Primary and secondary hemostasis. Anticoagulants

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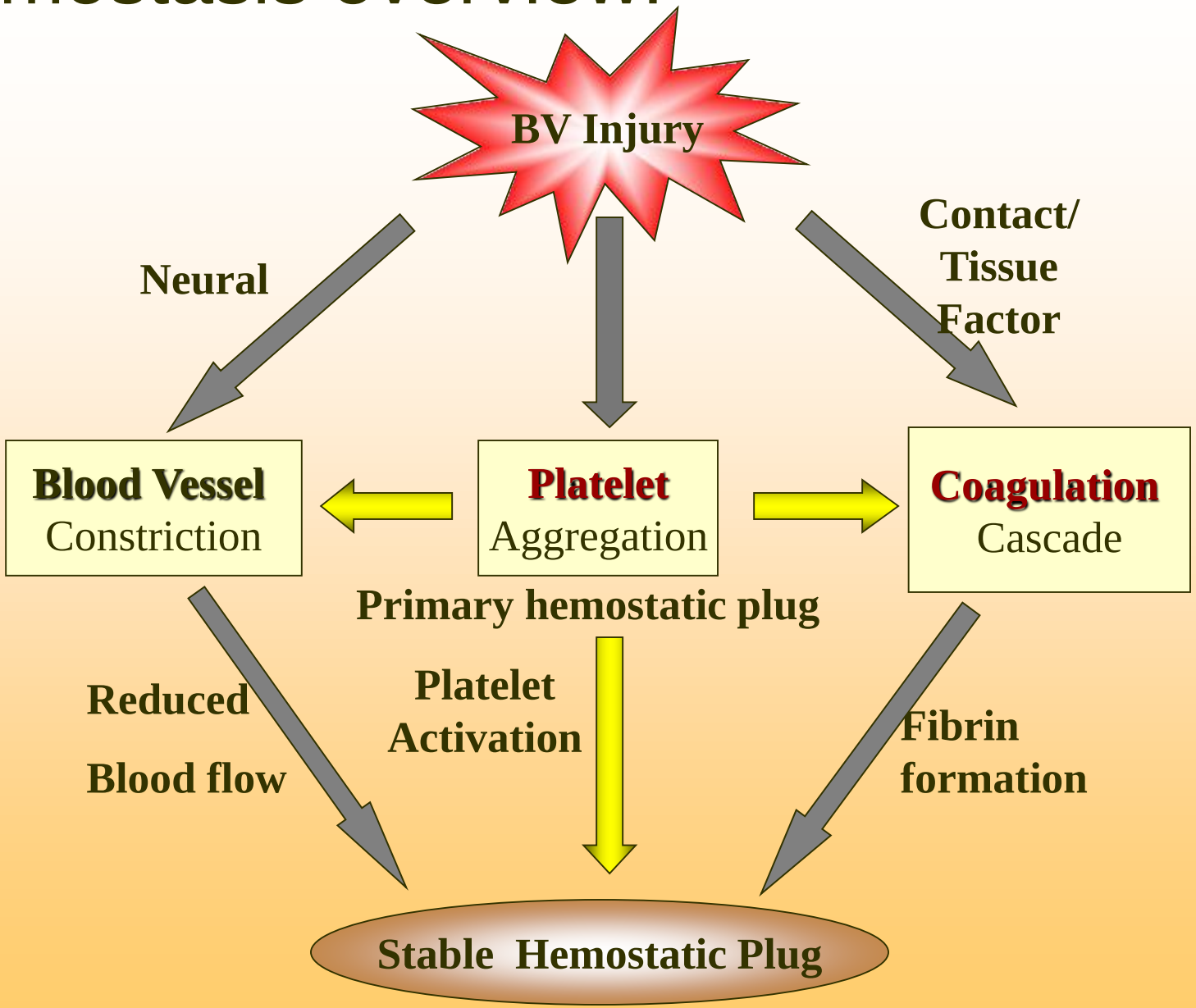
Introduction: Road map..

