The background features a light purple-to-blue gradient. Scattered across the surface are numerous water droplets of various sizes, some with highlights and shadows, giving them a 3D appearance. In the center, there is a faint, large, light-colored circular graphic that resembles a stylized cell or a molecular structure.

# HEMODYNAMIC DISORDERS, THROMBOEMBOLISM, AND SHOCK 2

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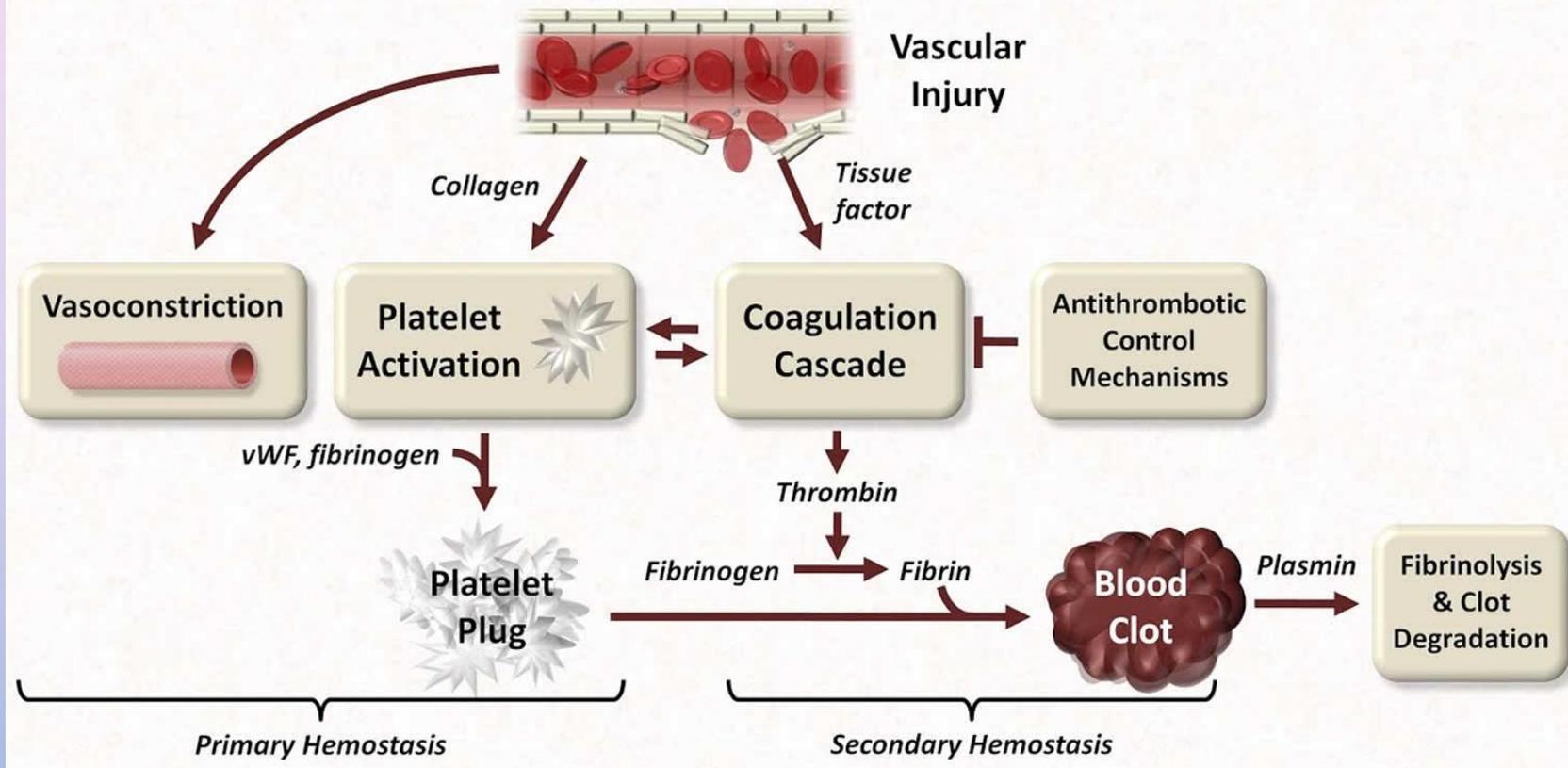
# HEMOSTASIS AND THROMBOSIS

- NORMAL HEMOSTASIS COMPRISES A SERIES OF REGULATED PROCESSES THAT CULMINATE IN THE FORMATION OF A BLOOD CLOT THAT LIMITS BLEEDING FROM AN INJURED VESSEL.
- THE PATHOLOGIC COUNTERPART OF HEMOSTASIS IS THROMBOSIS, THE FORMATION OF BLOOD CLOT (THROMBUS) WITHIN NON-TRAUMATIZED, INTACT VESSELS.

