Hemostasis and Bleeding Disorders (Part 1)

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Learning Objectives:

By the end of this session, you will be able to:

1. Describe Normal Hemostasis Mechanisms.
2. Describe the three mechanisms involved in hemostasis: Primary, Secondary, and Tertiary hemostasis.
3. Explain how the extrinsic and intrinsic coagulation pathways lead to the common pathway, and the coagulation factors involved in each.
4. Discuss disorders affecting hemostasis.
5. Outline the Clinical Assessment of Hemostasis.
6. Outline the Investigations for bleeding disorders.

HEMOSTASIS

Normal hemostasis

The normal response of body using interactions between different elements to:

1.Stop bleeding (loss of blood).

2.Keeping the blood within a damaged blood vessel.

Significance of Hemostasis:

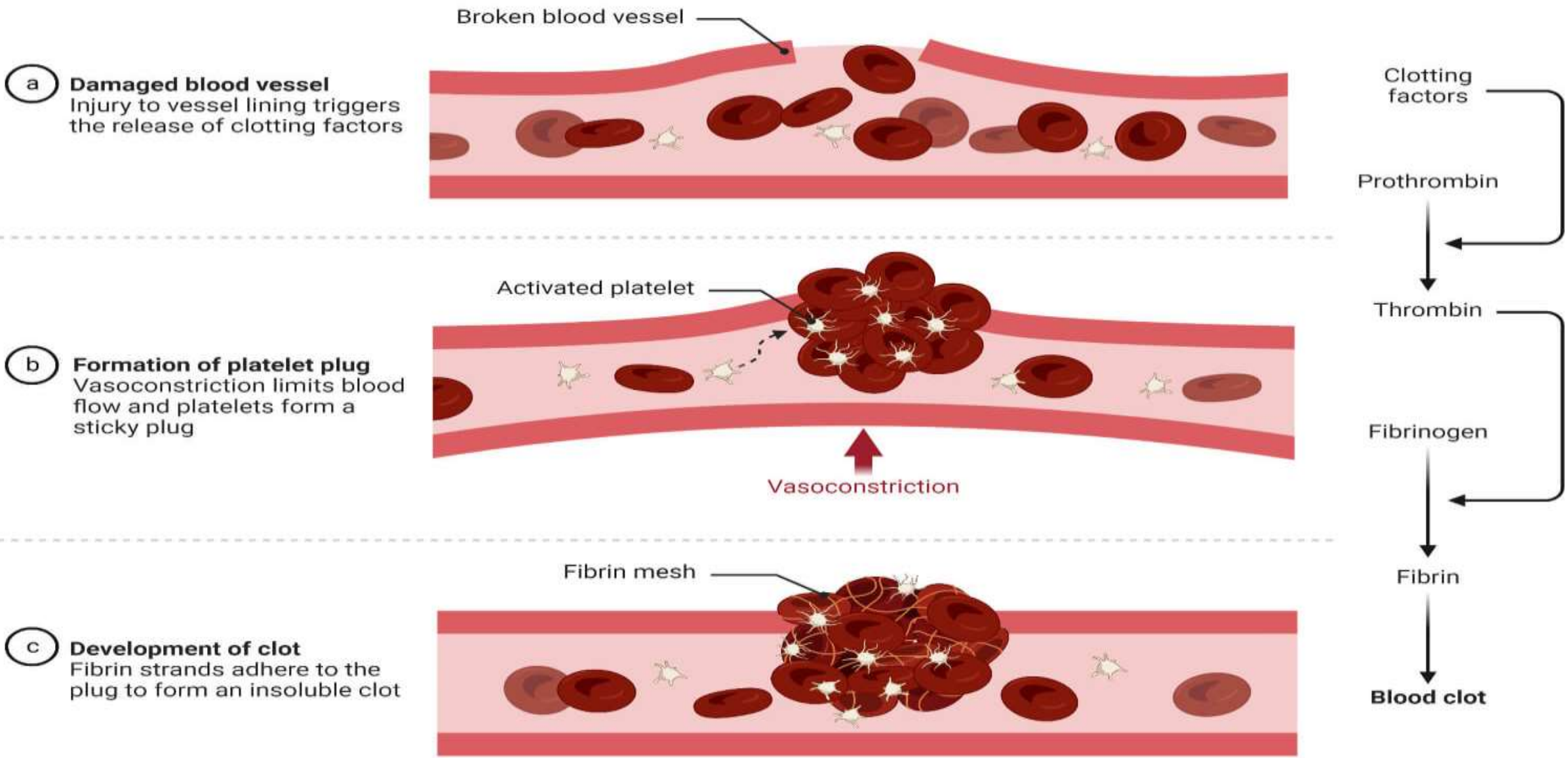
1) **Prevents excessive and uncontrolled blood loss and Anemia.**
2) **Helps to maintain homeostasis=** stable internal, external, chemical, and social conditions that are preserved by living systems which collectively help to keep life in balance.
3) **Prevents deposition of blood in the internal organs during burst of internal blood vessels** (by quickly checking the bleeding process).
4) **Triggers healing process of the ruptured blood vessel.**

