HEMOSTASIS PART -1-

Dr. ZAHRAA ALQAISI

HEMOSTASIS

Is the **physiological arrest** of hemorrhage at sites of vascular leakage.

There are mainly 5 **COMPONENTS** which interact together to ensure hemostasis, namely :

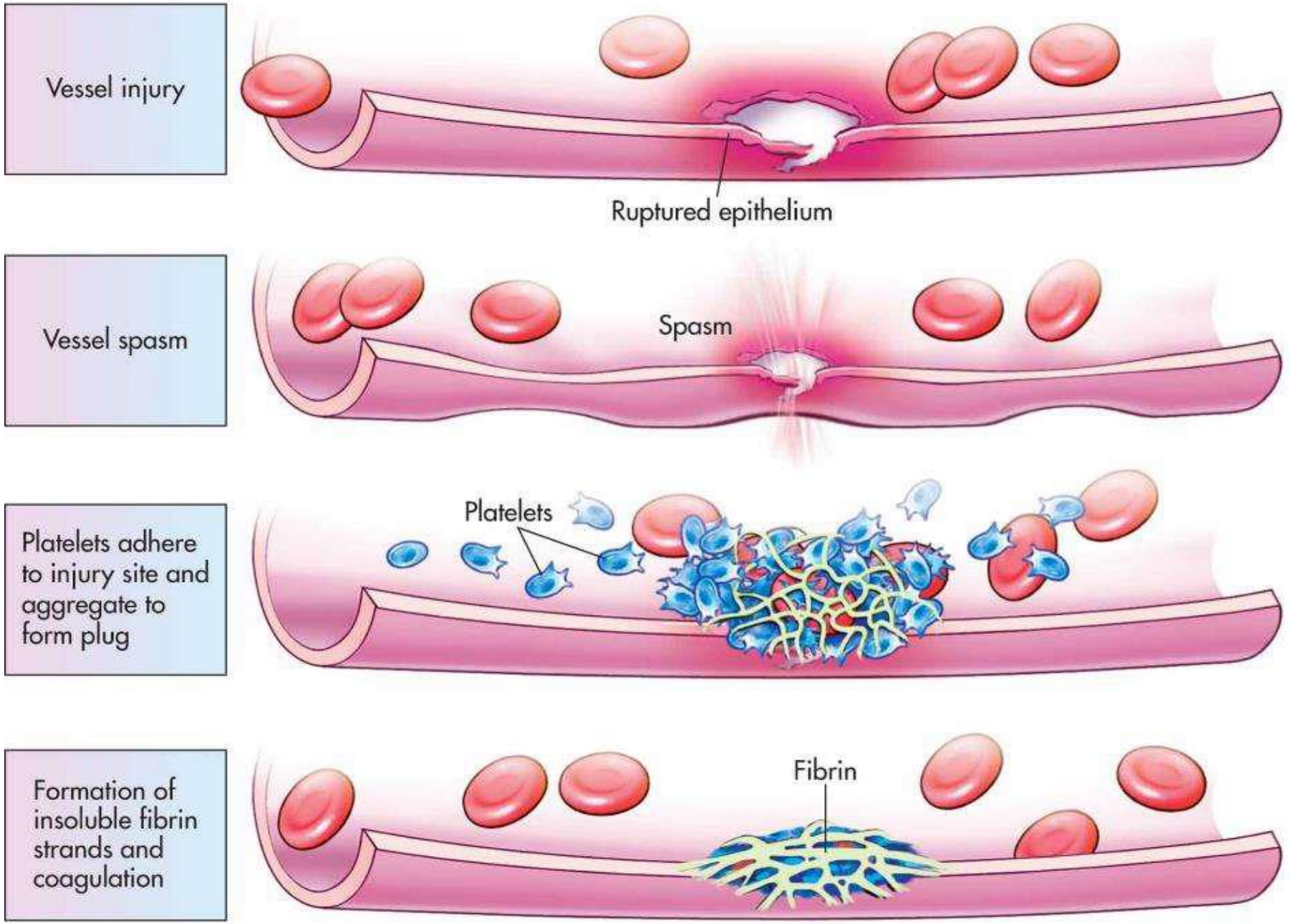
1) Blood vessels

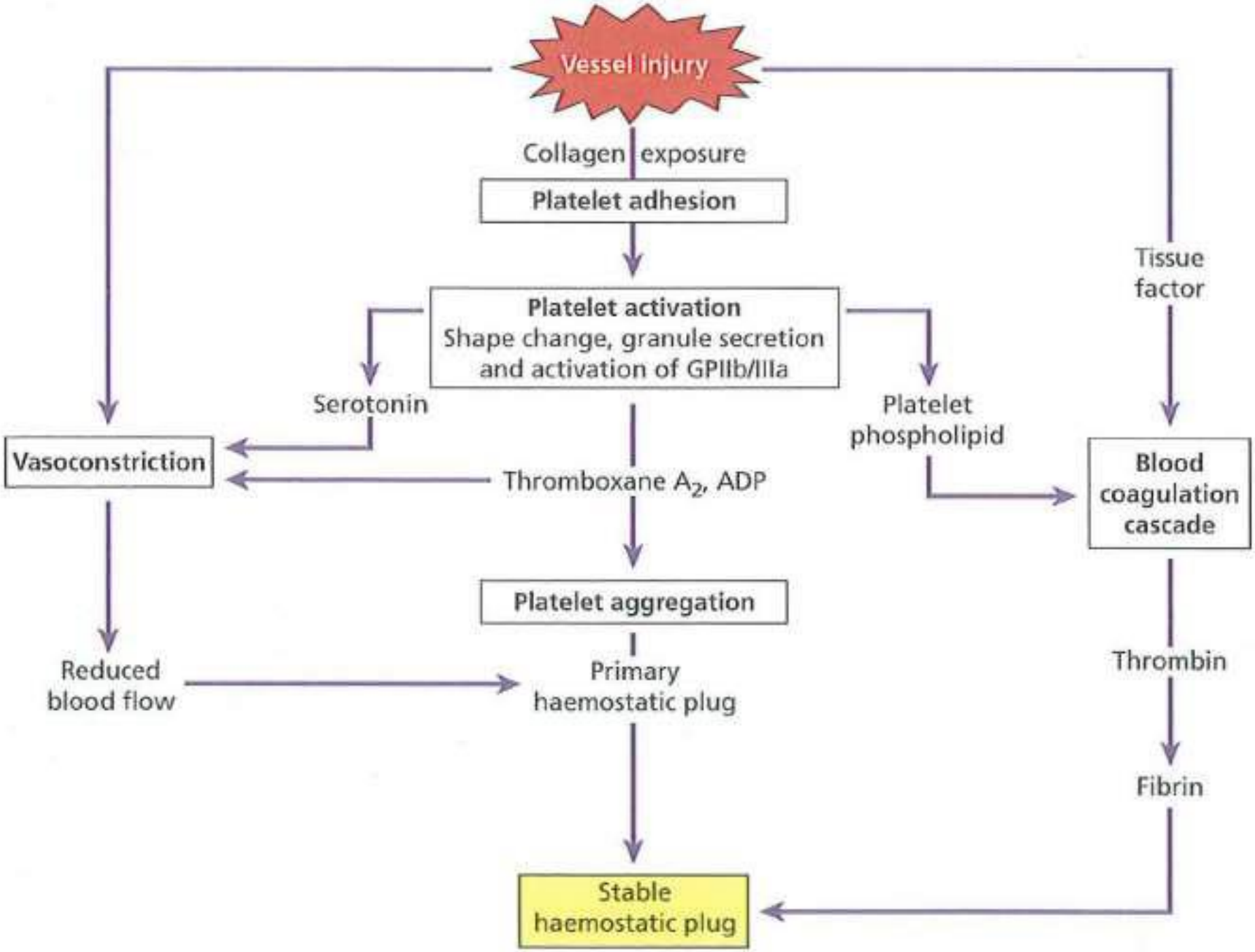
2) Platelets

3) Coagulation factors

