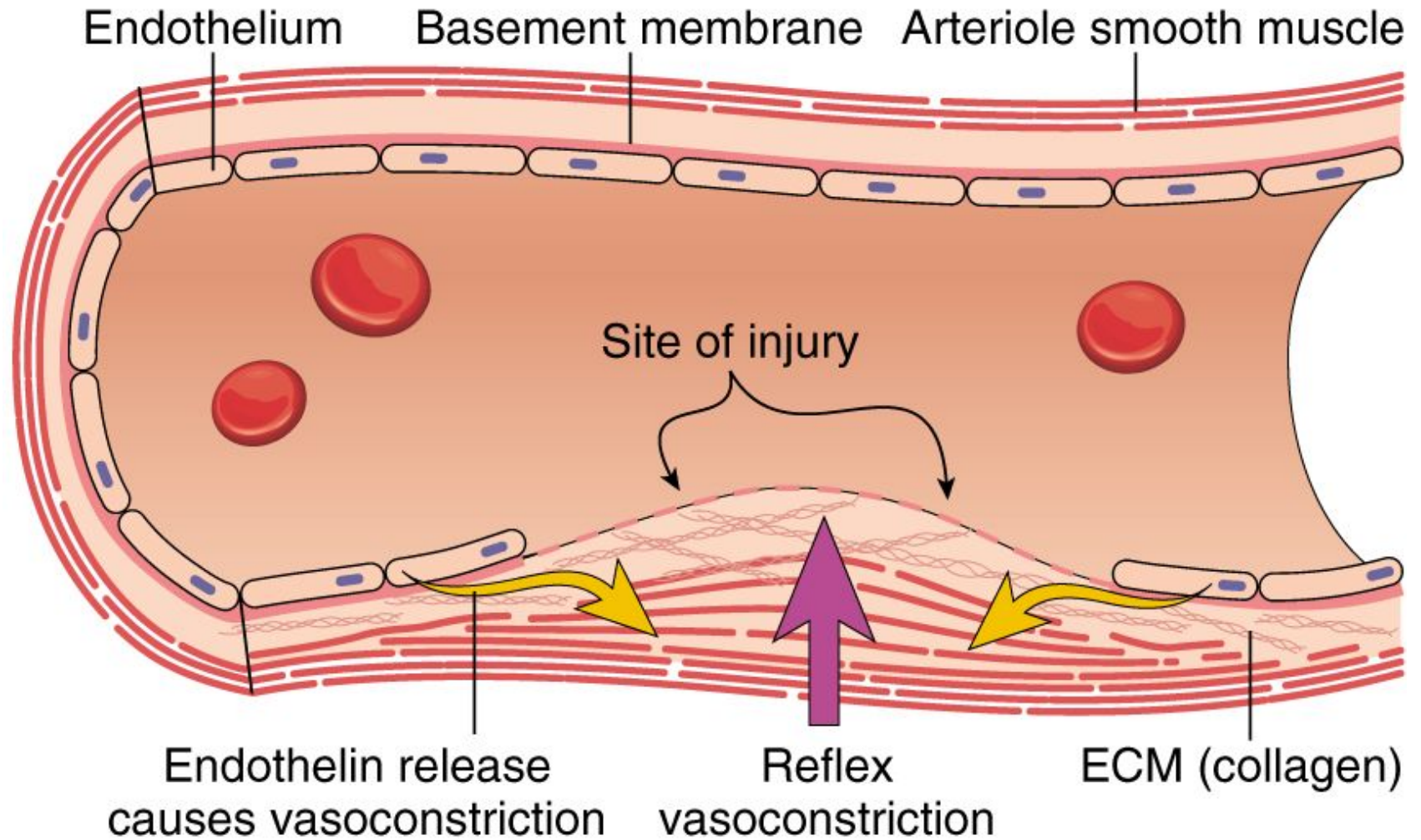
# Hemostasis:



# Process- *primary haemostasis*

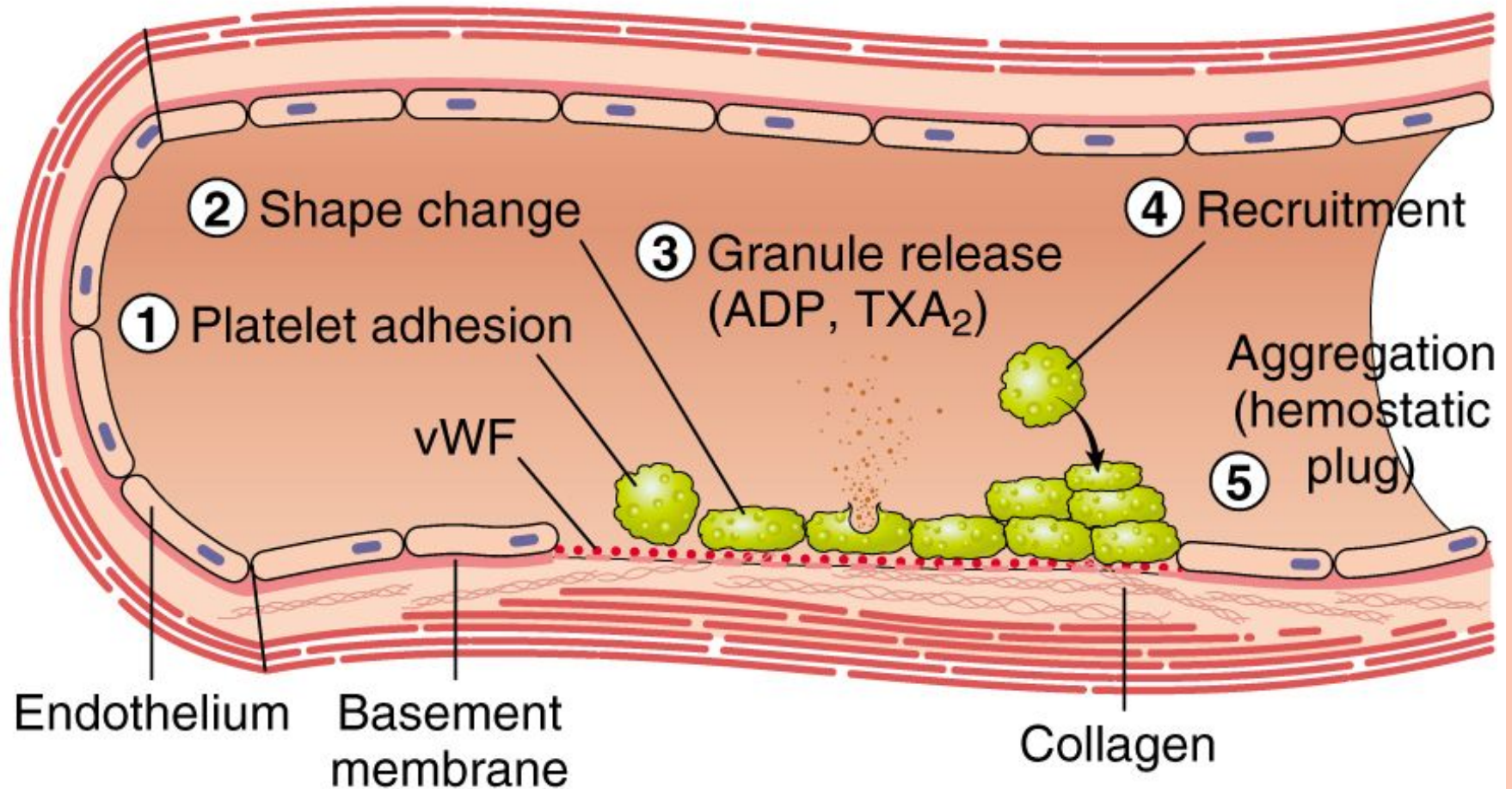
- ◆ In a normal individual, coagulation is initiated within 20 seconds after an injury occurs to the blood vessel damaging the endothelial cells.
- ◆ Platelets immediately form a haemostatic plug at the site of injury. This is called *primary haemostasis*.