Mechanism of Normal Hemostasis:

Including 4 Elements of interactions of rapidly sequenced steps:

1. Vascular spasm
2. Platelet plug formation
3. Blood coagulation or clotting system
4. Fibrinolysis system

Blood Clot Formation in Broken Vessel



1. Vascular Spasm :

blood vessels constrict = less blood to be lost.

- ***Response Triggered by:***

1) Direct injury to vascular smooth muscle
2) Chemicals released by endothelial cells and platelets.

- ***More effective spasm response in case of:***

1) Small blood vessels injury
2) Large amount of damage.

2. Platelet Plug Formation:

- **Platelets stick together + to the damaged endothelium = form a temporary seal = to cover the break in the vessel wall = forming a platelet plug in *15 seconds* (= Primary Hemostasis) and then degranulate = release chemicals= more platelets stick = release their chemicals**

>>>>>>>>>>>>Positive Feed Back Loop<<<<<<<<<<

3. Blood Coagulation or Blood Clotting:

= Called as [Secondary Hemostasis].

Sequential process by multiple interacting factors in the coagulation cascade = >>>>>Insoluble Fibrin Clot

- = reinforce the platelet plug = trapping blood cells and platelets to stay in the wound.

Although Without this process, wound healing not be possible >>>>>> cause severe health problems *if thrombus detached* from vessel wall >>>>> travels in the circulation >>>>>reaches the brain, heart, lungs >>>>>>>stroke, heart attack, pulmonary embolism

- **Main inhibitor of secondary hemostasis is anti-thrombin = inhibits thrombin + many activated coagulation proteins.**

. ***Defects in coagulation cascade = More Serious Bleeding than those due to defects of primary hemostasis.***

> **bleeding into cavities (chest, joints and skulls) + subcutaneous hematomas.**

Immediate Bleeding Type = occurs when there are ***problems in the primary*** **hemostasis elements.**