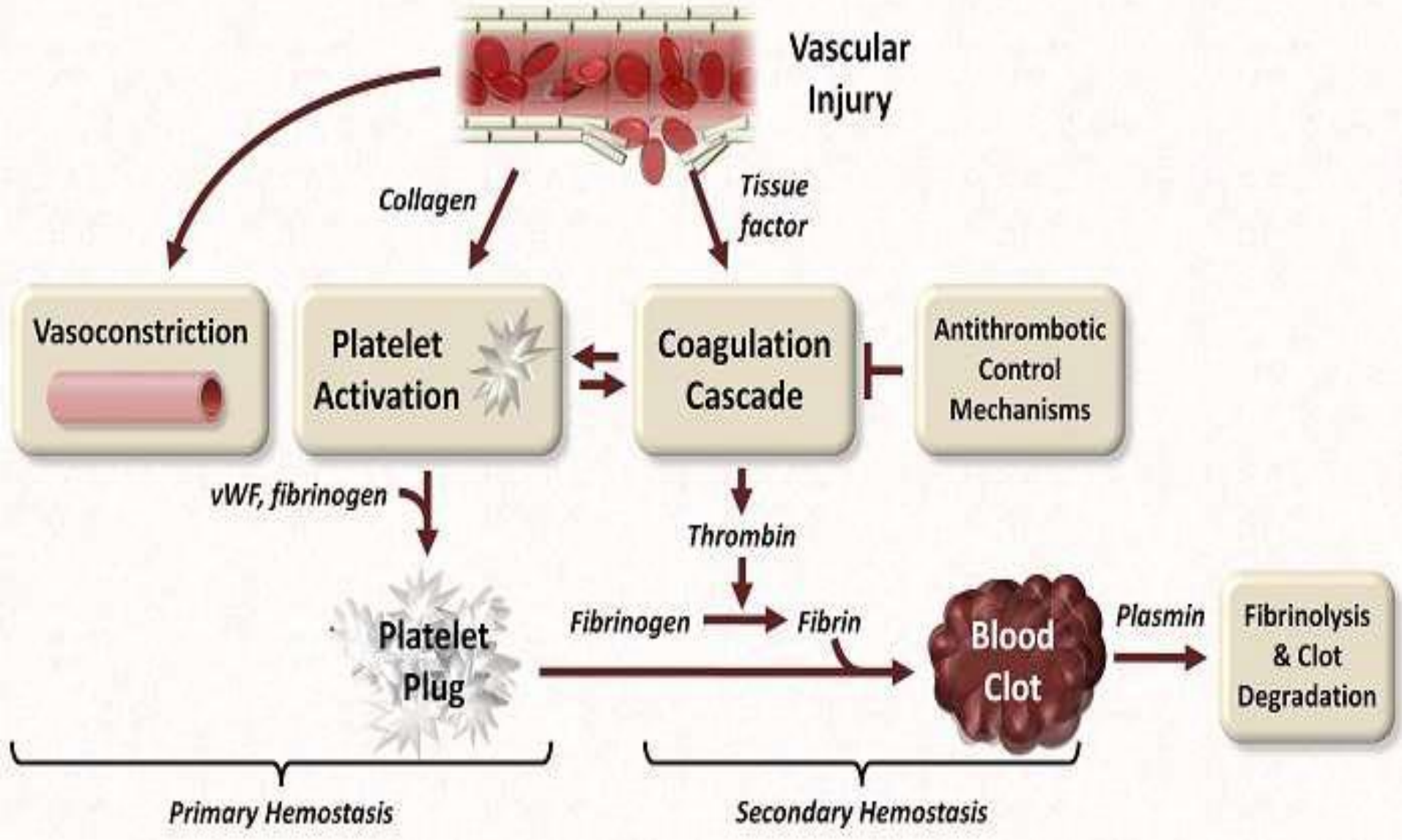
4) Coagulation inhibitors

5) Fibrinolytic system: Later it involves dissolution of the clot after repairing the vessel.

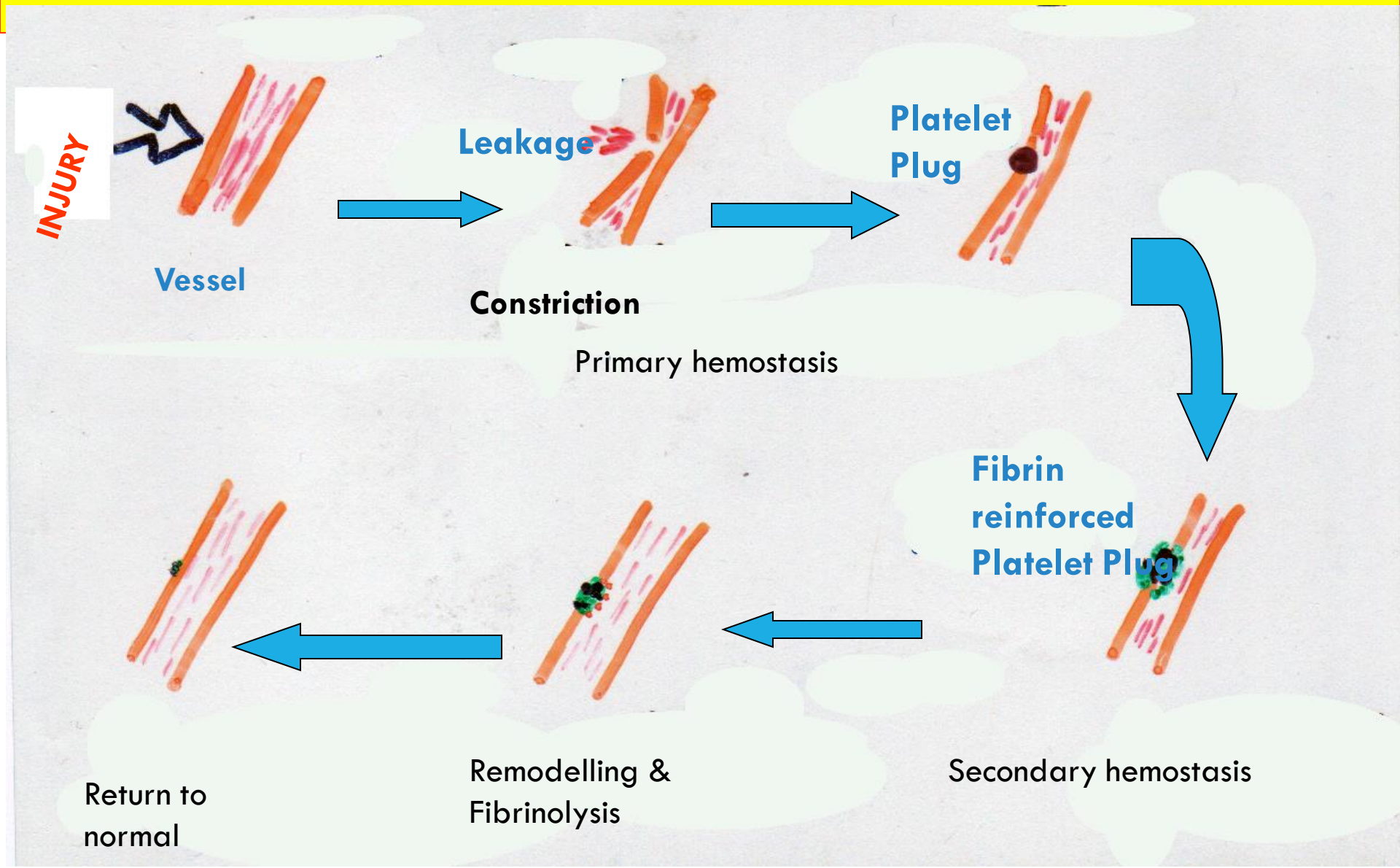

Vessel injury
Ruptured epithelium
Vessel spasm
Spasm
Platelets adhere to injury site and aggregate to form plug
Platelets
Formation of insoluble fibrin strands and coagulation
Fibrin