# NORMAL HEMOSTASIS

- HEMOSTASIS IS PROCESS INVOLVING PLATELETS, CLOTTING FACTORS, AND ENDOTHELIUM THAT OCCURS AT THE SITE OF VASCULAR INJURY AND CULMINATES IN THE FORMATION OF A BLOOD CLOT, WHICH SERVES TO PREVENT OR LIMIT THE EXTENT OF BLEEDING.

# Major Components of Hemostasis



# MAJOR COMPONENT OF HEMOSTASIS

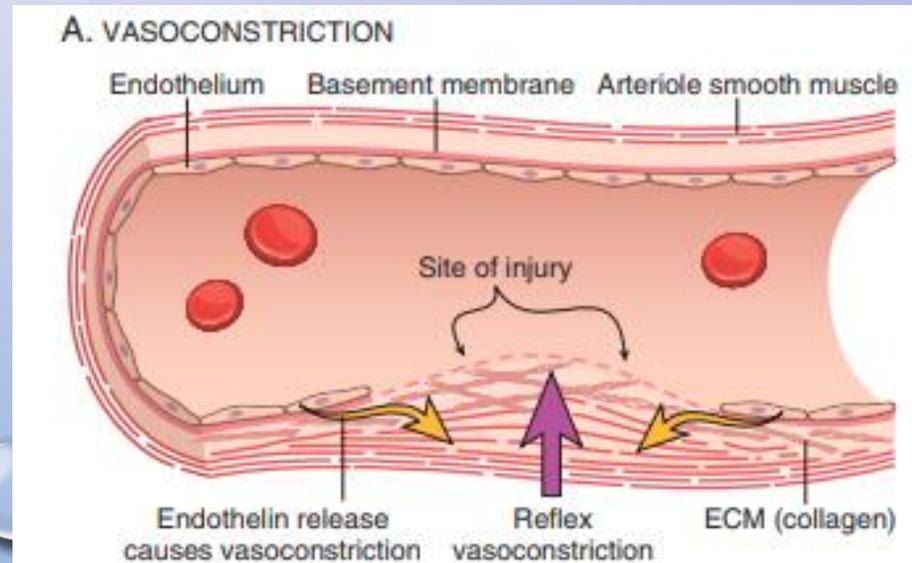
1.plateletes

2.Clotting factors

3.Endothelium

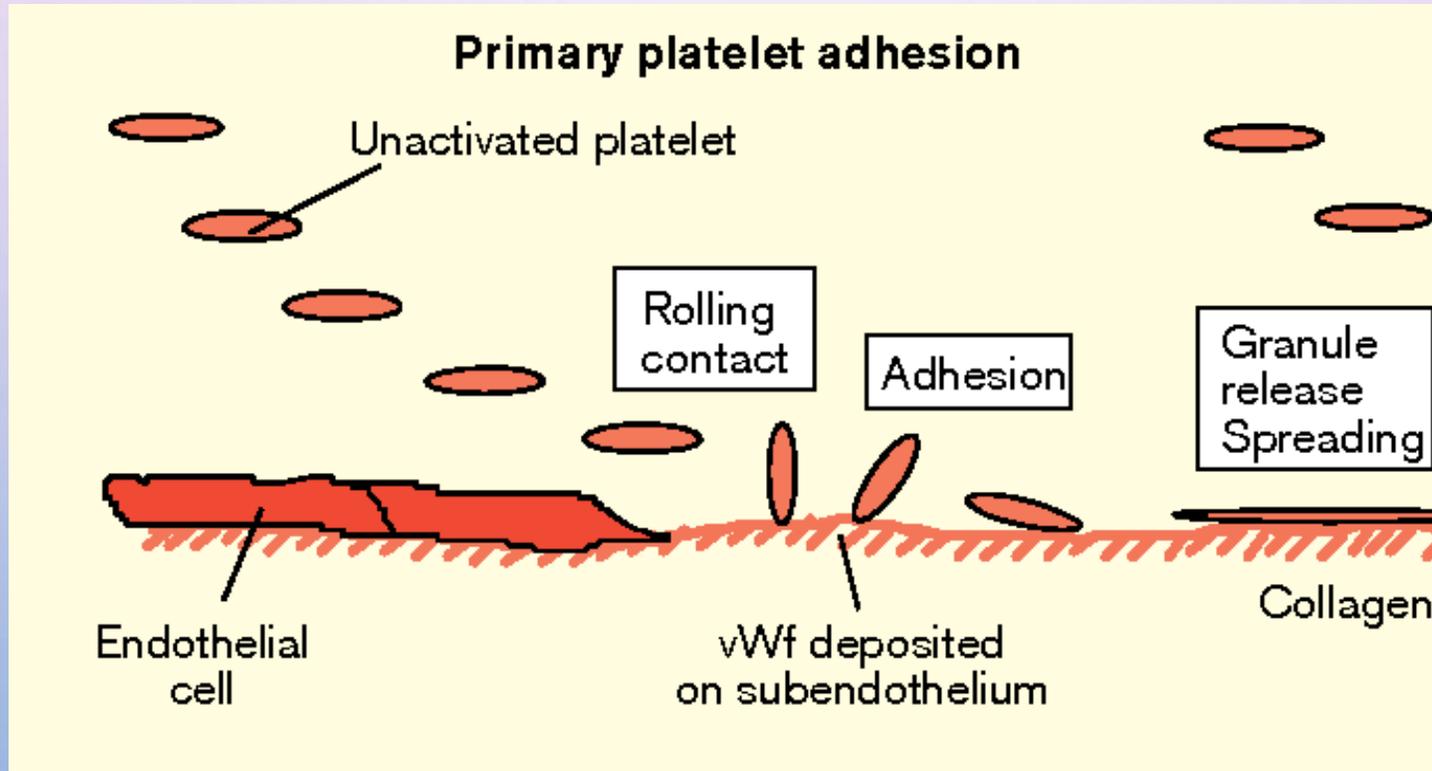
## THE GENERAL SEQUENCE OF EVENTS LEADING TO HEMOSTASIS AT A SITE OF VASCULAR INJURY INCLUDE: I. PRIMARY HEMOSTASIS