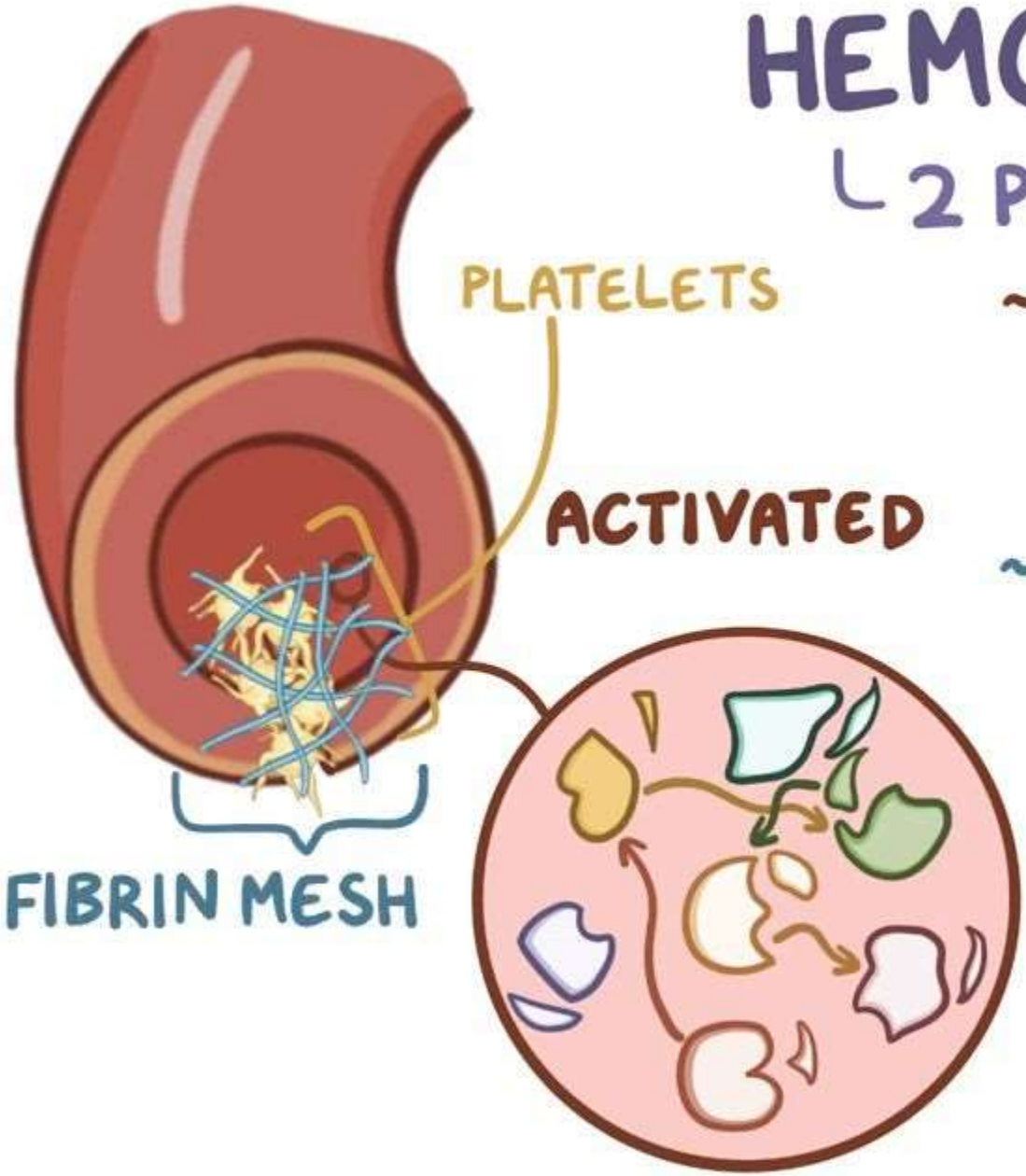
. ***Delayed Bleeding Type=*** occurs when there are ***problems in the secondary*** **hemostasis elements.**

4. Fibrinolytic System (Fibrinolysis):

- Initiated at same time of clotting process = to stop clotting progression= Called Tertiary Hemostasis.
- The blood clots are reorganized and resorbed = maintaining the patency of blood vessels.
- Main Responsible Enzyme = Plasmin.

HEMOSTASIS ~ STOPPING BLEEDING

└ 2 PHASES:



~ PRIMARY HEMOSTASIS

* FORMATION of PLATELET PLUG

(COAGULATION)