# A. VASOCONSTRICTION





## B. PRIMARY HEMOSTASIS

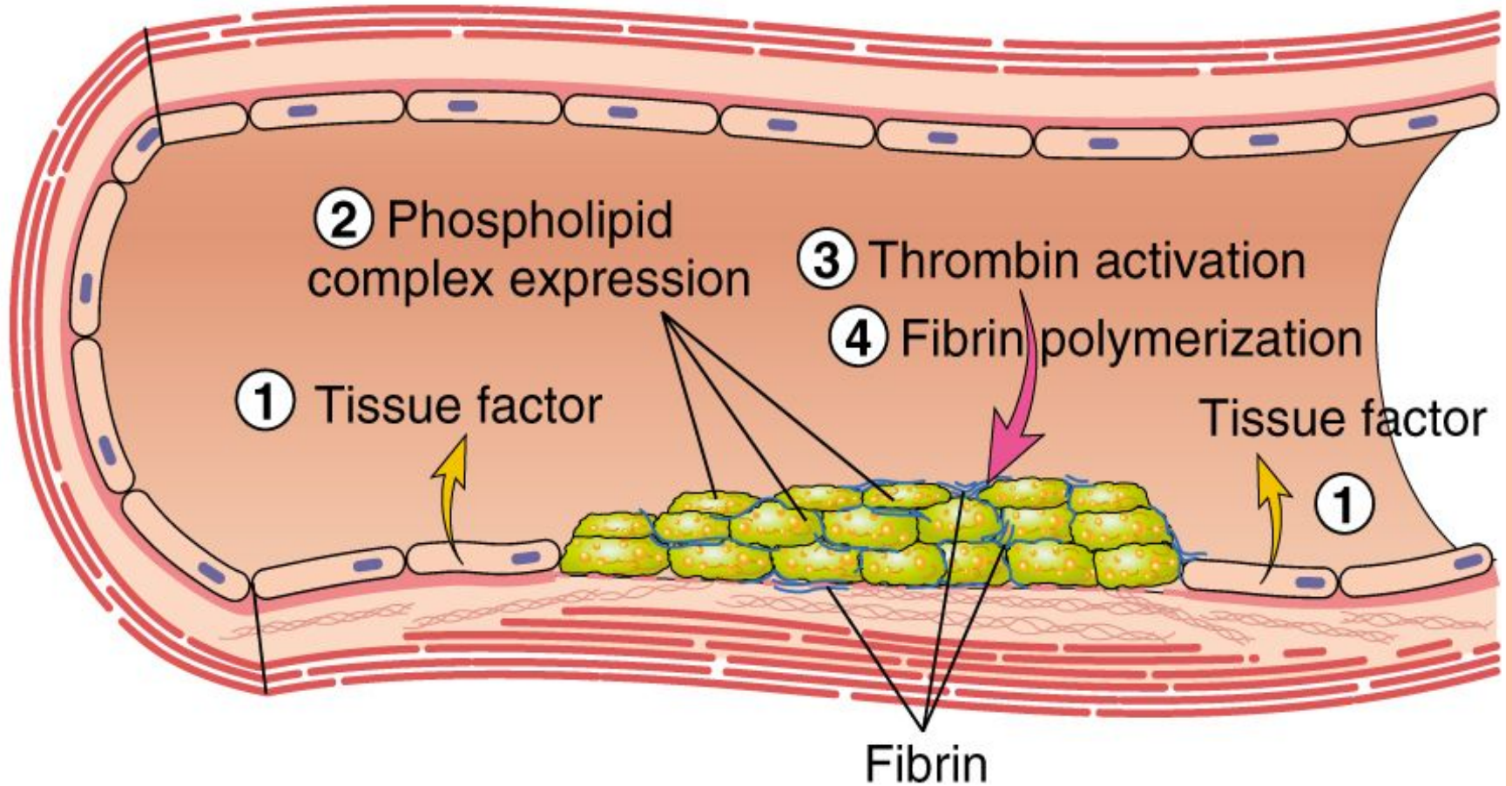


# Secondary haemostasis

- ◆ 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