- 1. ARTERIOLAR VASOCONSTRICTION:
- occurs immediately and markedly reduces blood flow to the injured area.
- it is mediated by reflex neurogenic mechanisms.
- it is augmented by endothelin, a potent endothelium-derived vasoconstrictor.
- this effect is transient, however, bleeding would resume if not followed by activation of platelets and coagulation factors.



- 2. PLATELET ACTIVATION

- THE FORMATION OF THE PLATELET PLUG.

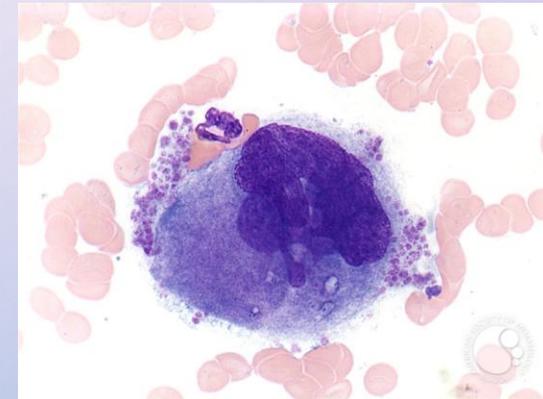


- PLATELETS

- platelets play a critical role in hemostasis by forming the primary plug that initially seals vascular defects and by providing a surface that binds and concentrates activated coagulation factors.
- platelets are disc-shaped anucleate cell fragments that are shed from megakaryocytes in the bone marrow into the bloodstream.

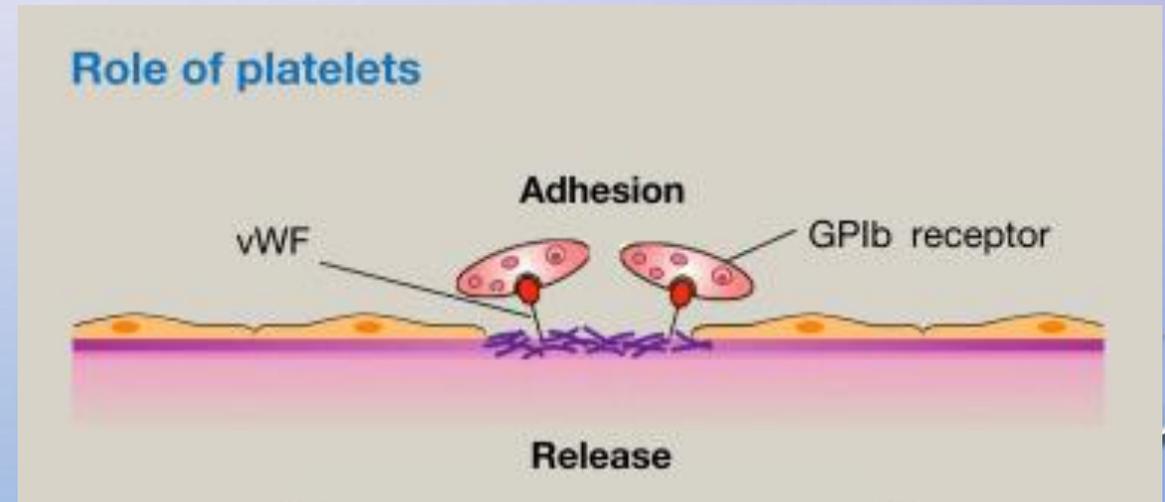
- Their function depends on several factors including:

- Glycoprotein receptors.
- A contractile cytoskeleton
- Two types of cytoplasmic granules.
- $\alpha$ -granules have the adhesion molecule p-selectin, and contain proteins involved in coagulation.
- dense (or  $\delta$ ) granules contain ADP and ATP , ionized calcium, serotonin, and epinephrine.



PLATELETS UNDERGO A SEQUENCE OF REACTIONS AFTER A TRAUMATIC VASCULAR INJURY THAT CULMINATE IN THE FORMATION OF A PLATELET PLUG

- 1. PLATELET ADHESION:
- is mediated via interactions with vwf, which acts as a bridge between the platelet surface receptor glycoprotein ib (gpib) and exposed collagen.





- **2. PLATELET ACTIVATION.**

- **A. CHANGES IN SHAPE** from smooth discs to spiky “sea urchins” with greatly increased surface area.

- alterations in glycoprotein iib/iiia that increase its affinity for fibrinogen

- the translocation of negatively charged phospholipids to the platelet surface

- **B. SECRETION OF GRANULE CONTENTS, e.g:**

- ✓ THROMBIN: ACTIVATES PLATELETS

- ✓ ADP: CREATE AN ADDITIONAL ROUNDS OF PLATELET ACTIVATION.

- ✓ THROMBOXANE A2 (TXA2): A POTENT INDUCER OF PLATELET AGGREGATION.

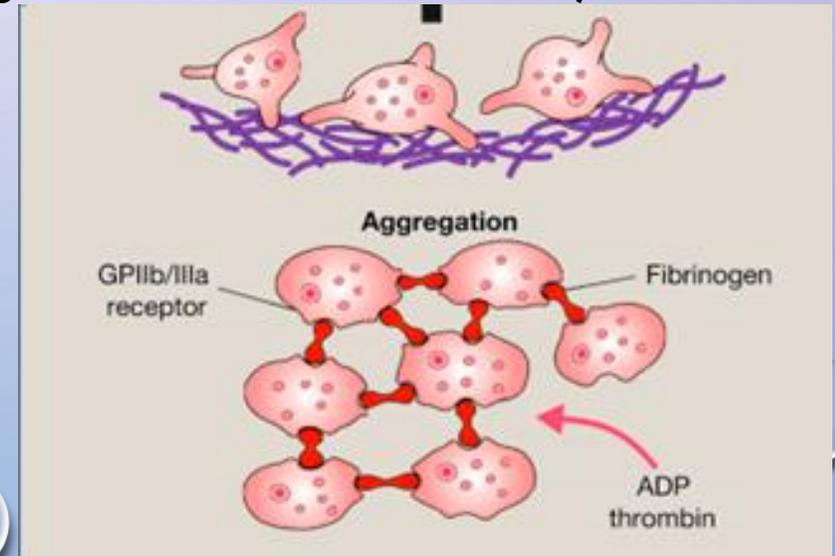
• 3. PLATELET AGGREGATION FOLLOWS THEIR ACTIVATION.

• The conformational change in glycoprotein iib/iiia allows binding of fibrinogen that forms bridges between adjacent platelets, leading to their aggregation.

✓ fibrinogen cause reversible aggregation

✓ thrombin cause irreversible aggregation (converts fibrinogen into insoluble fibrin).

✓ cytoskeleton cause contraction of the plug.