~ SECONDARY HEMOSTASIS

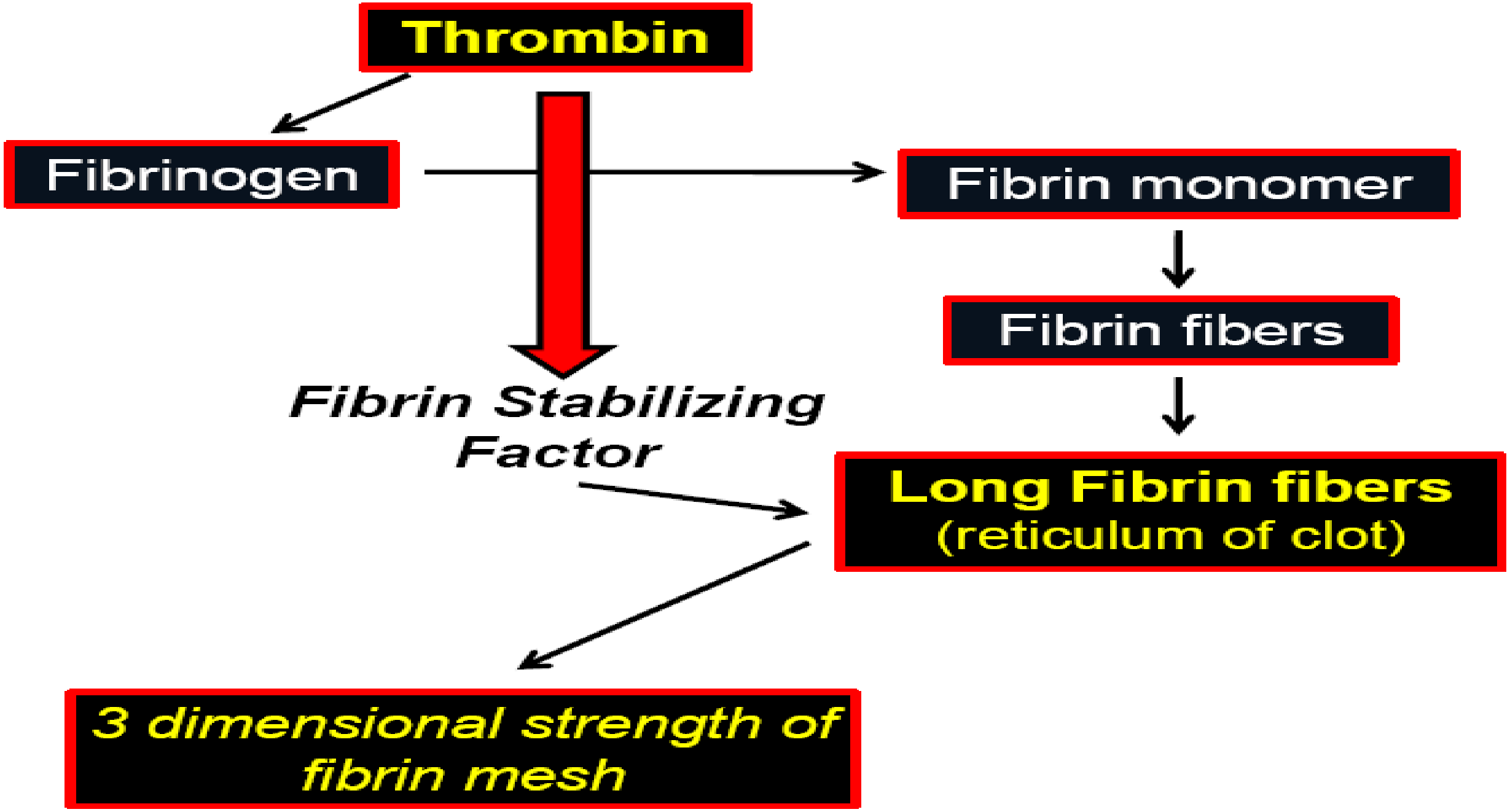
* CLOTTING FACTORS

↓

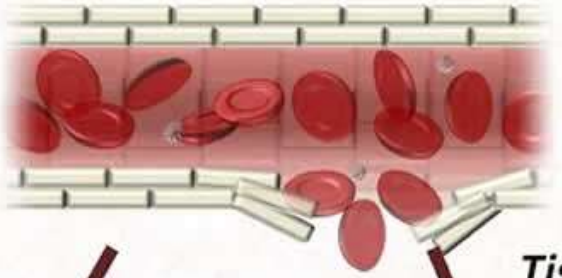
PROTEOLYTICALLY ACTIVATED

↓

ACTIVATION of FIBRIN (FACTOR Ia)


Thrombin
Fibrinogen
Fibrin monomer
Fibrin fibers
Fibrin Stabilizing Factor
Long Fibrin fibers
(reticulum of clot)
3 dimensional strength of fibrin mesh

Major Components of Hemostasis



Vascular Injury

Collagen

Tissue factor

Vasoconstriction

Platelet Activation

Coagulation Cascade

Antithrombotic Control Mechanisms

vWF, fibrinogen

Thrombin

Platelet Plug

Fibrinogen → *Fibrin*

Blood Clot

Plasmin

Fibrinolysis & Clot Degradation

Primary Hemostasis

Secondary Hemostasis

Tertiary Hemostasis

- ***Coagulation Cascade is traditionally separated into 3 pathways: intrinsic, extrinsic and common.***

- **Most clotting Factors manufactured in liver.**

- **Clotting factors in circulation =inactive form>>>> require activation.**

- **Once platelet plug formed= clotting factors are activated >>>>> create fibrin clot= acts as a mesh around platelet plug>>>> holding the plug in place.**

- **Red and white blood cells= caught up in the fibrin mesh >>>>>> causes the clot become more stronger.**