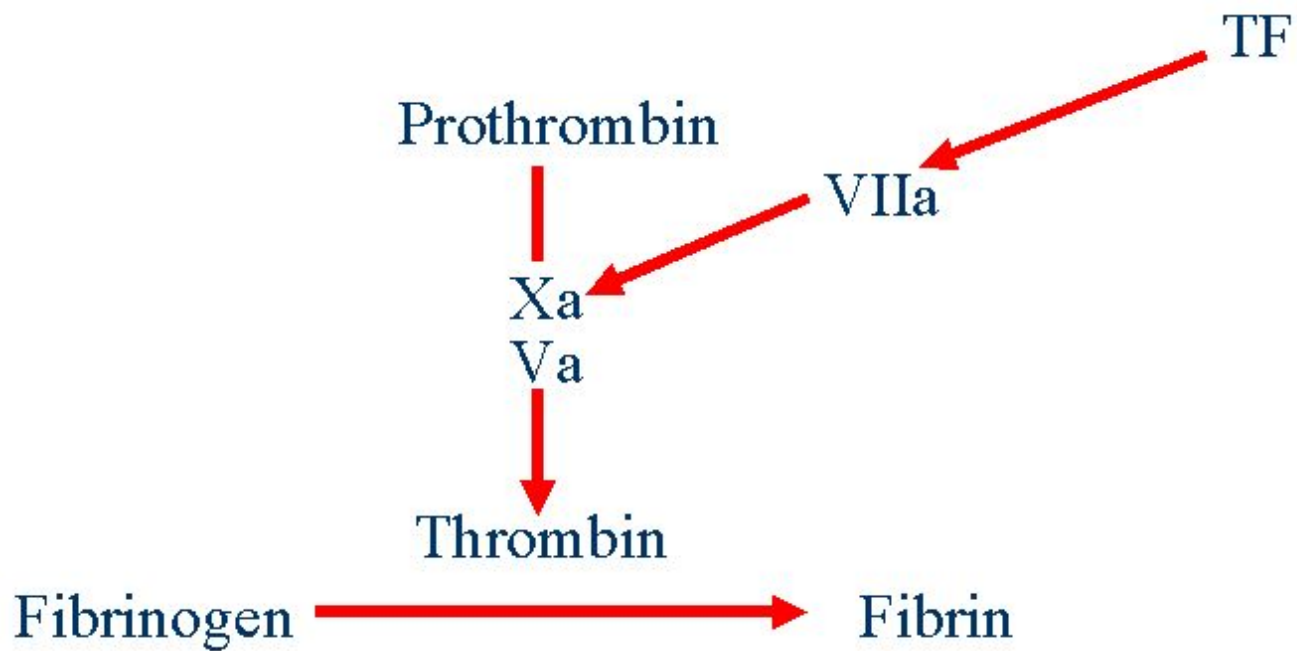
Fibrinogen



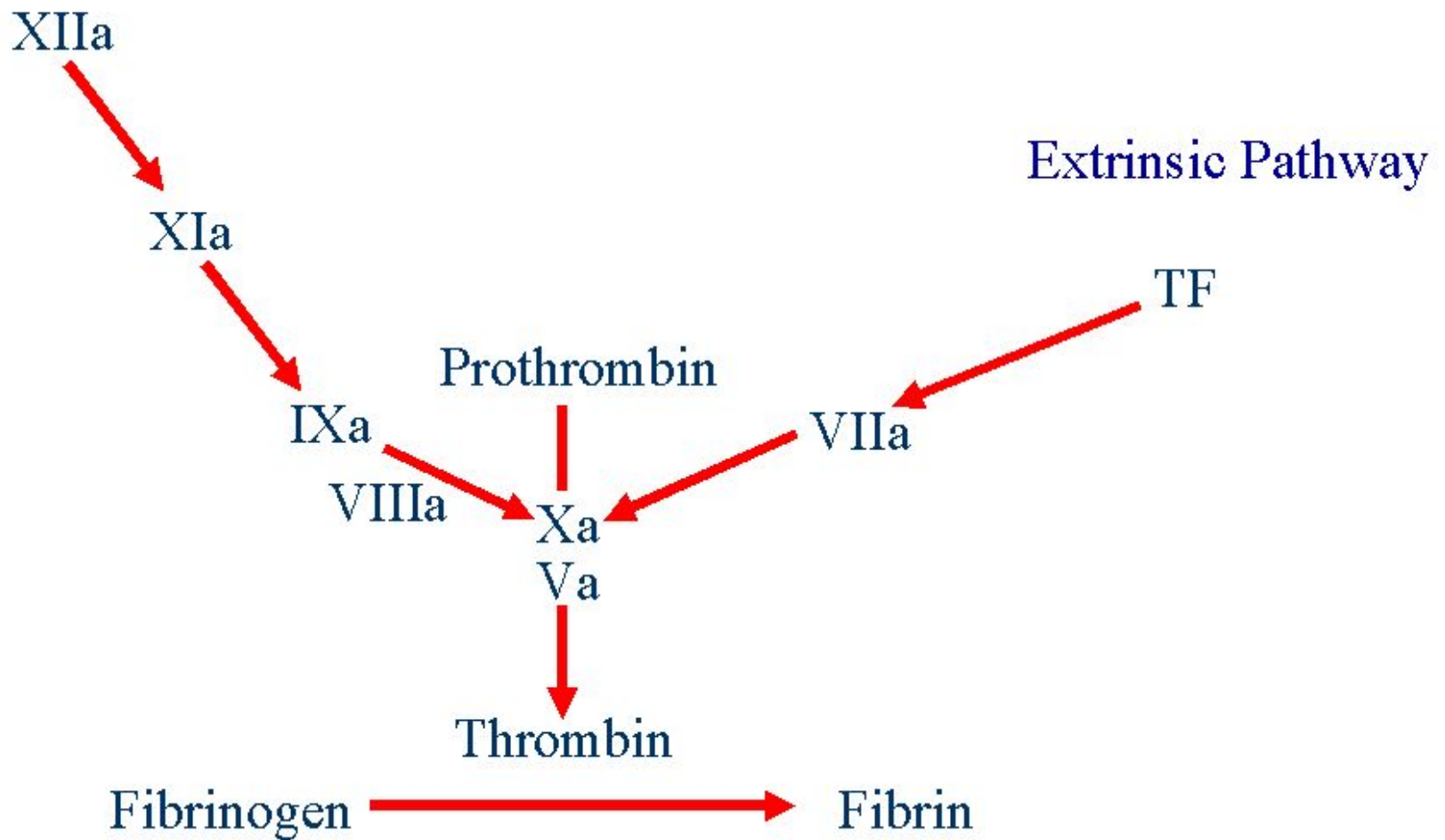
Fibrin