Vessel injury
Collagen exposure
Platelet adhesion
Platelet activation
Shape change, granule secretion
and activation of GPIIb/IIIa
Tissue factor
Serotonin
Platelet phospholipid
Vasoconstriction
Thromboxane A_2, ADP
Blood coagulation cascade
Platelet aggregation
Reduced blood flow
Primary haemostatic plug
Thrombin
Fibrin
Stable haemostatic plug

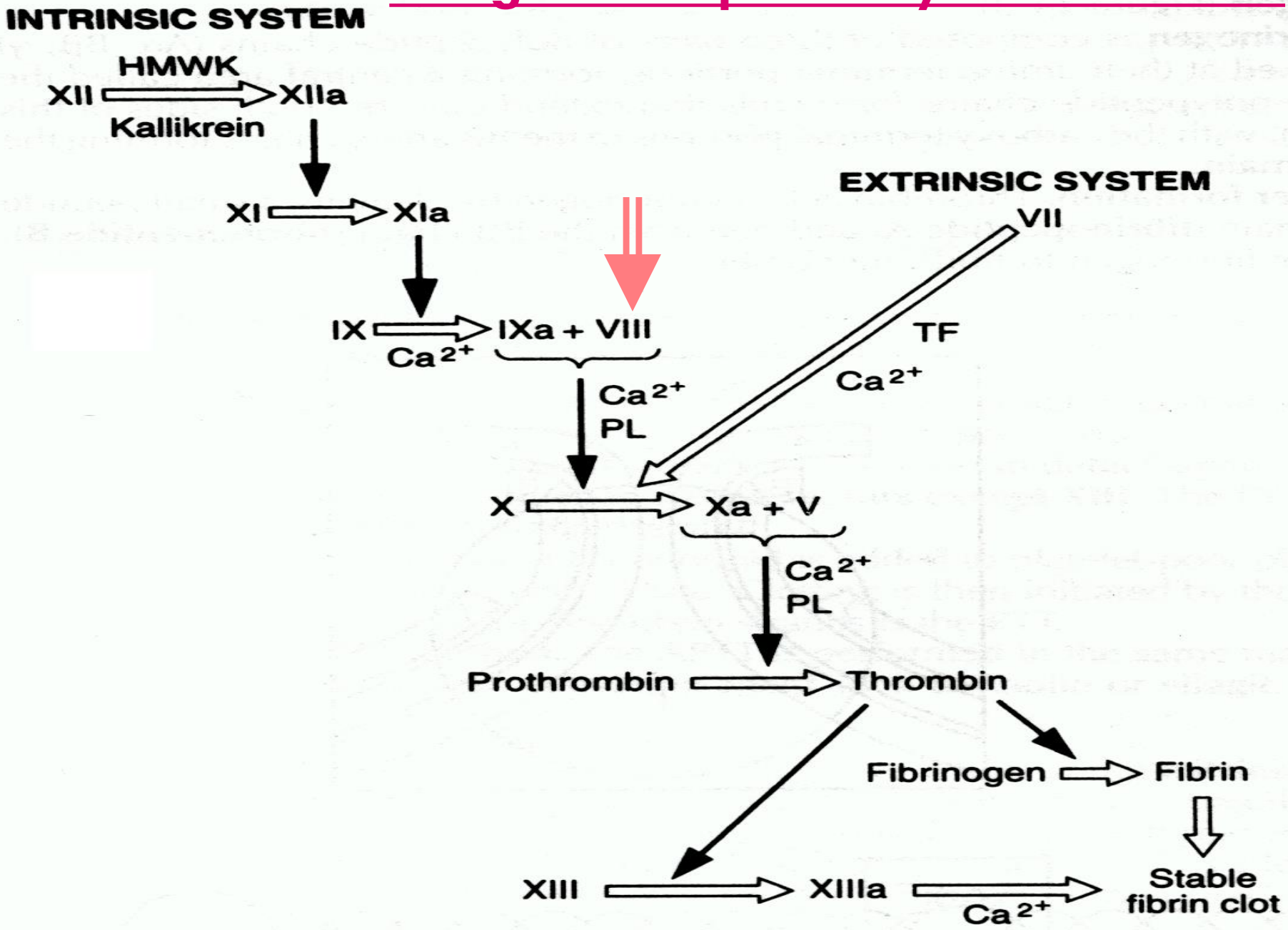