1. Extrinsic Pathway:

Main Pathway to Initiate Coagulation

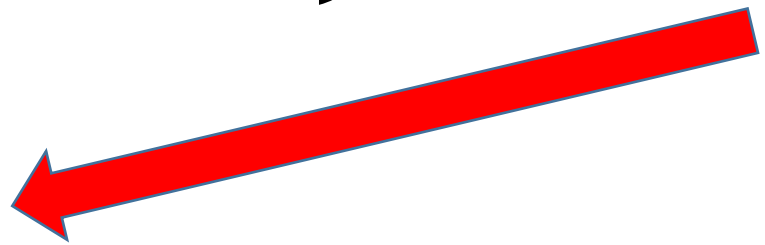
Initiated by exposure to Tissue Factor (factor III) released from Endothelial Cells and Monocytes

→ Activation of factor VII
→VIIa
→ Common Pathway.

2. Intrinsic Pathway:

- Amplifies Coagulation
- Involves Activation of factors XII, XI, IX, and VIII= factors(12, 11, 9, 8)

common pathway.



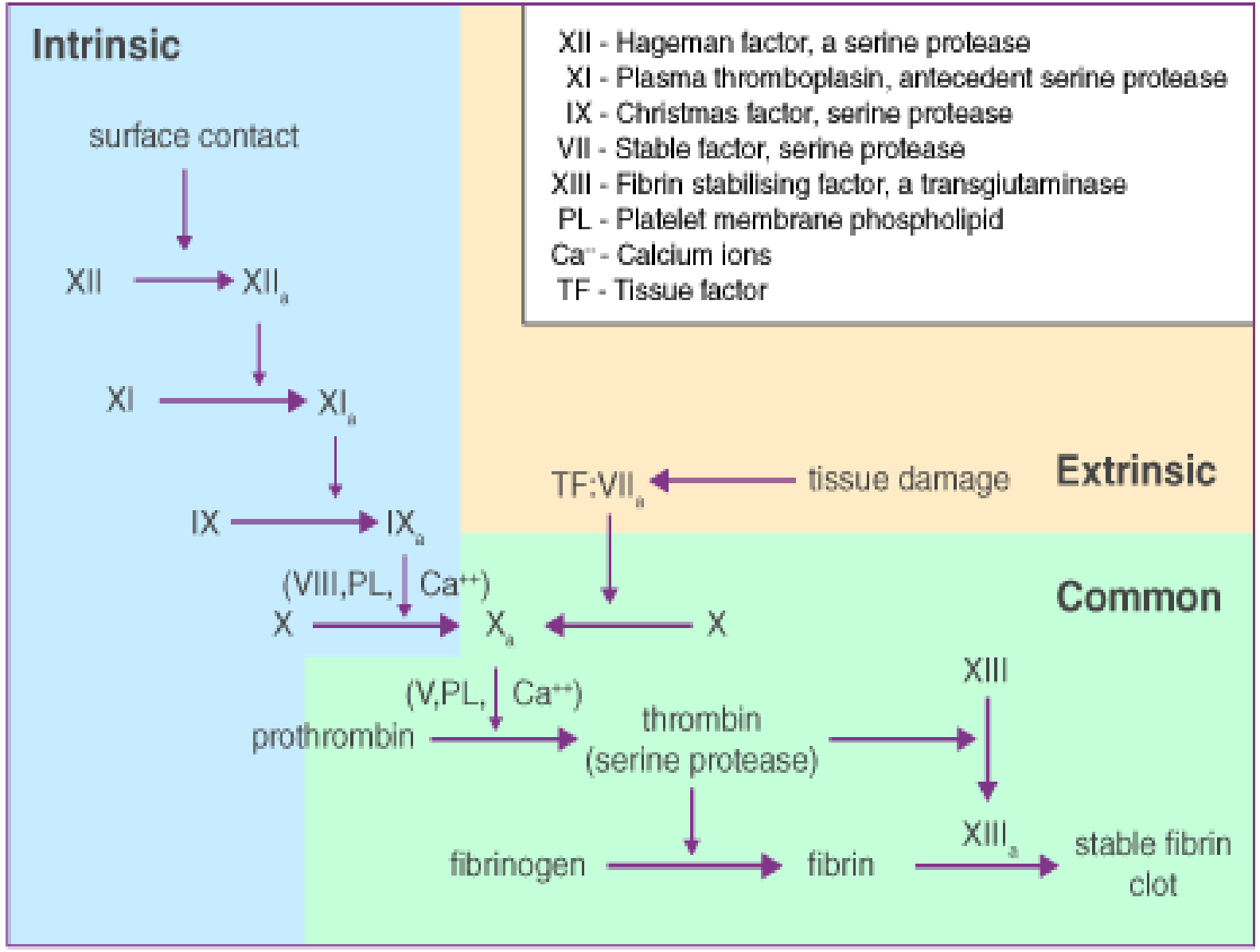
3. Common Pathway:

Activation of factors X= factor (10) → Xa= factor(10a) → prothrombin (factor II)= factor (2)

1….Thrombin>>>>> which forms clot by cleaving fibrinogen (factor I) = *soluble* fibrin.