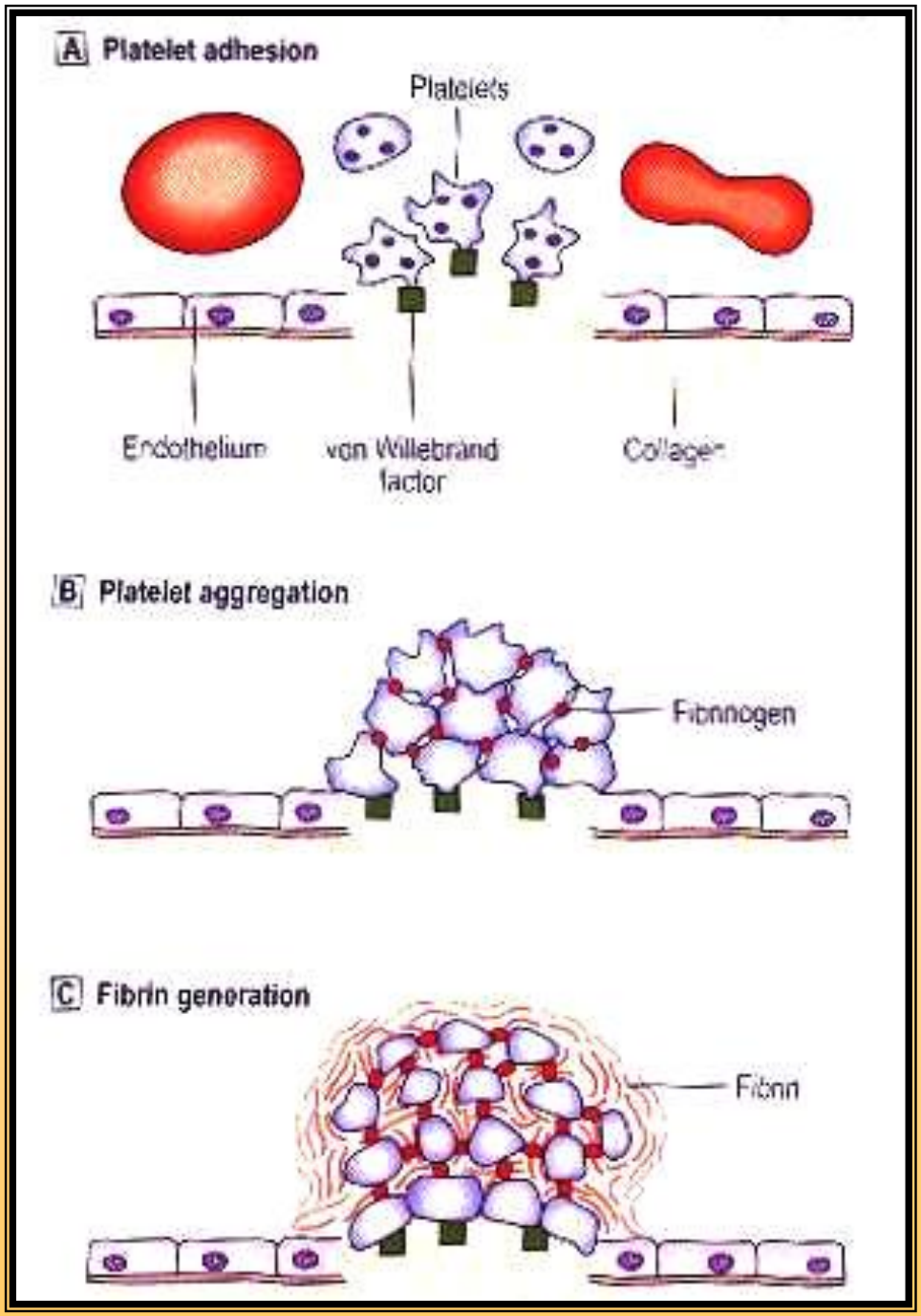
- Haemostasis – capacity to minimise loss of blood following injury to blood vessel.
- Blood vessel – Coagulation – Platelet act.
- Bleeding disorders – Bv, Plt, Coag.
- Laboratory tests of Haemostasis.
- Factor analysis, PLT function,

Haemostasis overview:



Coagulation:

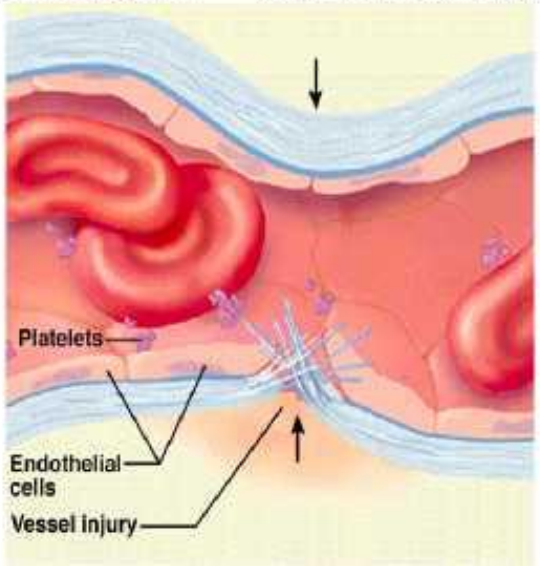
- Fibrinogen to Fibrin – Coag. Cascade
- Several factors – proenzymes-activation.
- Enzyme amplication –
- Plasma, Endothelium & Platelets
- Stable hemostatic plug.
- Clot lysis – starts soon after clot formation.



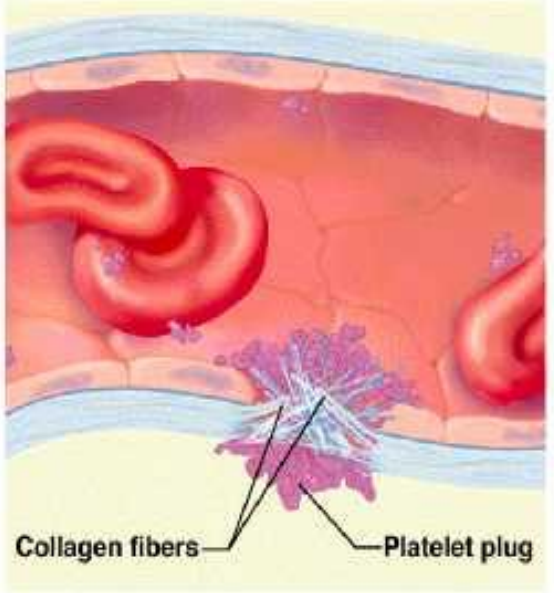
Haemostasis:

- Vasoconstriction – N
- Platelet activation
- Haemostatic plug
- Coagulation
- Stable clot formation
- Clot dissolution