Major Components of Hemostasis



RESPONSE TO VASCULAR INJURY



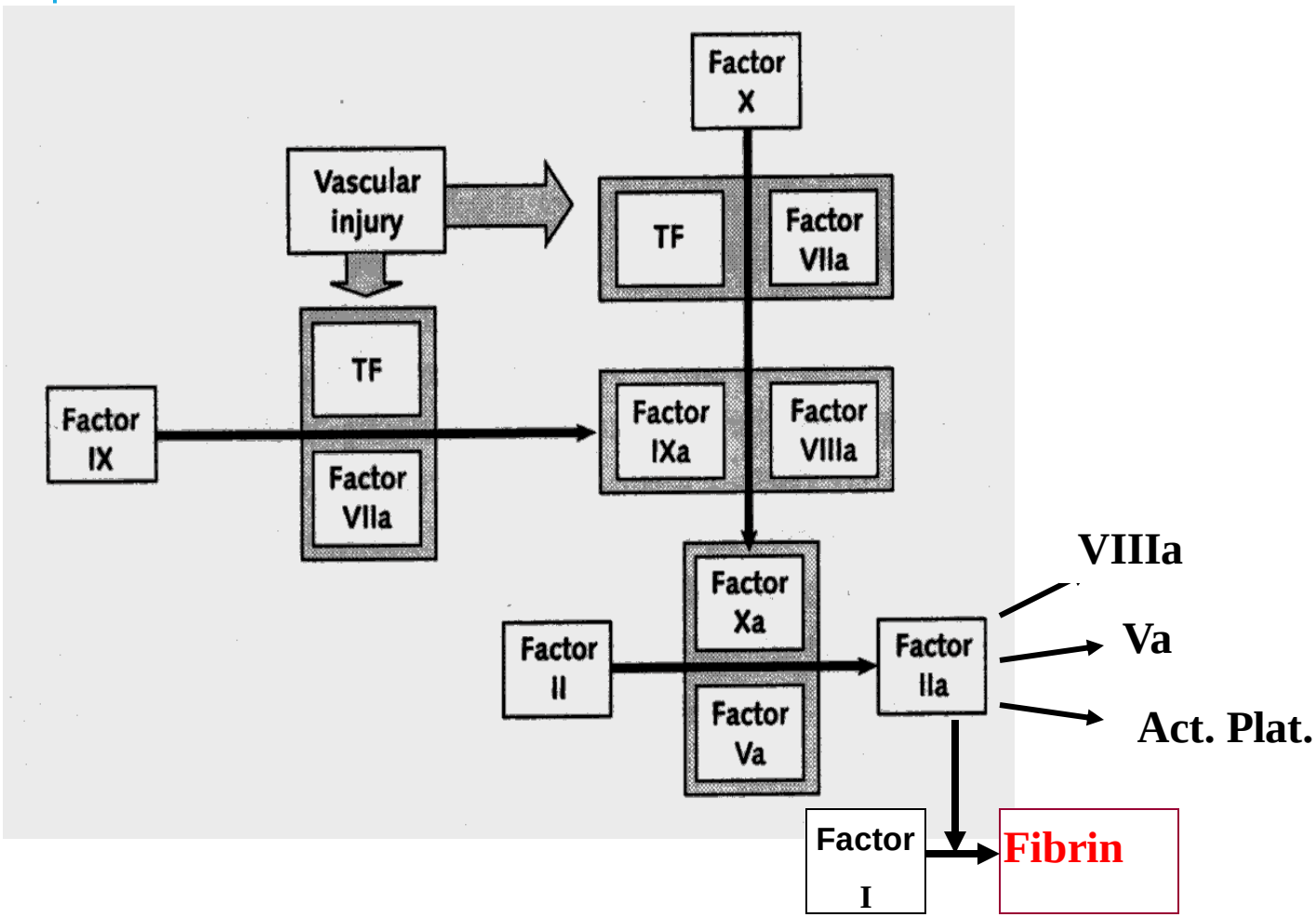
Coagulation pathways-Old version



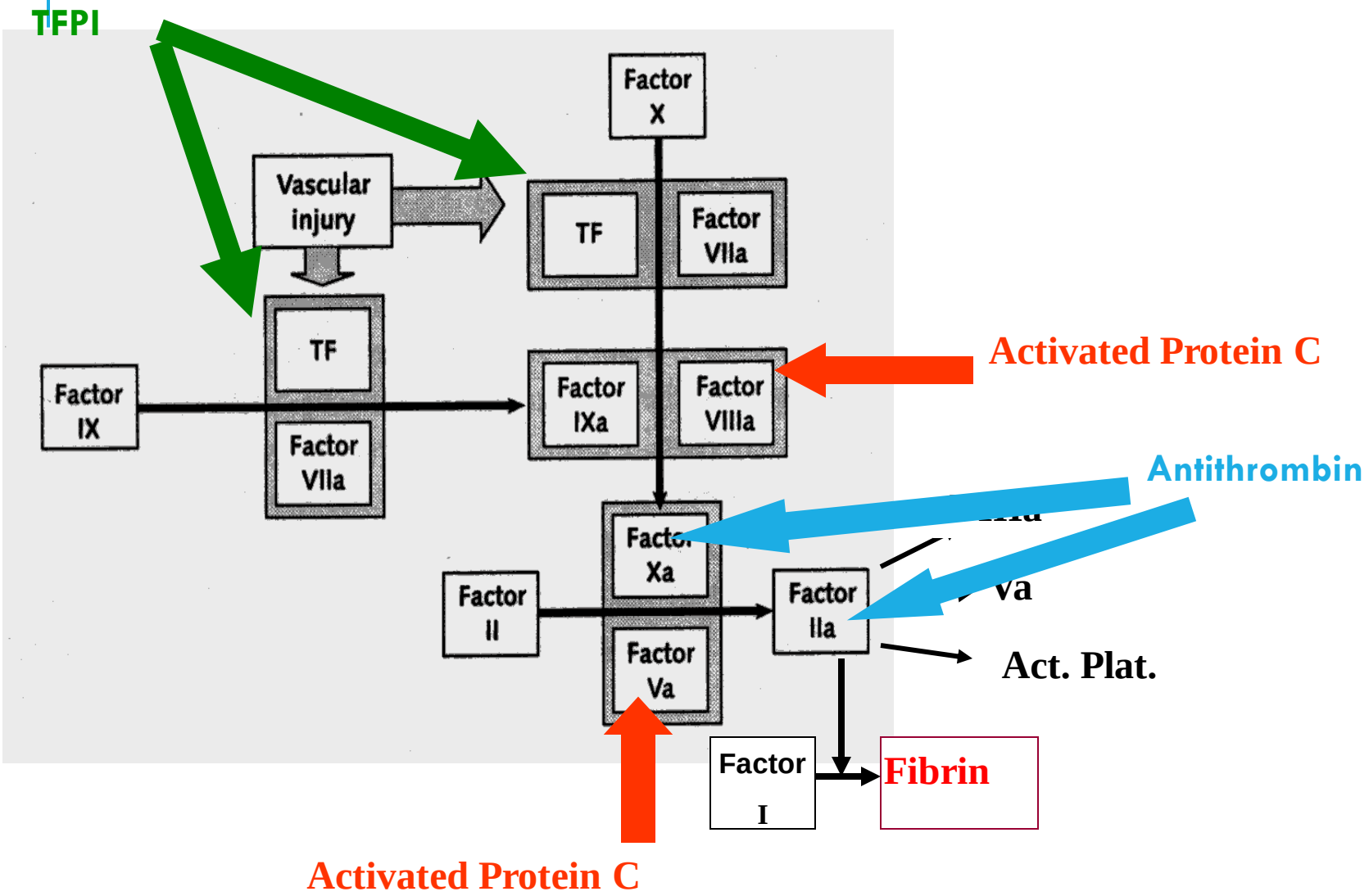
RELATION BETWEEN VONWILLEBRAND'S FACTOR (VWF) AND FACTOR VIII

vWF serves two unique functions in haemostasis, as a carrier for FVIII and as the bifunctional ligand mediating platelet GPIb α adhesion to collagen.