2…. Thrombin>>>>> also activates factor XIII= factor(13), which, together with calcium → stabilize the soluble fibrin, forming cross-linked *(insoluble)* fibrin.

BLOOD COAGULATION PATHWAY



Factor	Name	Pathway
I	Fibrinogen	Both
II	Prothrombin	Both
III	Tissue Factor	Extrinsic
IV	Calcium	Both
V	Proaccelerin	Both
VI	Accelerin	Both
VII	Proconvertin	Extrinsic
VIII	Antihemophiliac	Intrinsic
IX	Christmas Factor	Intrinsic
X	Stuart-Prower Factor	Both
XI	Plasmathromboplastin antecedent (PTA)	Intrinsic
XII	Hageman Factor	Intrinsic
XIII	Protransglutaminase	Both

- ***Natural hemostasis is most desired…….***

Other Means for Achieving Hemostasis = Vital for Survival in Many Emergencies.

- **Hemostasis during Surgical procedures achieved by various other ways by:**

1) **Direct pressure**
2) **Ligation**
3) **Hemostatic agent (chemical and/or mechanical).**

Clinical Assessment of Patient with bleeding disorder:

A. History:

1) Fami

1)Duration of bleeding

1)Coexisting illness

2)Drug therapy.

===Indicate whether the disorder is congenital or acquired.

===Predispose to bleeding = Should be inquired

During Clinical Examination:

Check For:

I. **Bruising**

II. **Purpura.**

III. **Telangiectasia on lips (indicates hereditary hemorrhagic telangiectasia).**

IV. **Swollen joints**

V. **Hemarthrosis.**

VI. **Hepatomegaly.**

VII. **Splenomegaly.**

- **Muscle and joint bleeds indicate= a coagulation defect.**
- **Purpura, prolonged bleeding from cuts, epistaxis, GI hemorrhage, excessive post-surgical bleeding and menorrhagia suggest=**

1) **Platelet Disorder**
2) **Thrombocytopenia**
3) **Von Willebrand Disease.**

Blood Coagulation Tests

Investigations for Bleeding Disorders:

Initial screening tests:

1) **Platelet count**
2) **Bleeding time (BT)**
3) **Prothrombin time (PT)**
4) **Partial thromboplastin time (PTT)**
5) **Thrombin time (TT)**

1..Platelet Count:

quantitative evaluation of platelet

- **Normal platelet count =**

150000 - 400000 cells/mm^3.

- **A thrombocytopenia= platelet count of < 150000 cells/mm^3**

= major postoperative bleeding.

2..Bleeding Time(BT):

Evaluation adequacy of platelet function

- **Time for standardized skin incision to stop bleeding =formation of a temporary hemostatic plug.**
- **Normal BT= 1 and 6 minutes**

(depends on the way the test is performed).

Prolonged bleeding time:

1)Platelet abnormalities

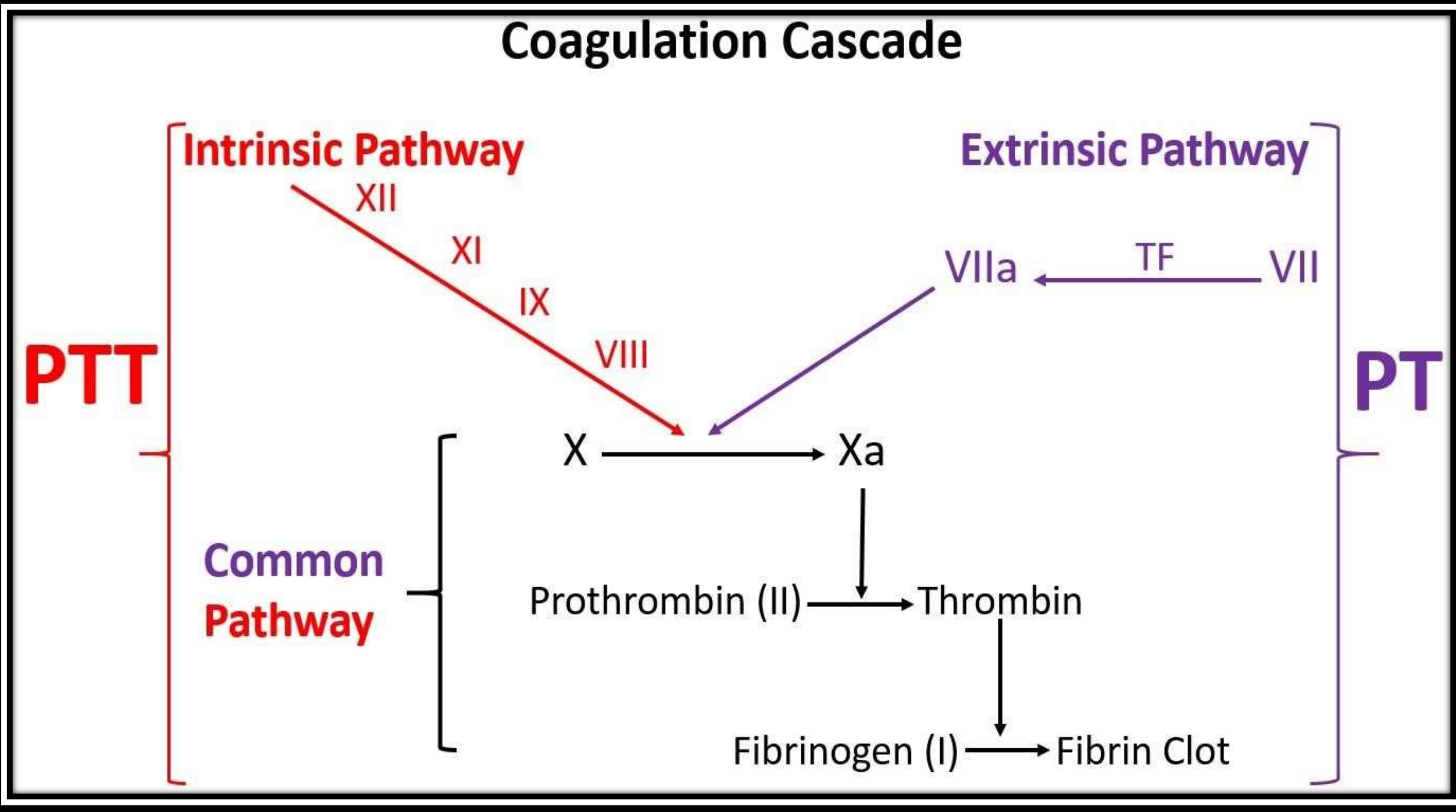
2)Medications affect platelet function.

Types of Coagulation Tests

Prothrombin Time (PT)
Evaulates ability to clot

International Normalized Ratio (INR)
Ensures that results from a PT test are the same from one lab to another

Partial Thromboplastin Time (PTT)
Determines if blood-thinning therapy is effective


Coagulation Cascade
Intrinsic Pathway
Extrinsic Pathway
XII
XI
IX
VIII
VIIa
TF
VII
PTT
PT
X
Xa
Common Pathway
Prothrombin (II)
Thrombin
Fibrinogen (I)
Fibrin Clot

3..Prothrombin Time (PT):

- **Normal PT = 10 and 15 seconds.**
- **Assess:**

1) **Extrinsic pathway = (Factor VII)**
2) **Common pathway=**

1. **Factor V**
2. **Factor X**
3. **Prothrombin (II)**
4. **Fibrinogen.**

- **PT = Monitor oral anticoagulant therapy (such as warfarin).**
- **Prolonged PT:**

1) **Deficiencies of these factors**
2) **Liver disease.**

- **International Normalized Ratio (INR):**
- **=PT ratio= Patient's PT / Control PT.**
- **Normal INR = Approximately 1.**
- **INR above 1 = Clotting Takes Longer Time >normal.**

3.. Partial Thromboplastin Time (PTT):

- Normal PTT = 25-35 seconds
- Assess:

1. Intrinsic pathway + Common pathway.
2. Tests for all factors except for factor VII.

PTT =

1) Monitor heparin therapy.
2) Best single screening test for coagulation disorders.