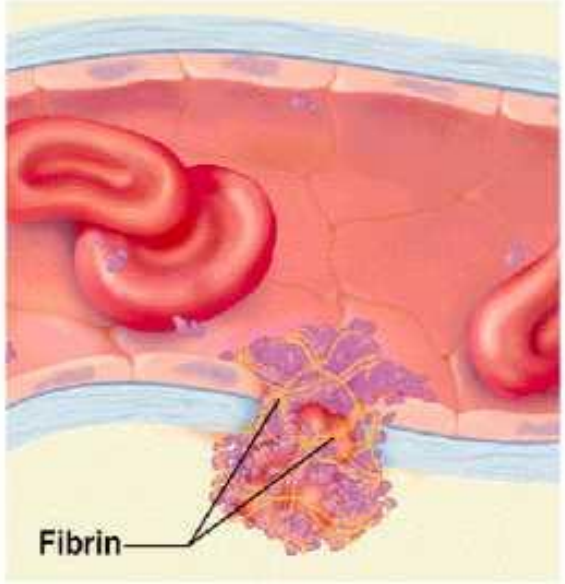
Hemostasis — Vasoconstriction



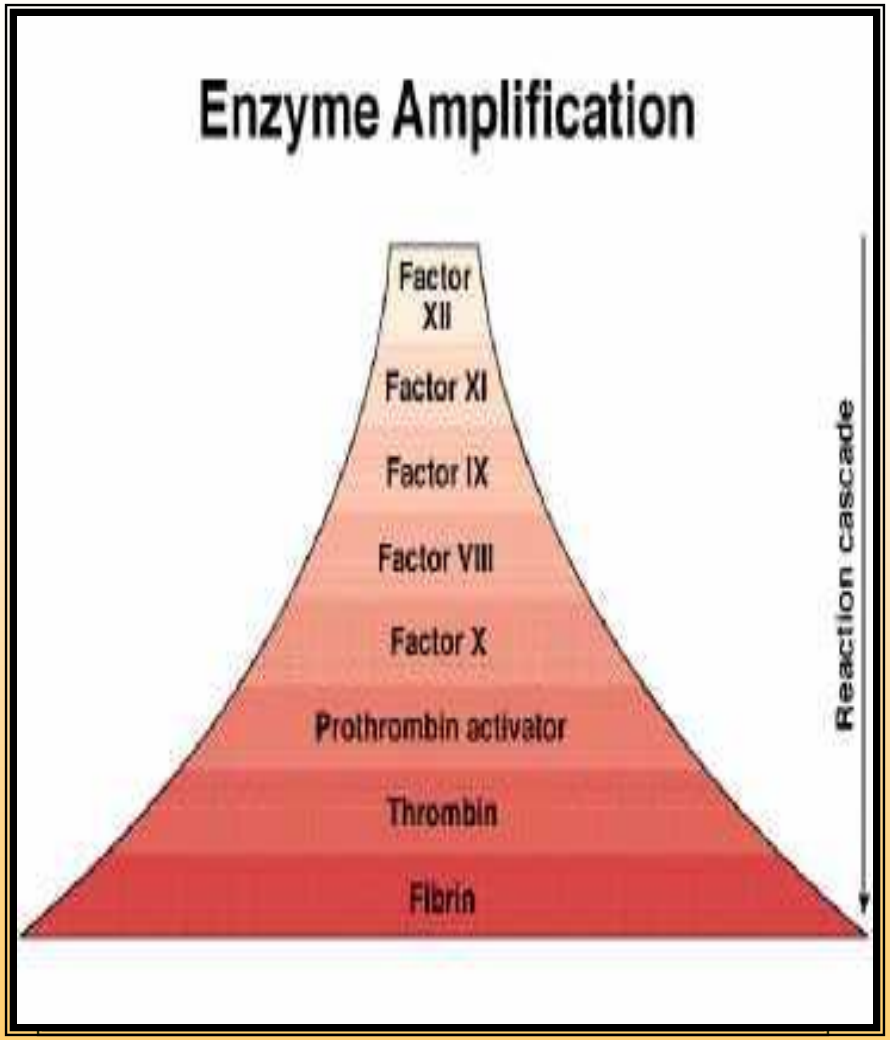
Hemostasis — Platelet Plug