## Extrinsic Pathway



## Intrinsic pathway







# 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:

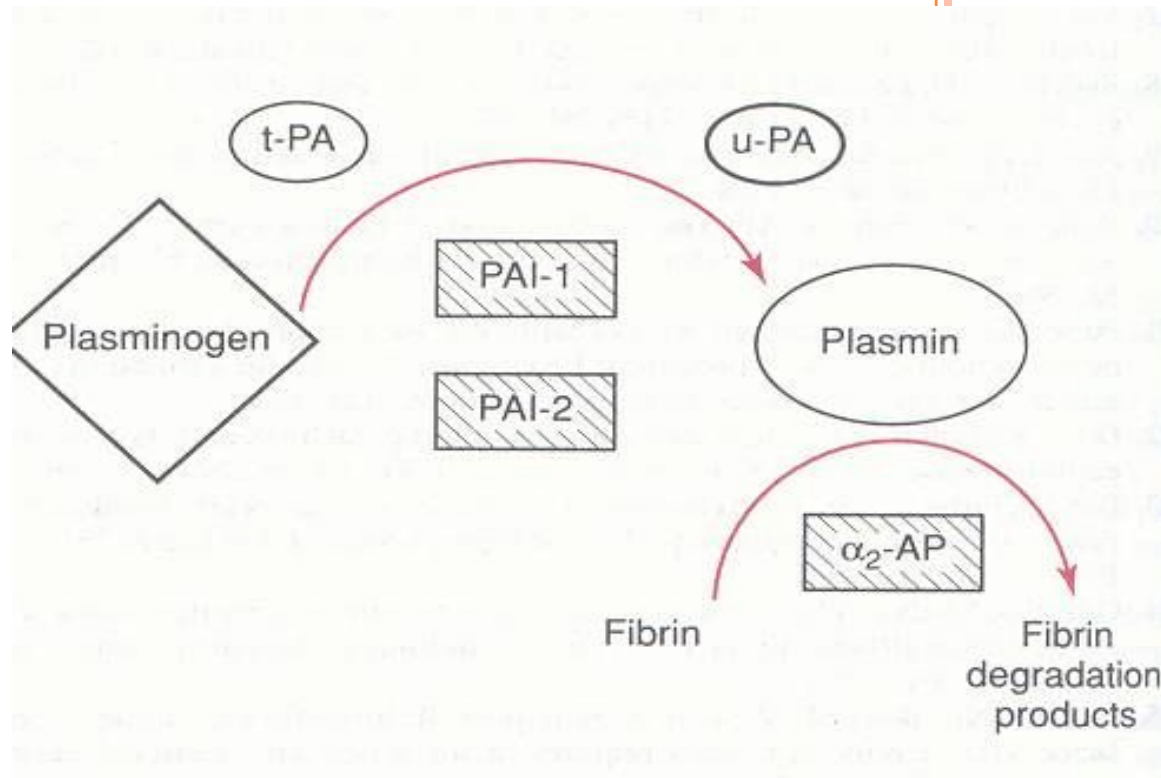