COAGULATION PATHWAYS-NEW VERSION

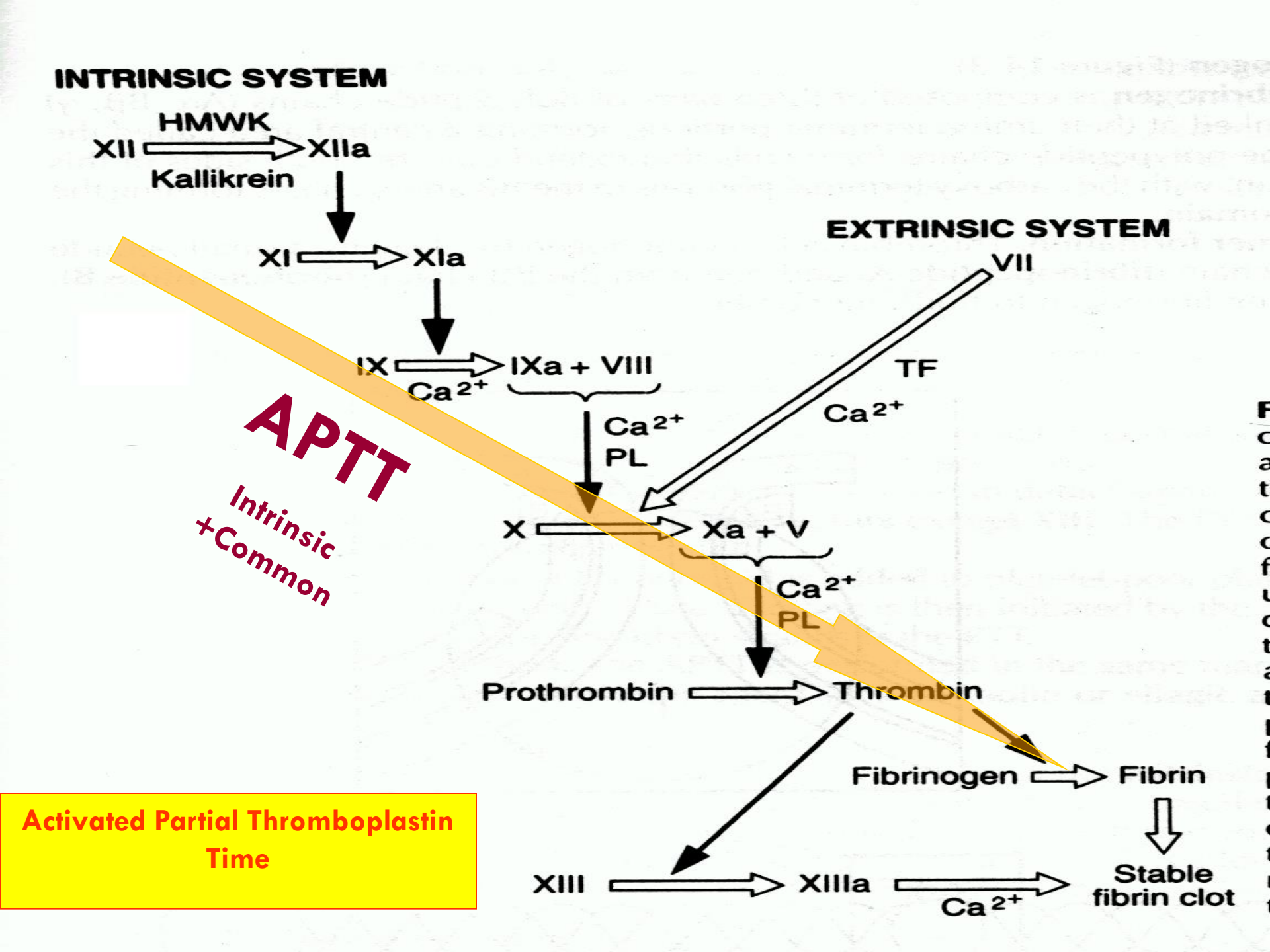


NATURAL COAGULATION PATHWAY INHIBITORS

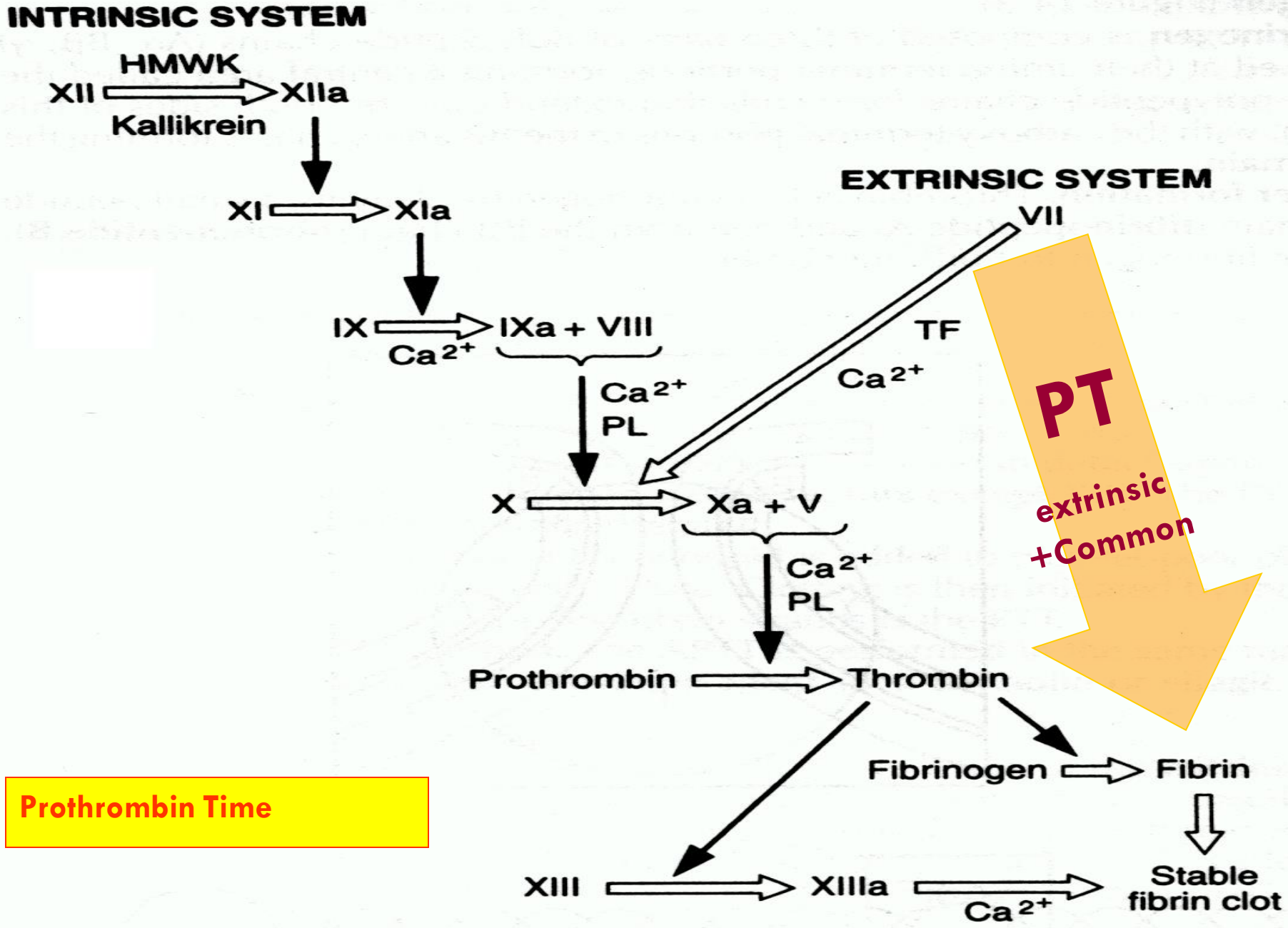


Basic Screening tests for Hemostasis :