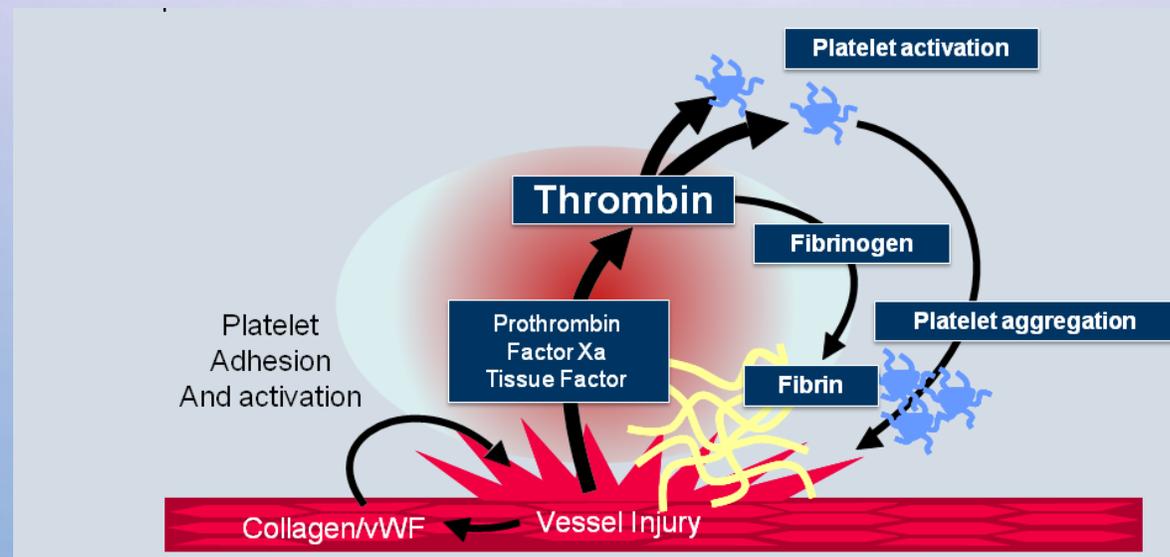


- II .SECONDARY HEMOSTASIS:

- DEPOSITION OF FIBRIN.

- VASCULAR INJURY EXPOSES TISSUE FACTOR AT THE SITE OF INJURY.

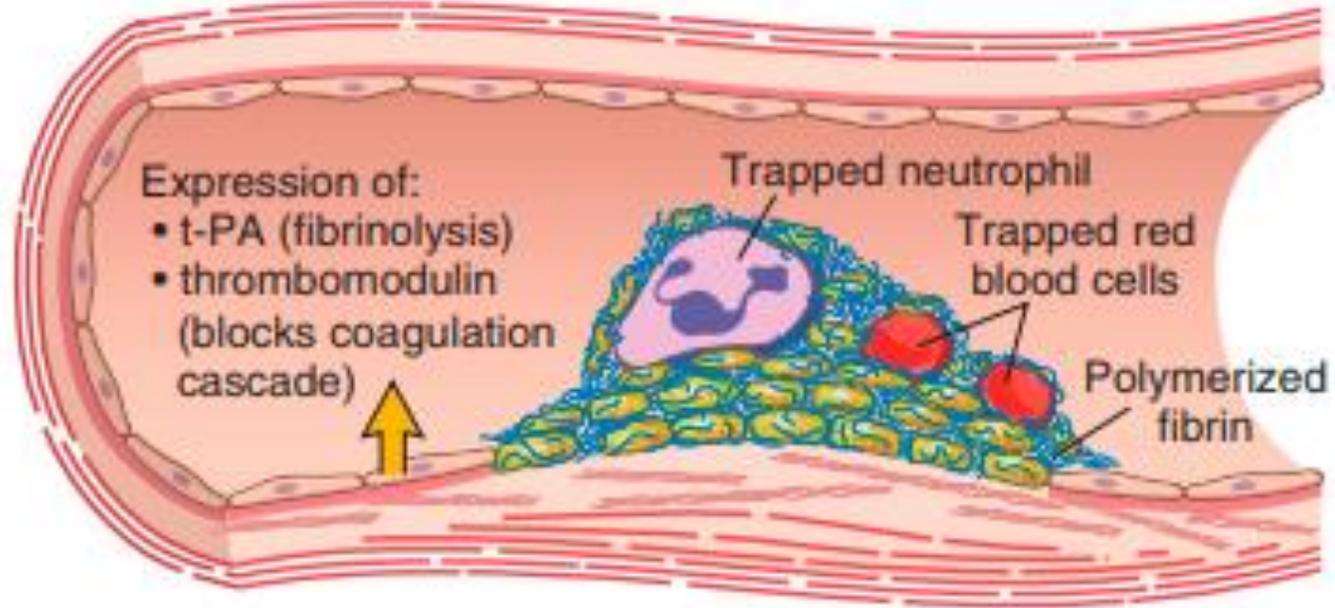
- TISSUE FACTOR BINDS AND ACTIVATES FACTOR VII , SETTING IN MOTION A CASCADE OF REACTIONS THAT CULMINATES IN THROMBIN GENERATION.