Hemostasis — Blood Clot

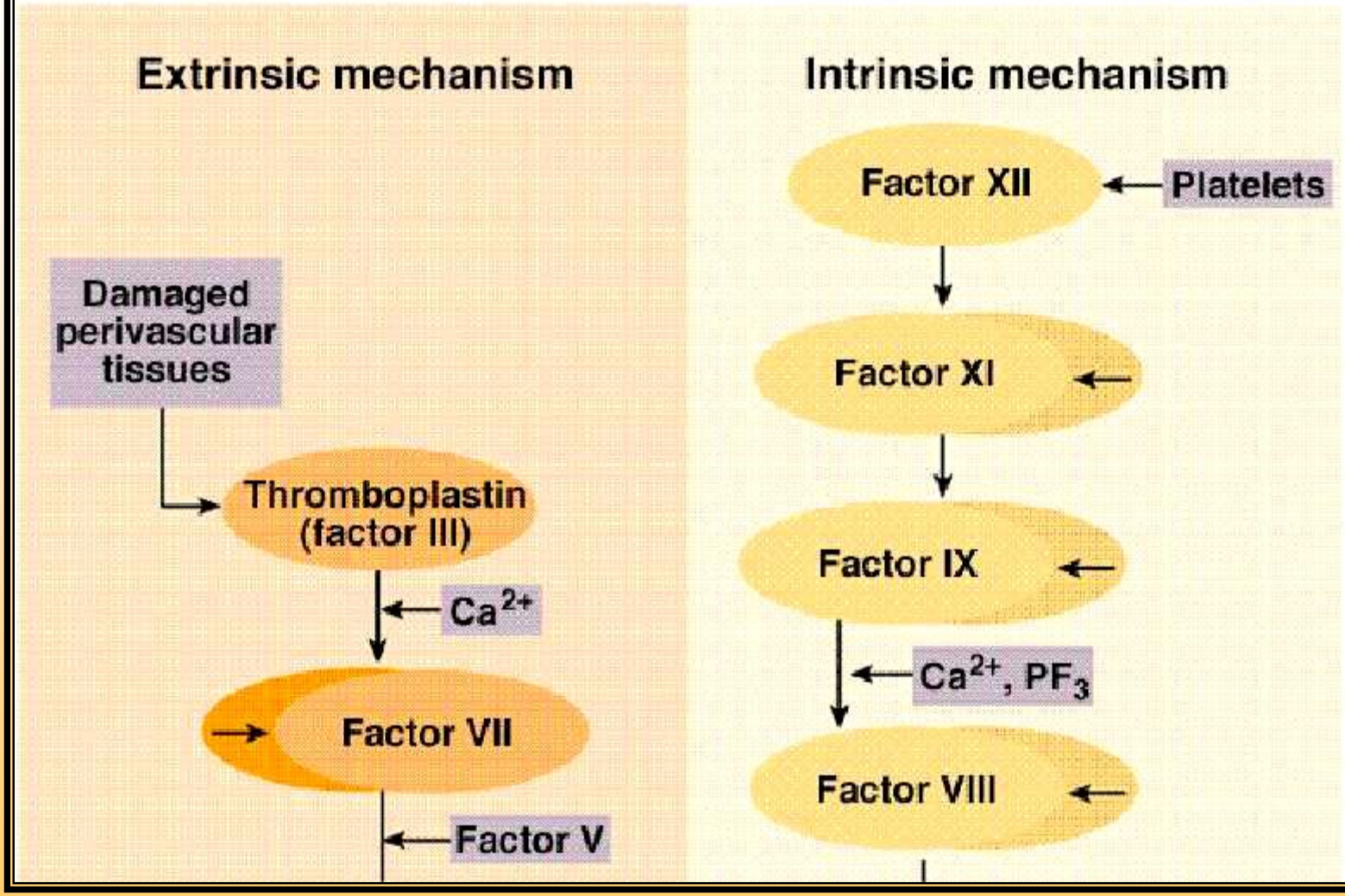


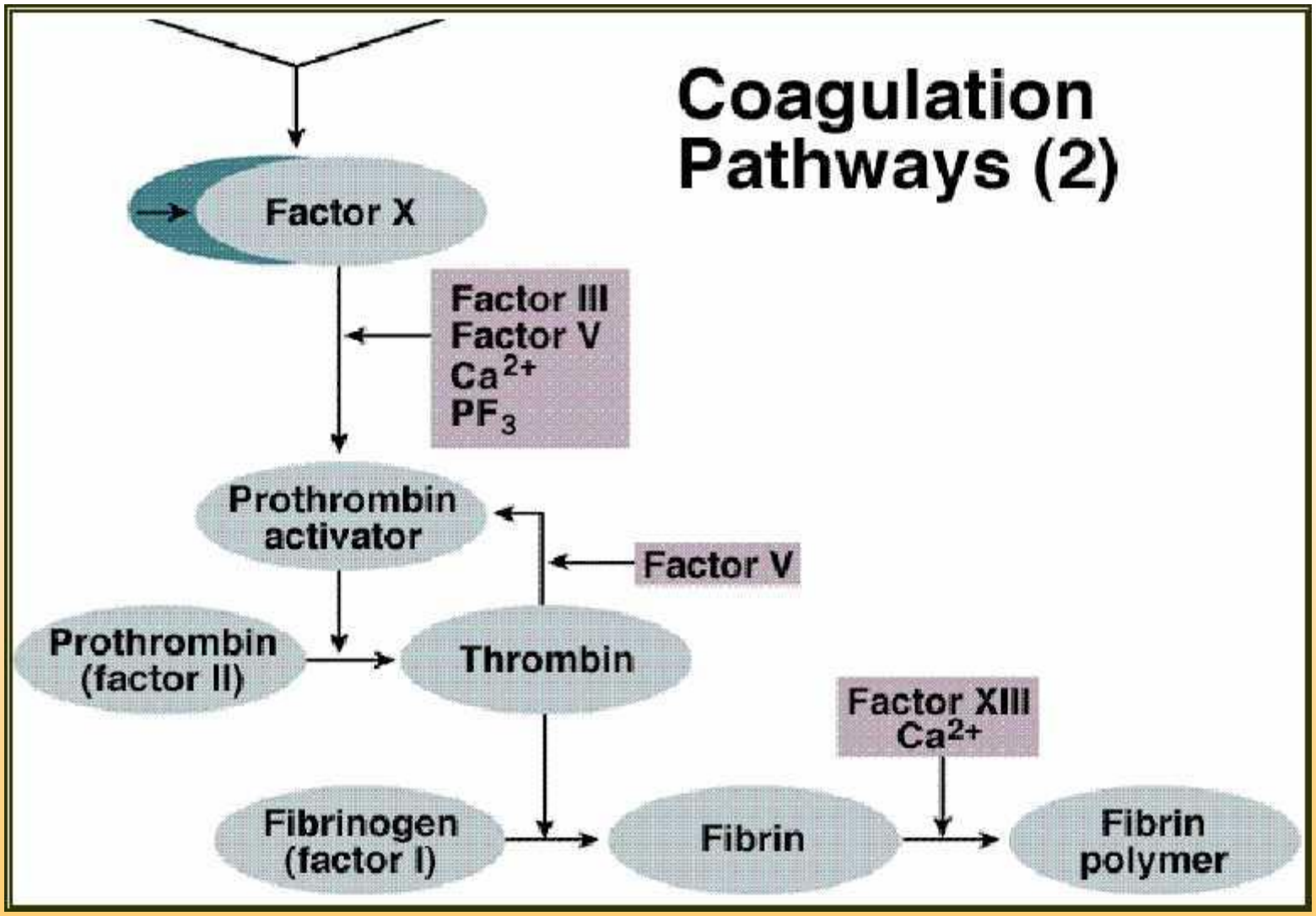
Coagulation:

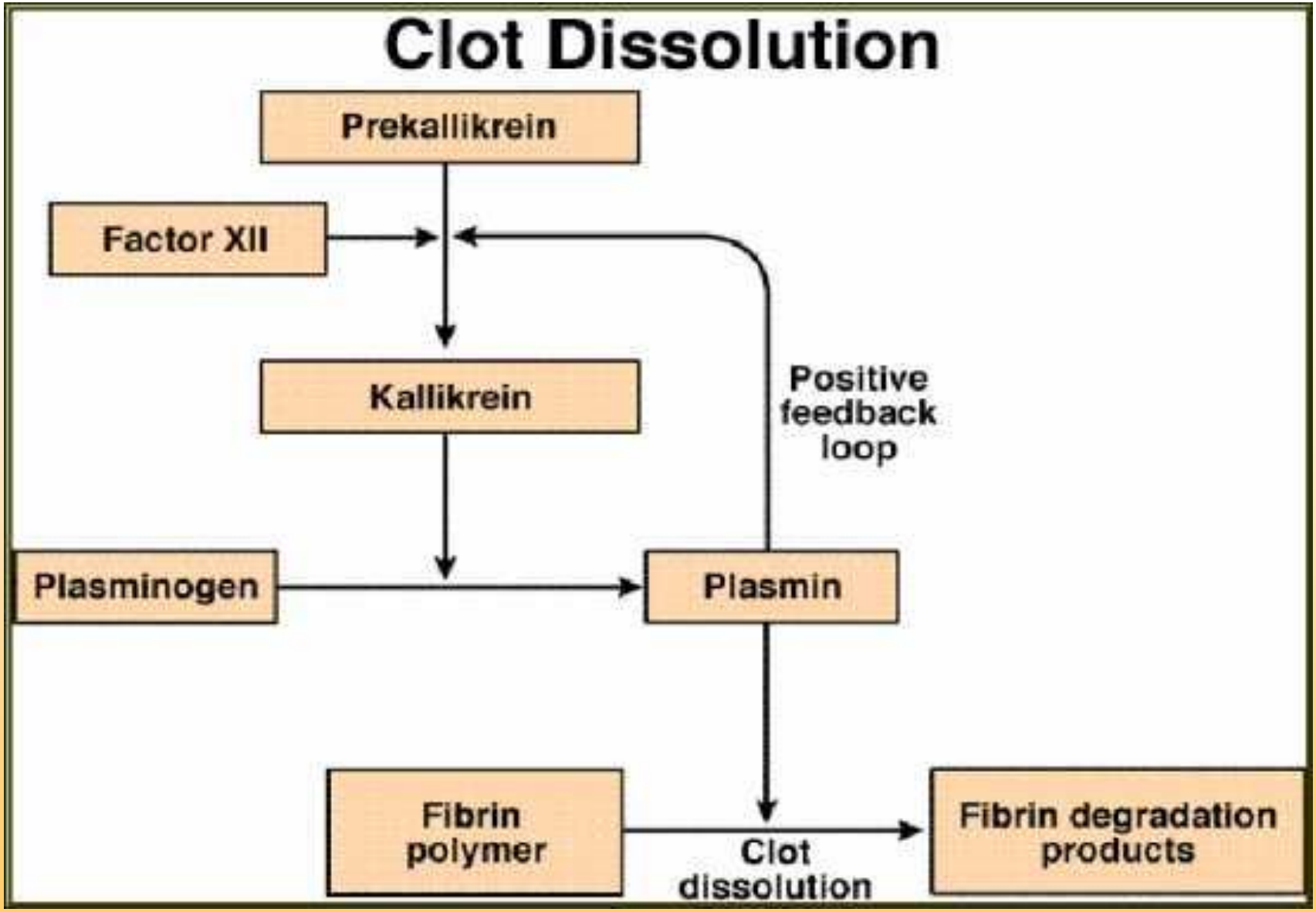


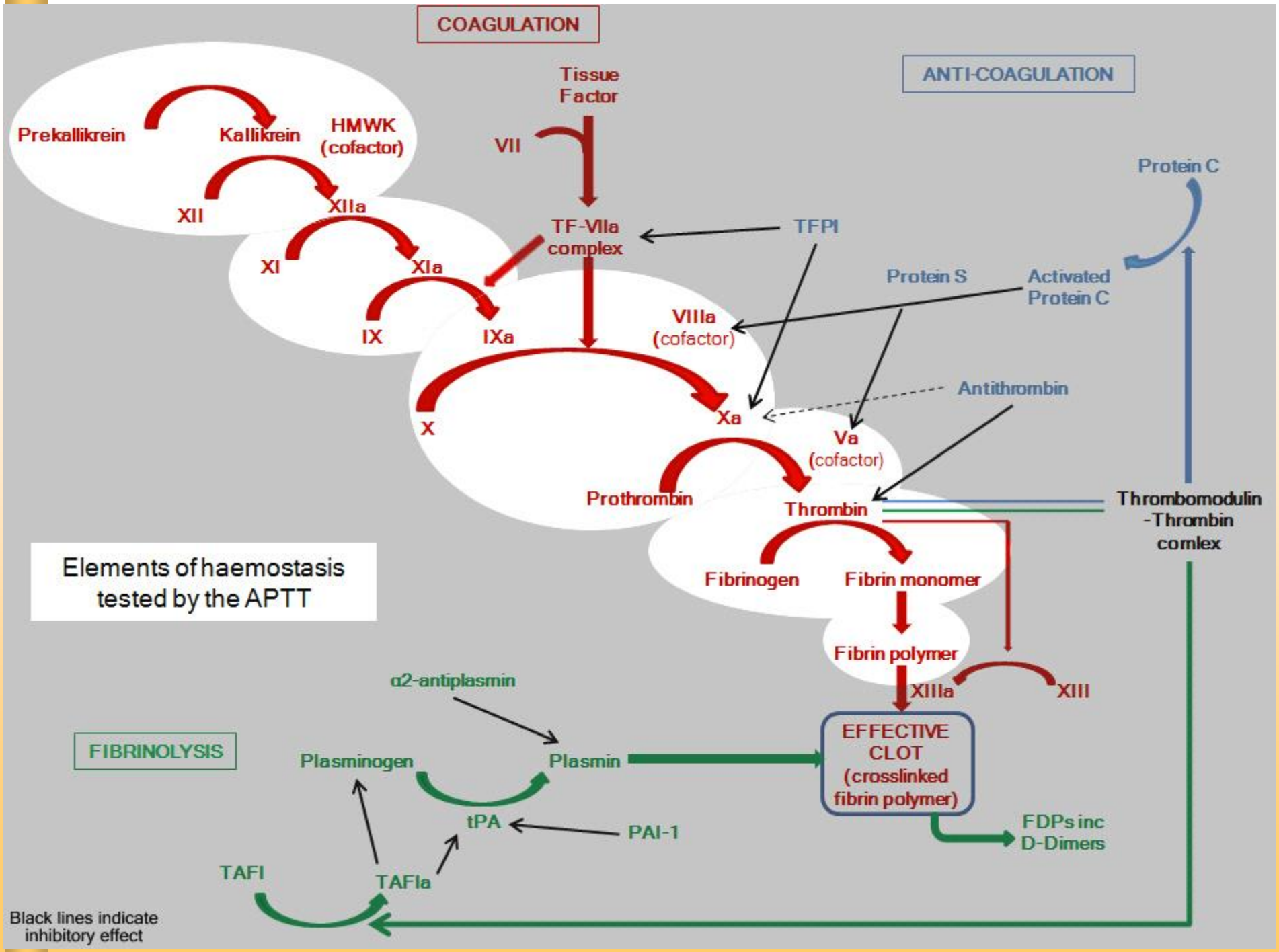
- Contact activation- Intrinsic system
- Tissue factor activation – Extrinsic
- Common path- amplification
- Fibrin formation
- Fibrin lysis.