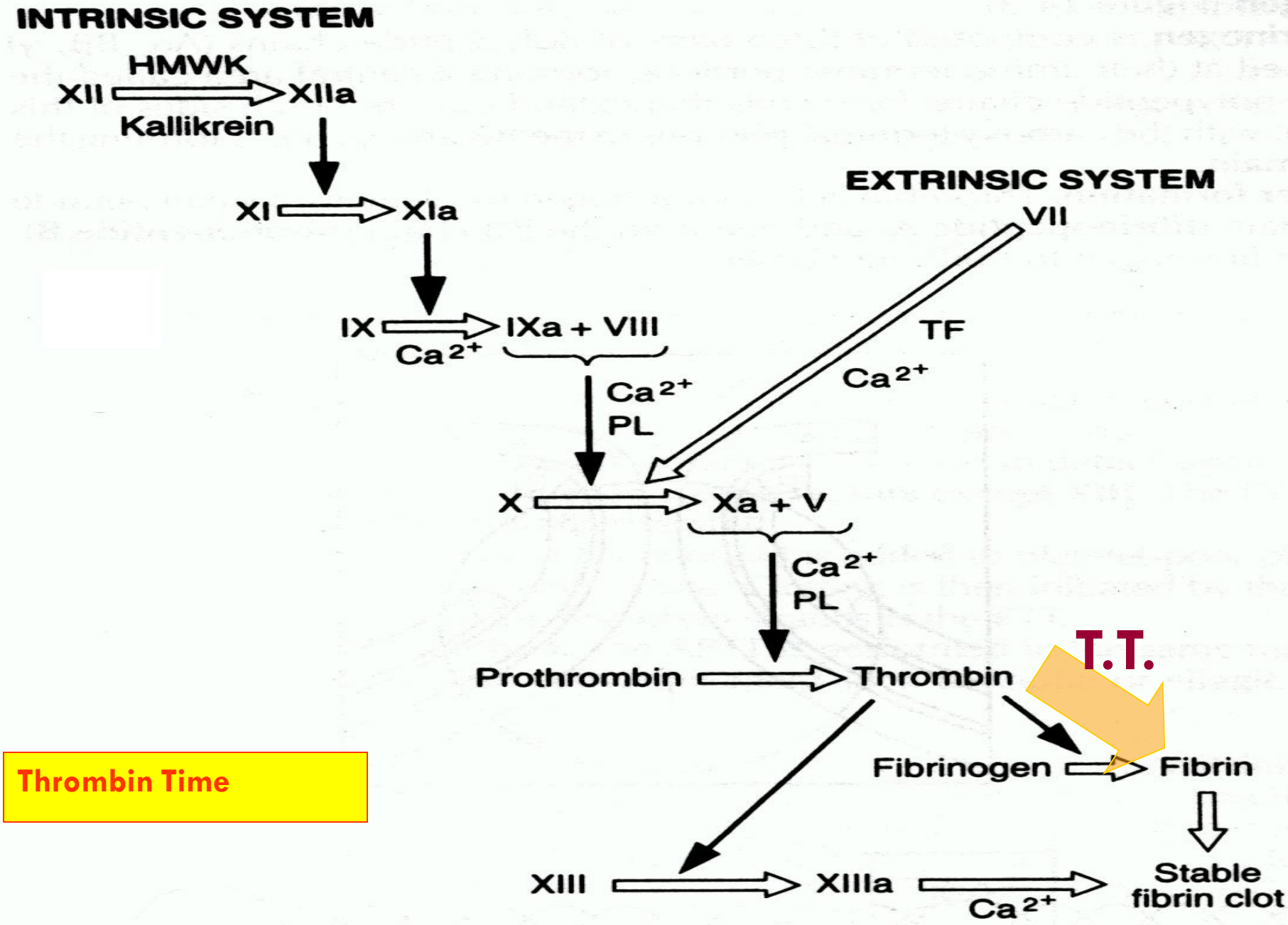
1. Platelets count (Normal range 150 000 – 450 000/cmm) : a reduced platelets count is associated with increased liability to bleeding.
2. Bleeding time (NR 2 – 10 minutes) : is prolonged if there is reduced platelets count or number, or if there is a vascular defect.
3. Prothrombin Time (PT) :this is a test which tests the extrinsic and the common pathway of the coagulation (PT will be prolonged by deficiencies in FVII,FX, FV, FII or fibrinogen).
4. Activated Partial Thromboplastine Time (APTT):This test is used to test for intrinsic and the common pathway (APTT will be prolonged by deficiencies of FXII,FXI, FIX, FVIII, FX, FV, FII, fibrinogen)
5. Thrombin time (TT) :this tests the last step in the coagulation pathway i.e. the conversion of Fibrinogen (factor I) to fibrin.



Activated Partial Thromboplastin Time



Prothrombin Time



Thrombin Time

BLEEDING TENDENCY

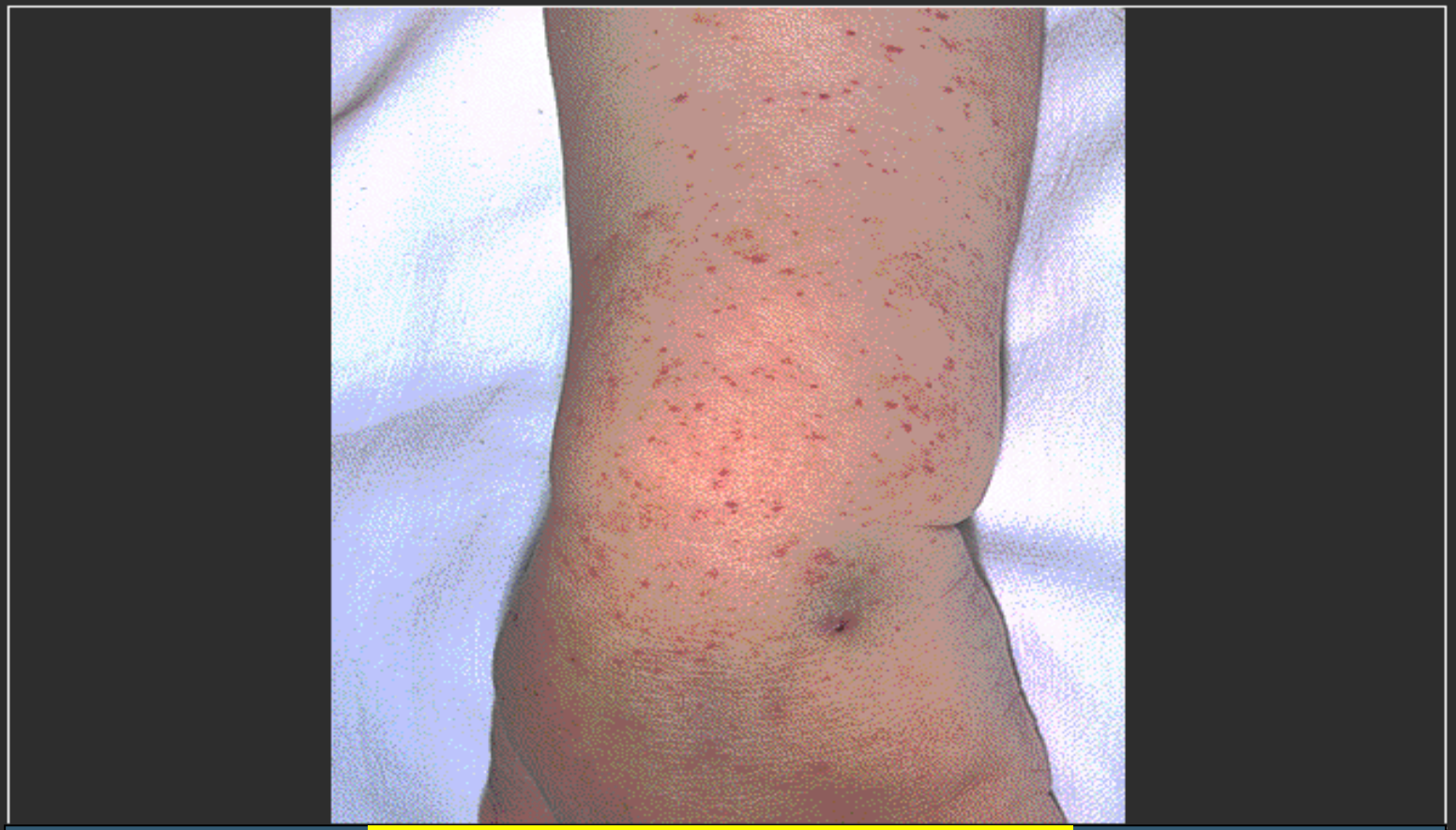
- ***Dry purpura :*** cutaneous purpura (petechiae, ecchymosis, easy bruising).
- ***Wet purpura :*** mucosal bleeding (oozing gums, blood blisters in mouth, epistaxis, hematuria, menorrhagia, melena, bleeding per rectum), fundal hemorrhages.
- There are **2 main causes are:**

1. **Platelets disorders:** May either be due to reduced platelets count (thrombocytopenia) or function
2. **Coagulation Disorders:** caused by deficiency of clotting factors and lead to defects in normal clot formation process.

Table 41.1 Main specific clinical differences between diseases of coagulation factors and platelet disorders.