## ◆ **Screening tests:**

- 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)**

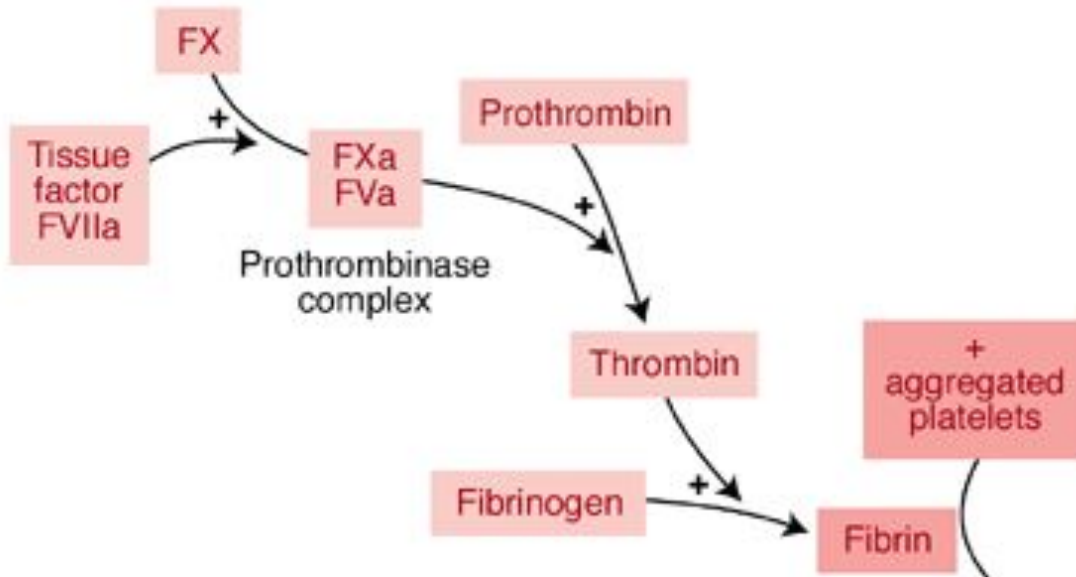
**PAI-1 (PLASMINOGEN ACTIVATOR INHIBITOR 1)**