4..Thrombin Time (TT):

- This test **bypasses** → intrinsic, extrinsic, and most of the common pathway.
- For example= patients with hemophilia A= have Normal TT.
- **Normal TT = 9 - 13 seconds.**
- **Abnormal TT = Caused by =**

1)Excessive plasmin

2)Fibrin Split Products.

- Thrombin converts: Fibrinogen → insoluble fibrin= essential portion of a blood clot.

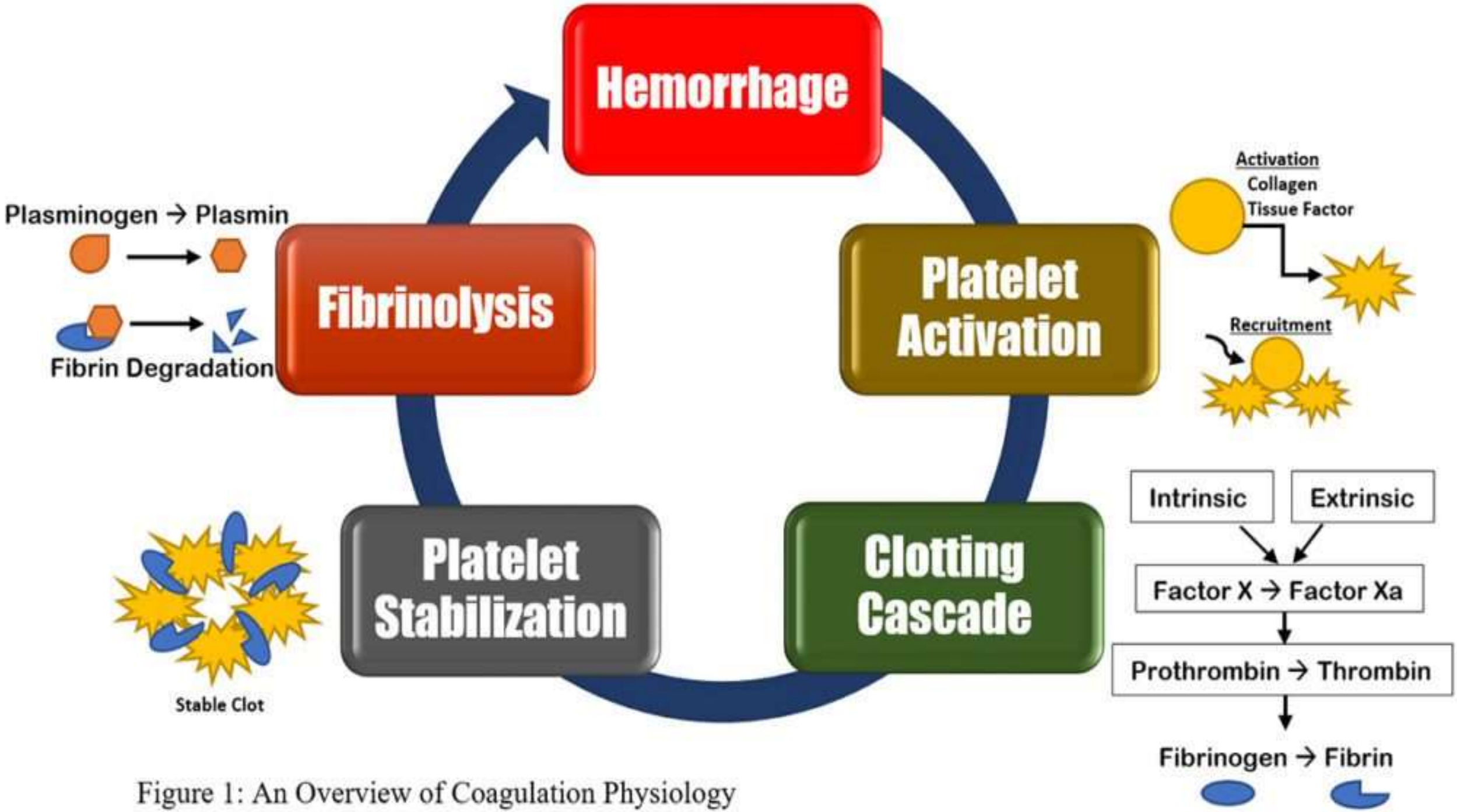


Figure 1: An Overview of Coagulation Physiology

Any questions?

Thank You For Your Attention