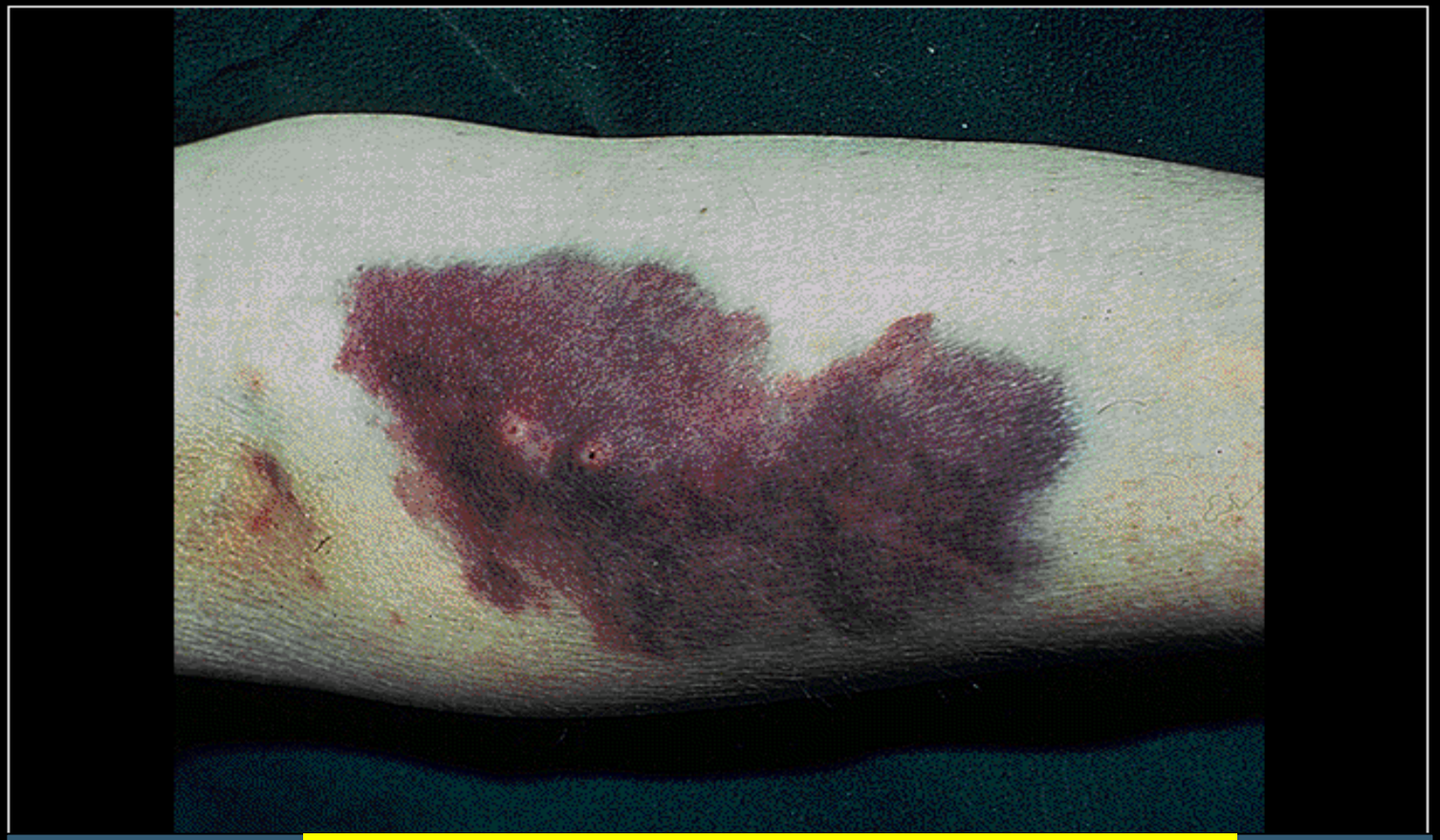
Findings	Disorders of	
	Coagulation	**Platelets/vessels**
Onset of bleeding	Delayed after trauma	Spontaneous or immediately after trauma
Mucosal bleeding	Rare	Common
Petechiae	Rare	Characteristic
Deep haematomas	Characteristic	Rare
Ecchymoses	Large and solitary	Small and multiple
Haemarthrosis	Characteristic	Rare
Bleeding from superficial cuts and scratches	Minimal	Persistent; often profuse
Sex of patient	80–90% male	Equal

BLEEDING TENDENCY : DRY PURPURA

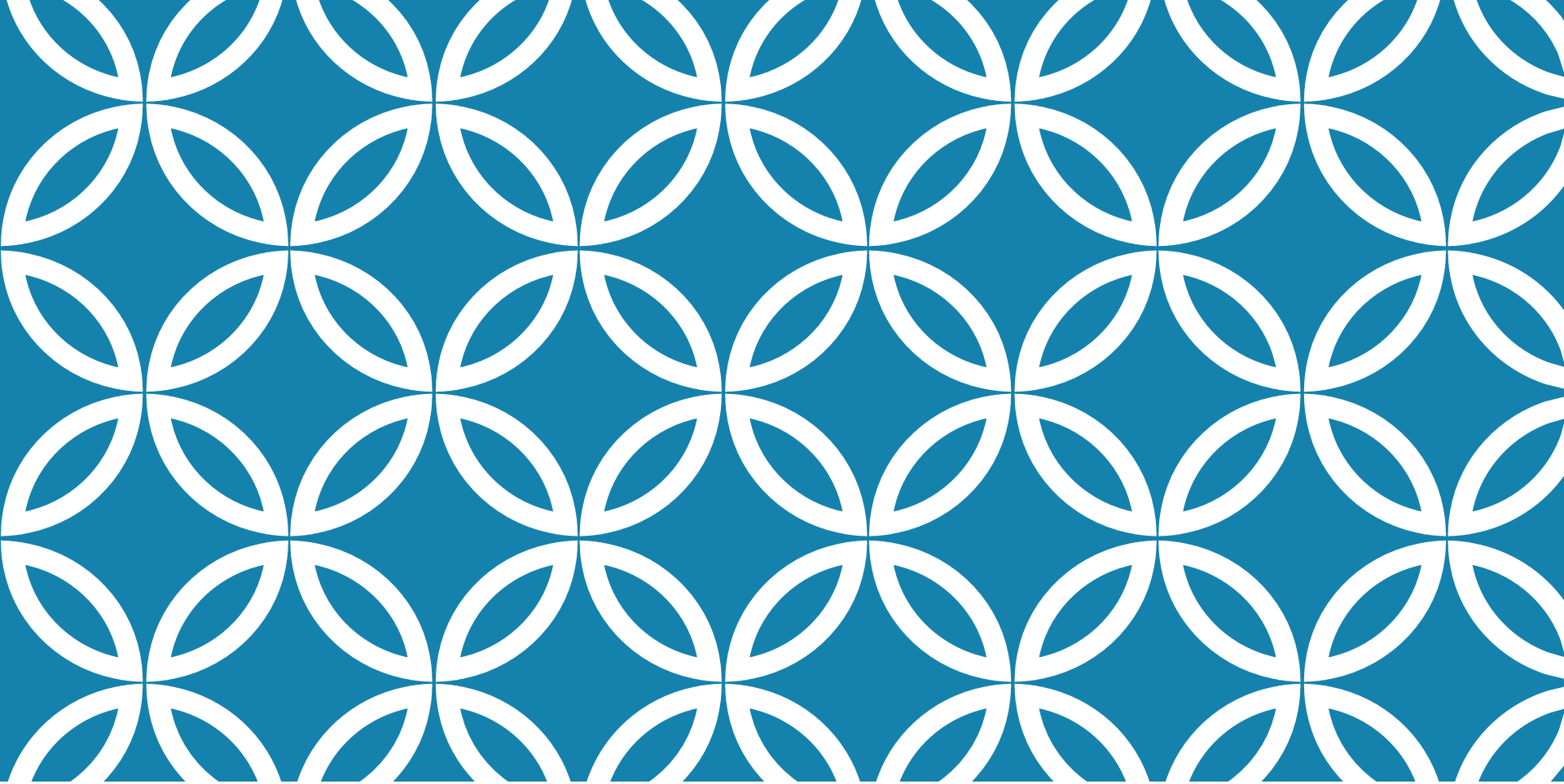


Petechiae < 3mm

BLEEDING TENDENCY: DRY PURPURA



Ecchymosis > 3mm



PLATELETS DISORDERS

CAUSES OF THROMBOCYTOPENIA

Reduced production of platelets .