Coagulation Pathways (1)




Coagulation Pathways (2)
Factor X
Factor III
Factor V
Ca^{2+}
PF_3
Prothrombin activator
Factor V
Prothrombin (factor II)
Thrombin
Factor XIII
Ca^{2+}
Fibrinogen (factor I)
Fibrin
Fibrin polymer


Clot Dissolution
Prekallikrein
Factor XII
Kallikrein
Positive feedback loop
Plasminogen
Plasmin
Fibrin polymer
Clot dissolution
Fibrin degradation products


COAGULATION
ANTI-COAGULATION
Tissue Factor
VII
Prekallikrein
Kallikrein
HMWK (cofactor)
XII
XIIa
XI
XIa
IX
IXa
TF-VIIa complex
TFPI
Protein C
Protein S
Activated Protein C
VIIIa (cofactor)
X
Xa
Antithrombin
Va (cofactor)
Prothrombin
Thrombin
Thrombomodulin -Thrombin comlex
Fibrinogen
Fibrin monomer
Fibrin polymer
XIIIa
XIII
Elements of haemostasis tested by the APTT
α2-antiplasmin
FIBRINOLYSIS
Plasminogen
Plasmin
EFFECTIVE CLOT (crosslinked fibrin polymer)
tPA
PAI-1
FDPs inc D-Dimers
TAFI
TAFIa
Black lines indicate inhibitory effect

Routine Investigations:

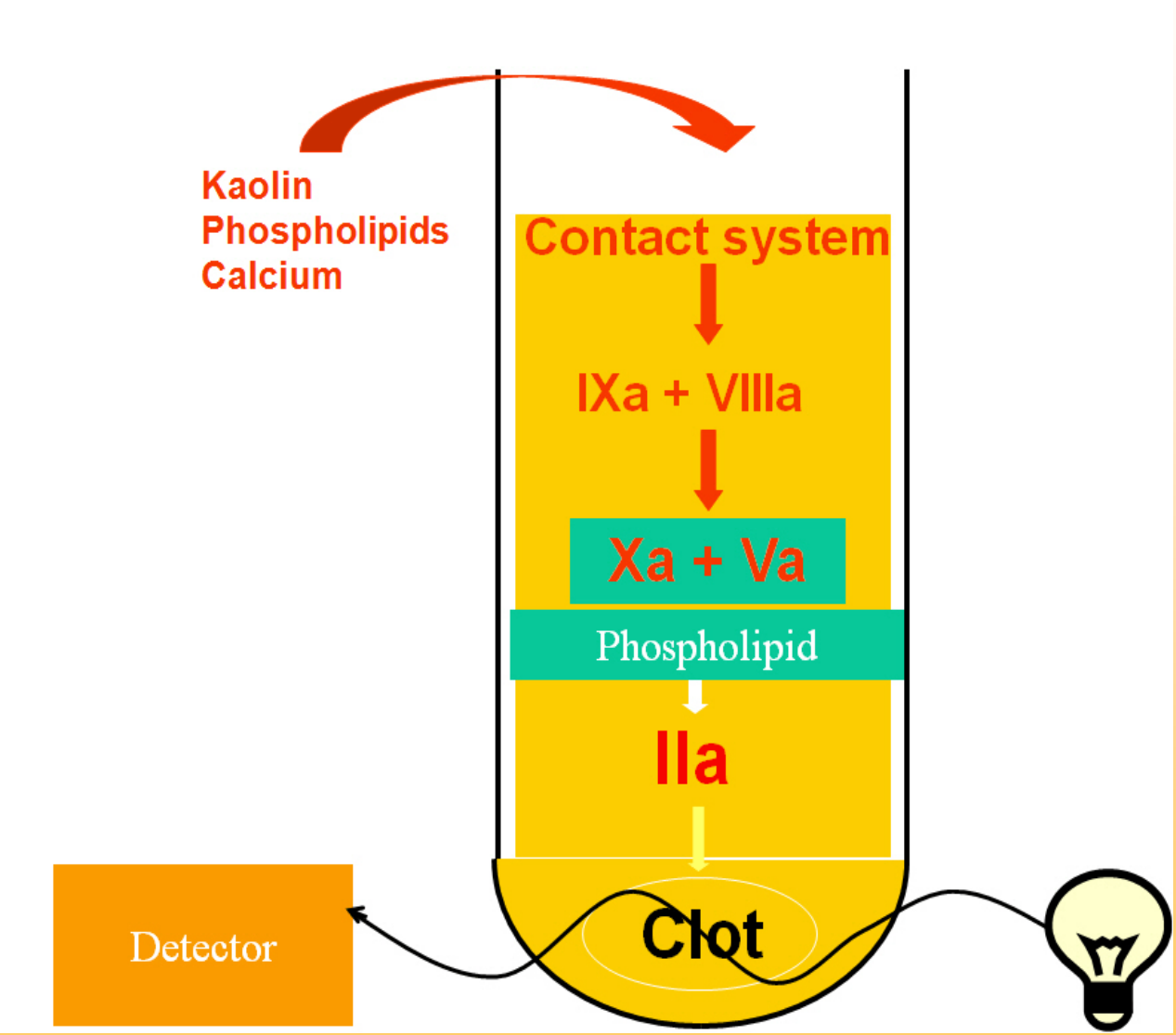
- **Bleeding time – BV, PLT**
  - ivy template method - 2-4 min
- **Clotting time** – inaccurate – 10-15min
- **Prothrombin time** –Extrinsic – 11-15 sec
  - Acquired diseases, liver dis, warfarin therapy
- **aPTT** –Activated Partial Thromboplastin Time - Intrinsic
  - Haemophilia, Congenital.
- **Trombin Time:** Fibrinogen