**PAI-2 (PLASMINOGEN ACTIVATOR INHIBITOR 2)**

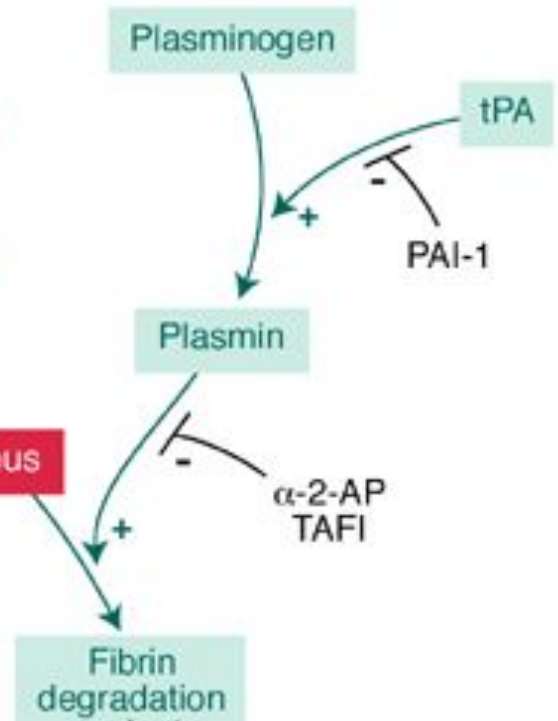
**$\alpha_2$ -AP ( $\alpha_2$ -ANTI PLASMIN)**



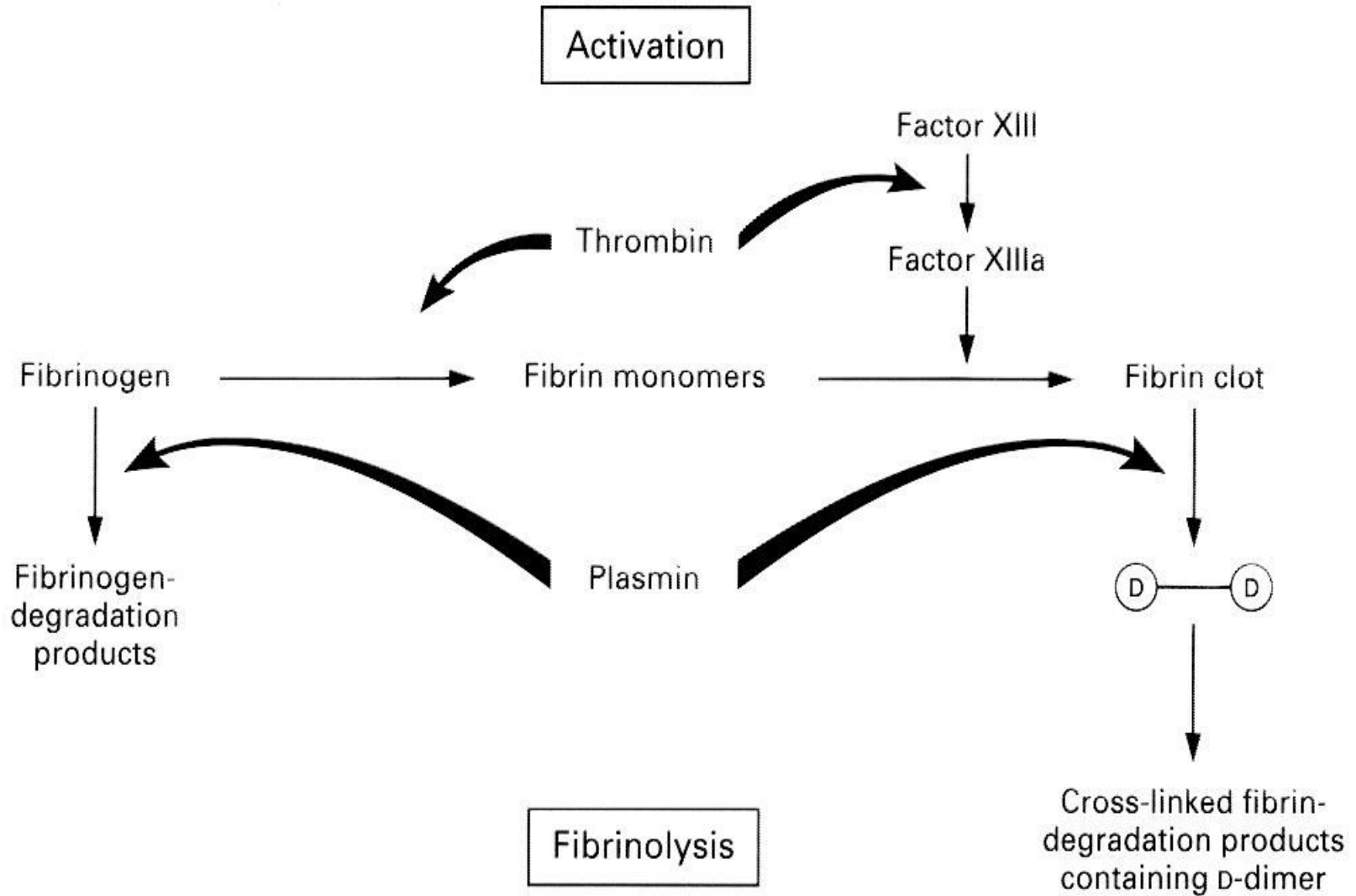
TAFI (thrombin  
activatable  
fibrinolysis  
inhibitor)