1. **Acute leukemia .**
2. **Aplastic Anemia .**
3. **Cytotoxic drugs.**
4. **Marrow infiltration by malignant disease.**
5. **Myelofibrosis.**

Increased platelets consumption (with normal or increased production)

1. **Autoimmune Thrombocytopenic Purpura (AITP).**
2. **Alloimmune thrombocytopenia.**
3. **Drug induced immune Purpura.**
4. **Hypersplenism (increased consumption of platelets by hyperactive enlarged spleen).**
5. **Dissaminated Intravascular coagulation (DIC) .**

AUTOIMMUNE THROMBOCYTOPENIC PURPURA

A relatively common hematological disorder, the main feature of which is bleeding tendency due to thrombocytopenia, and could be classified into:

1. **Idiopathic thrombocytopenic purpura (ITP):** Immune (autoimmune, idiopathic) thrombocytopenic purpura is a common acquired autoimmune disorder defined by a low platelet count secondary to accelerated platelet destruction by antiplatelet antibodies. usually affecting young or middle aged adults, without precedent or associated illness
2. **Secondary autoimmune thrombocytopenia :** resembles ITP clinically, but associated Autoimmune disorder, or malignancy (SLE, CTD, LPD, Solid tumors, AIDS etc).
3. **Acute Post-viral auto-immune thrombocytopenia:** acute usually self-limiting thrombocytopenic purpura, typically seen in children following acute viral infection or immunization.

Table 42.2 Potential causes of thrombocytopenia in ITP.

- Autoantibody opsonization of platelets leading to destruction by the reticuloendothelial system
- Autoantibody opsonization of megakaryocytes, with inhibition of megakaryocyte growth, differentiation and platelet release
- Autoantibody-induced megakaryocyte apoptosis
- Relative thrombopoietin deficiency
- Molecular mimicry and immune complex formation
- T-cell direct lysis of platelets

CLINICAL FEATURES OF AITP

Clinical parameter	Acute	Chronic
Peak age (yr.)	2-8	20-40
Sex distribution	F=M	3F:1M
Onset	Sudden	Insidious
Duration	usually weeks	often months/years.
Associated disorders	post-viral	1. Idiopathic. 2. Secondary.

N.B.: *Splenomegaly is not a feature of AITP, except if secondary*

HEMATOLOGICAL FINDINGS :

Blood Picture :

Main feature reduced platelets (<80x10^9/L).

Normal or reduced Hb.

Leucocytes often normal.

Bone marrow shows :

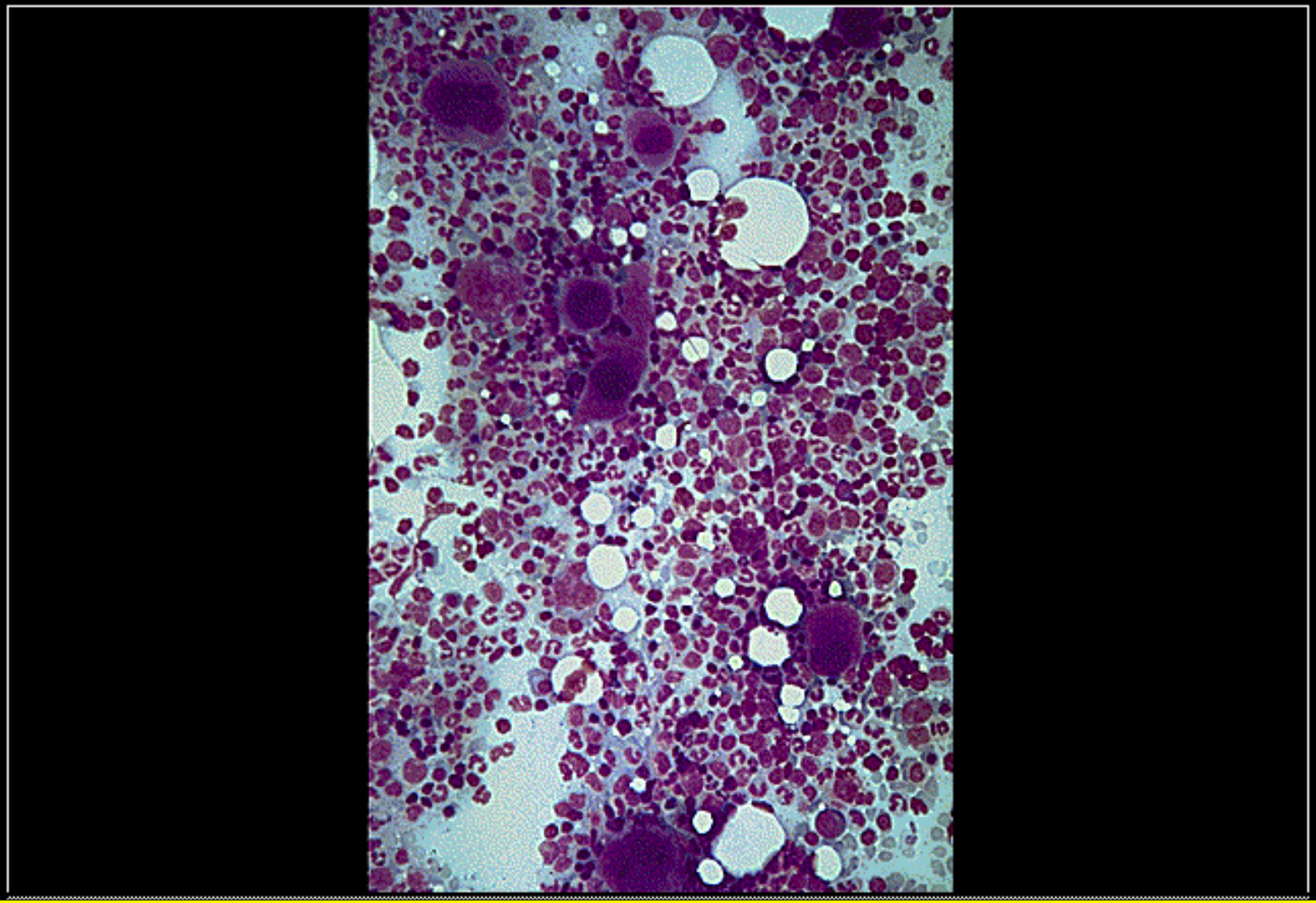
Usually normal cellularity.

Mainly increased or normal no. of Megakaryocytes.

Normal erythro and granulopoiesis.

No excess blasts or foreign cells.

Diagnosis is confirmed by demonstration of platelets auto-antibodies.



Bone marrow Aspirate in AITP

Increased Megakaryocytes

MANAGEMENT OF AITP :

- **Traditionally**, treatments have been grouped into first line, second line, third line
- **First-line** therapies comprise corticosteroids, IVIg and anti-D. These three treatments work fairly quickly (within 24–48 hours) and their efficacy rates are high at around 70–80%.
- If patients fail to respond to first-line treatment they may then be given a **second-line drug**, such as azathioprine, mycophenolate mofetil or a TPO receptor agonist

Table 42.5 Treatment options after first-line therapy.

Non-approved second-line treatments

- Azathioprine
- Dexamethasone
- Methylprednisolone
- Ciclosporin
- Mycophenolate mofetil
- Cyclophosphamide
- Danazol
- Dapsone
- Vincristine
- Rituximab

Surgical second-line treatment

- Splenectomy

Approved second-line treatments

- Romiplostim
- Eltrombopag

- **In Acute Post-viral ITP :** majority recover spontaneously within 3 months. The recommended treatment is IV Immunoglobulin.
- **In chronic ITP :** management includes steroids, followed by splenectomy if necessary


Thank
you