(common path) – 12-17 sec

  - DIC -(**Disseminated intravascular coagulation)** &
  - Heparin therapy.
- **FDP** – Fibrinogen Degradation Products – DIC

Method

A schematic of the APTT is shown below



Special Investigations:

- **Specific Factor Assays**
- **Platelet function studies –**
  - **Aggregometry,**
  - **Adhesion studies**
  - **Immuno-fluorescence**
- **Electrophoresis**
- **Bone marrow examination – plt**
- **Molecular Biology – FISH**

Bleeding: Clinical Features

1. Local - Vs - General, spontaneous . .
2. Hematoma & Joint bleed - Coagulation
3. Skin/Mucosal Petechiae & Purpura – PLT
4. wound / surgical bleeding –

- Immediate - (PLT)
- Delayed - (Coagulation)

Platelet

Petechiae, Purpura

Coagulation

Hematoma, Joint bl.

Disorders of Hemostasis

- **Vascular disorders**
  - Scurvy, easy bruising,
- **Platelet disorders**
  - Low Number or abnormal function
- **Coagulation disorders**
  - Factor deficiency.
- **Mixed/Consumption: DIC**

Haemophilia

- Congenital deficiency -Factor **8 (A)** or **9 (B)**
- Bleeding – Haematoma, joint etc.
- Gene on X chromosome.
  - (Carrier females, Males suffer)
- Prolonged **PTT** but normal **PT**.

Factor replacement – Life long.

Ideopathic T. Purpura - ITP

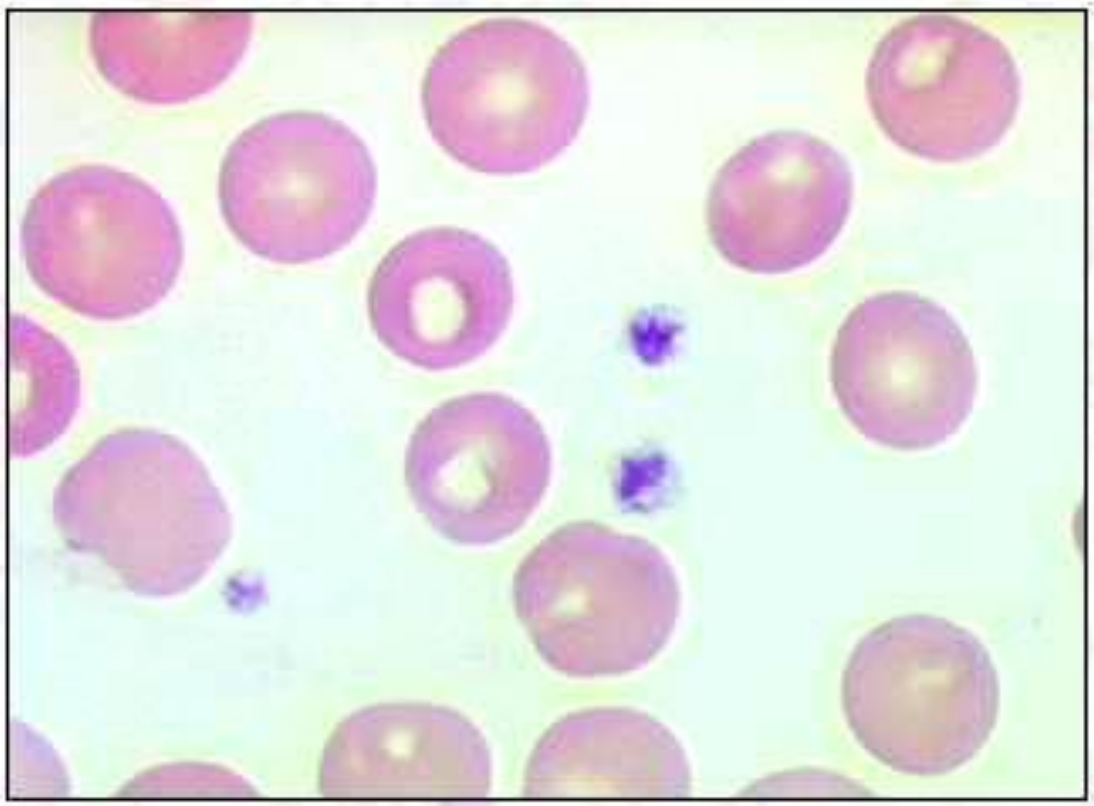
- Young female – 20-35y
- Easy bruising, Petechiae, menorrhagia
- Anti PLT Antibody (IgG) – destruction of plt
- Low Platelet number.