- III. CLOT STABILIZATION AND RESORPTION:

- POLYMERIZED FIBRIN AND PLATELET AGGREGATES UNDERGO CONTRACTION TO FORM A SOLID, PERMANENT PLUG THAT PREVENTS FURTHER HEMORRHAGE.
  
- ENTRAPPED RED CELLS AND LEUKOCYTES ARE ALSO FOUND IN HEMOSTATIC PLUGS, IN PART DUE TO ADHERENCE OF LEUKOCYTES TO P-SELECTIN EXPRESSED ON ACTIVATED PLATELET
  
- AT THIS STAGE, COUNTERREGULATORY MECHANISMS (E.G., TISSUE PLASMINOGEN ACTIVATOR, T-PA MADE BY ENDOTHELIAL CELLS) ARE SET INTO MOTION THAT LIMIT CLOTTING TO THE SITE OF INJURY , AND EVENTUALLY LEAD TO CLOT RESORPTION AND TISSUE REPAIR.

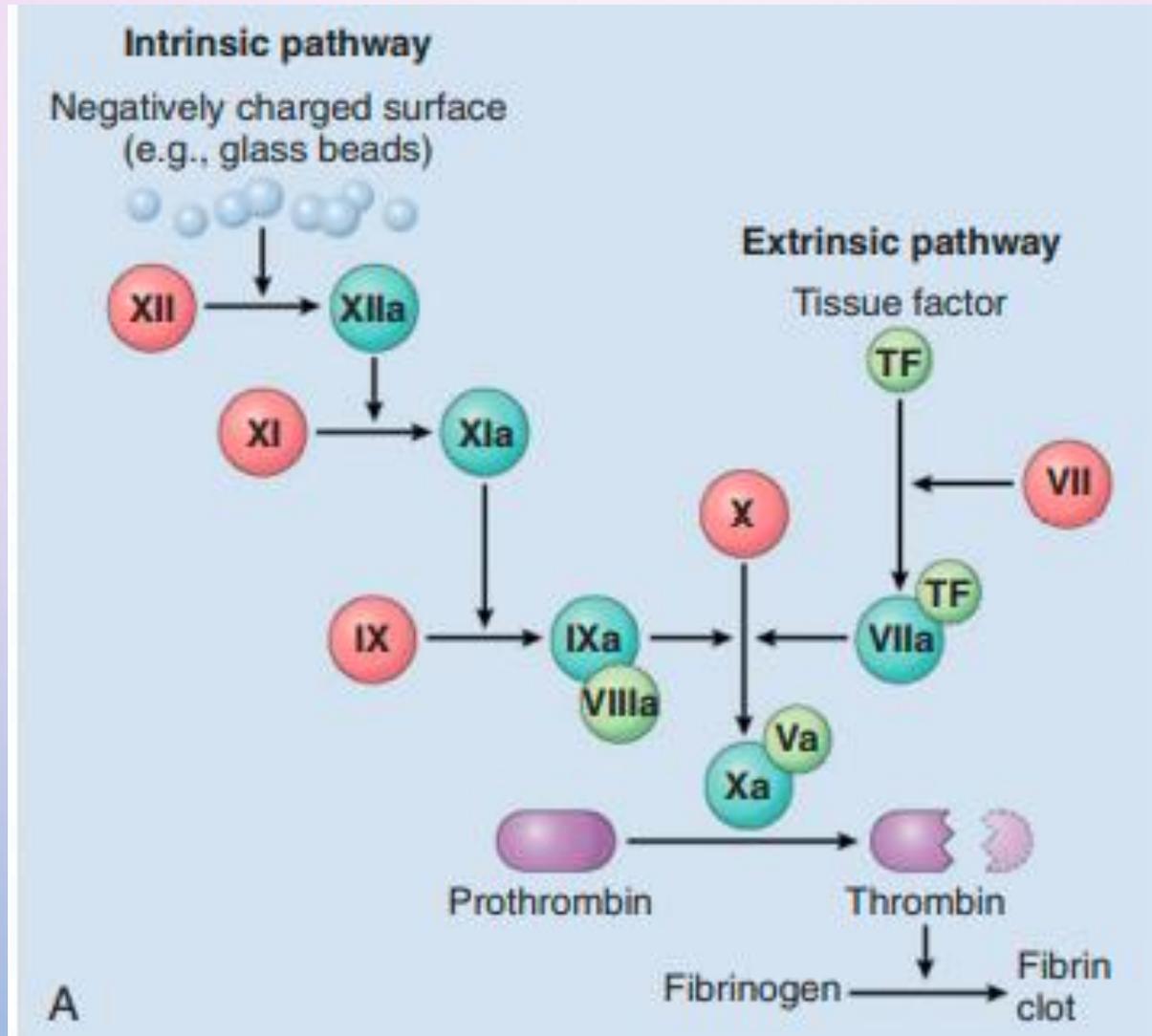
## D. CLOT RESORPTION



# COAGULATION CASCADE

- the coagulation cascade is a series of amplifying enzymatic reactions that lead to the deposition of an insoluble fibrin clot.
- each reaction step involves an enzyme (an activated coagulation factor), a substrate (an inactive proenzyme form of a coagulation factor), and a cofactor (a reaction accelerator).
- these components are assembled on a negatively charged phospholipid surface, which is provided by activated platelets. assembly of reaction complexes also depends on calcium