### b Plasmin-mediated fibrinolysis



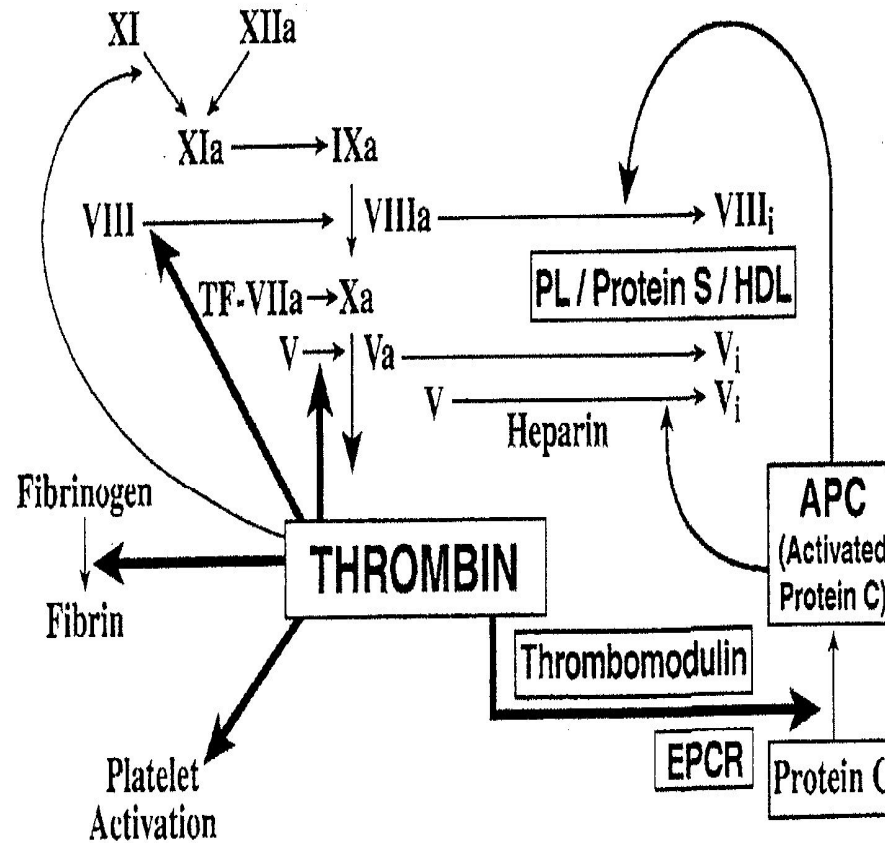




# COAGULATION INHIBITORS

## Blood Coagulation Pathways

## Protein C Pathway



- Anti Thrombin inhibitor
- Inhibition of Factor VIIa by TFPI