PTT



PT



vitamin K antagonists

Mnemonic for  
Vitamin K Dependent Clotting Factors

"Two plus seven is nine NOT ten!"

2 7 9 10



Coagulation cascade has traditionally been divided into the extrinsic and intrinsic pathways



- 1.THE PROTHROMBIN TIME (PT)
- ASSAY ASSESSES THE FUNCTION OF THE PROTEINS IN THE EXTRINSIC PATHWAY (FACTORS VII, X, V, II (PROTHROMBIN), AND FIBRINOGEN).
- THE PARTIAL THROMBOPLASTIN TIME (PTT)
- ASSAY SCREENS THE FUNCTION OF THE PROTEINS IN THE INTRINSIC PATHWAY (FACTORS XII, XI, IX, VIII, X, V, II, AND FIBRINOGEN).

## AMONG THROMBIN'S MOST IMPORTANT ACTIVITIES ARE THE FOLLOWING:

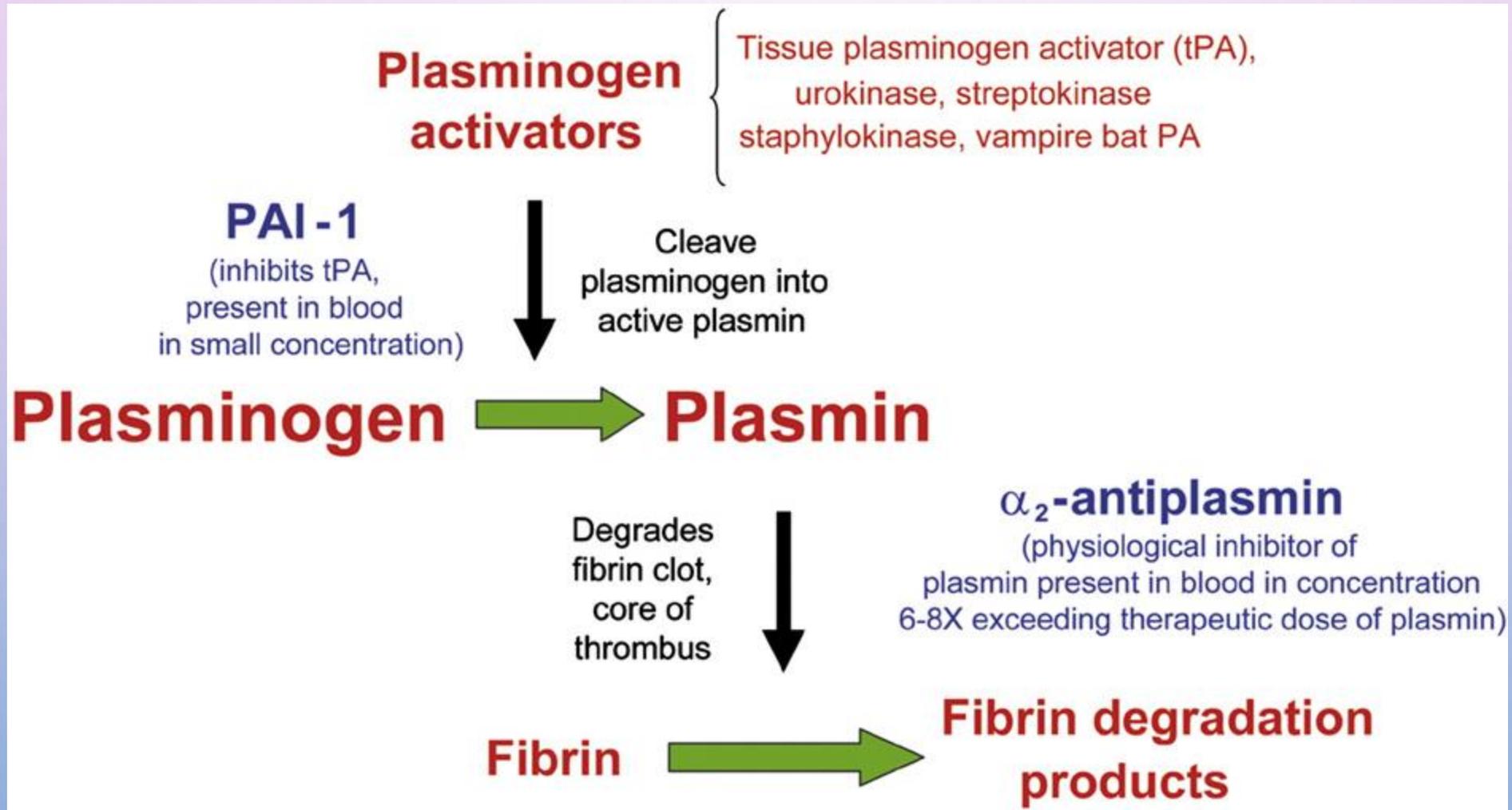
- 1. CONVERSION OF FIBRINOGEN INTO CROSSLINKED FIBRIN.
- THROMBIN DIRECTLY CONVERTS SOLUBLE FIBRINOGEN INTO FIBRIN MONOMERS THAT POLYMERIZE INTO AN INSOLUBLE FIBRIL.
- 2. PLATELET ACTIVATION.
- 4. ANTI-COAGULANT EFFECTS.
- ENCOUNTERING NORMAL ENDOTHELIUM, THROMBIN CHANGES FROM A PROCOAGULANT TO AN ANTICOAGULANT.



# FACTORS THAT LIMIT COAGULATION.

- COAGULATION MUST BE RESTRICTED TO THE SITE OF VASCULAR INJURY TO PREVENT DANGEROUS CONSEQUENCES THROUGH:
  - 1.SIMPLE DILUTION:
  - BLOOD FLOWING AT THE SITE OF INJURY WASHES OUT ACTIVATED COAGULATION FACTORS, WHICH ARE RAPIDLY REMOVED BY THE LIVER.
  - 2.REQUIREMENT FOR NEGATIVELY CHARGED PHOSPHOLIPIDS
  - 3. FIBRINOLYTIC CASCADE:
  - THROUGH THE ENZYMATIC ACTIVITY OF PLASMIN, WHICH BREAKS DOWN FIBRIN AND INTERFERES WITH ITS POLYMERIZATION.

# fibrinolytic cascade



- AN ELEVATED LEVEL OF BREAKDOWN PRODUCTS OF FIBRINOGEN (D-DIMERS) ARE A USEFUL CLINICAL MARKERS OF SEVERAL THROMBOTIC STATES

## D-Dimer test



# ENDOTHELIUM

- THE BALANCE BETWEEN THE ANTICOAGULANT AND PROCOAGULANT ACTIVITIES OF ENDOTHELIUM OFTEN DETERMINES WHETHER CLOT FORMATION, PROPAGATION, OR DISSOLUTION OCCURS.

- 1. PLATELET INHIBITORY EFFECTS:

- ✓ SERVE AS A BARRIER THAT SHIELDS PLATELETS FROM SUBENDOTHELIAL VWF AND COLLAGEN.
- ✓ RELEASES A NUMBER OF FACTORS THAT INHIBIT PLATELET ACTIVATION AND AGGREGATION. AMONG THE MOST IMPORTANT ARE PROSTACYCLIN (PGI<sub>2</sub>), NITRIC OXIDE (NO).
- ✓ ENDOTHELIAL CELLS BIND AND ALTER THE ACTIVITY OF THROMBIN, WHICH IS ONE OF THE MOST POTENT ACTIVATORS OF PLATELETS.

- 2. ANTICOAGULANT EFFECTS.

- NORMAL ENDOTHELIUM SHIELDS COAGULATION FACTORS FROM TISSUE FACTOR IN VESSEL WALLS AND EXPRESSES MULTIPLE FACTORS THAT ACTIVELY OPPOSE COAGULATION:
- MOST NOTABLY THROMBOMODULIN, ENDOTHELIAL PROTEIN C RECEPTOR, HEPARIN-LIKE MOLECULES, AND TISSUE FACTOR PATHWAY INHIBITOR.