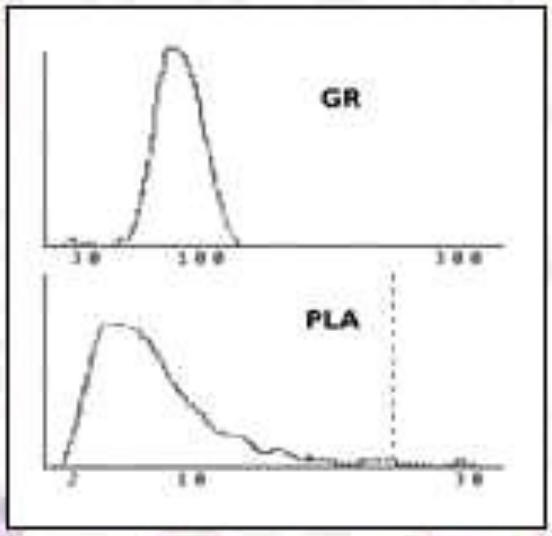
Disorders of platelets

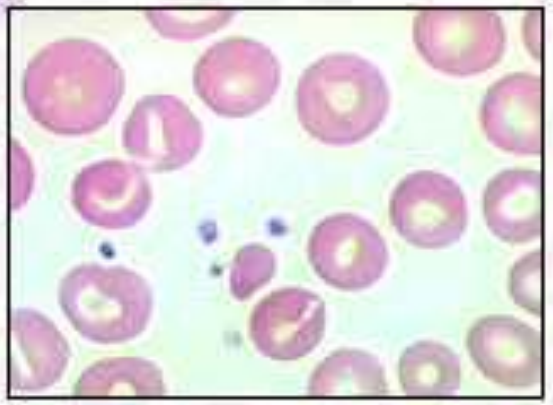
- **Decreased Number: Thrombocytopenia**
  - **Decreased Production**
  - **Decreased Survival – Immune (ITP)**
  - **Increased utilization - DIC**
- **Defective Platelet function:**
  - **Acquired – Drugs – Aspirin, MPS, MDS**
  - **Congenital – Eg. Thrombasthenia.**

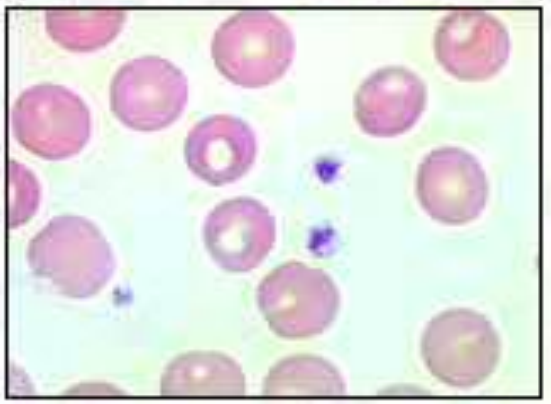
Normal platelets (number and form)

Platelets: 211 000/mm3









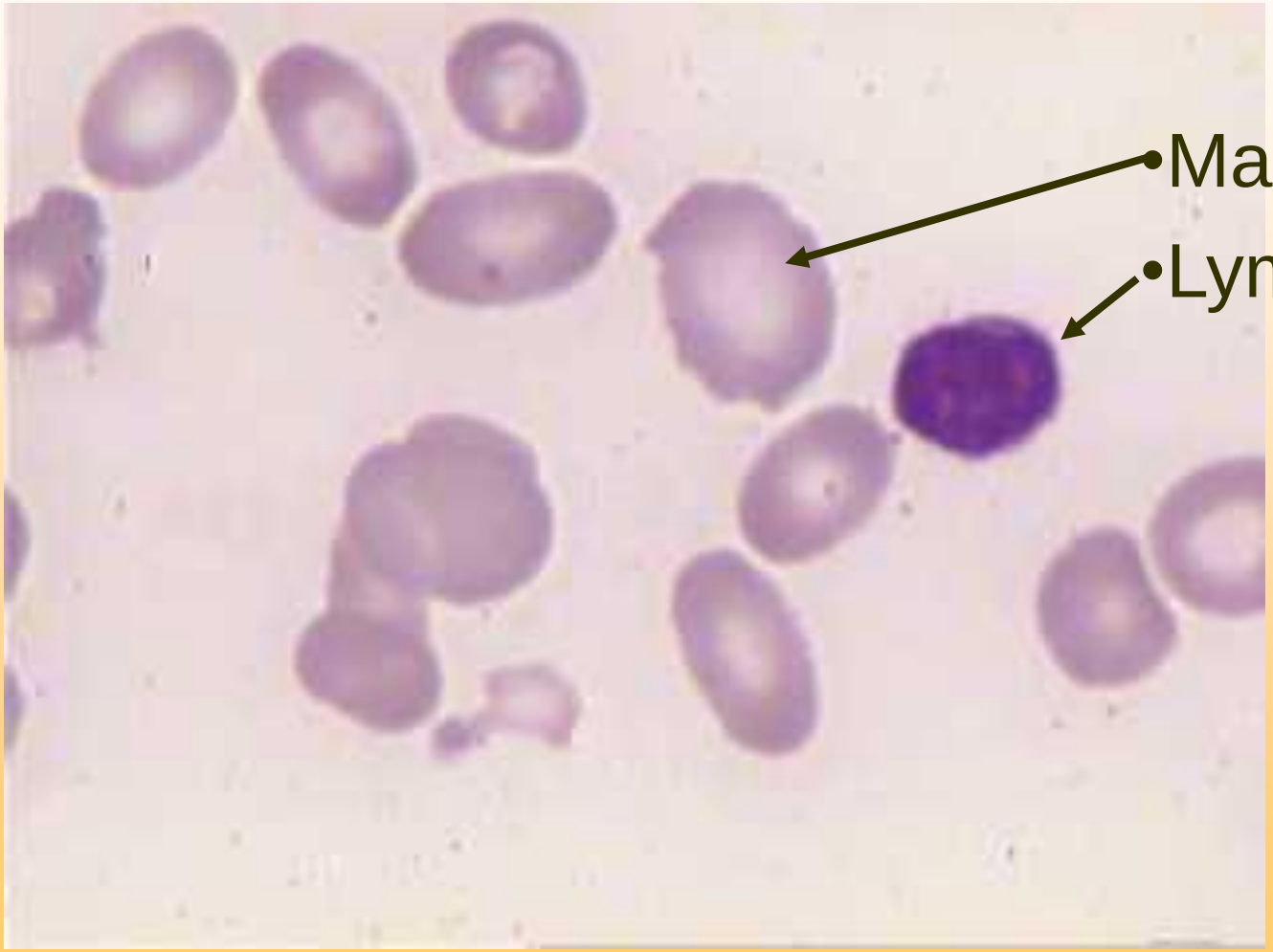
Clinical Cases

Nail bed - Hematoma

- Red
- Blue/Gr
- Brown

Contusion - Hematoma

Megaloblastic Anemia

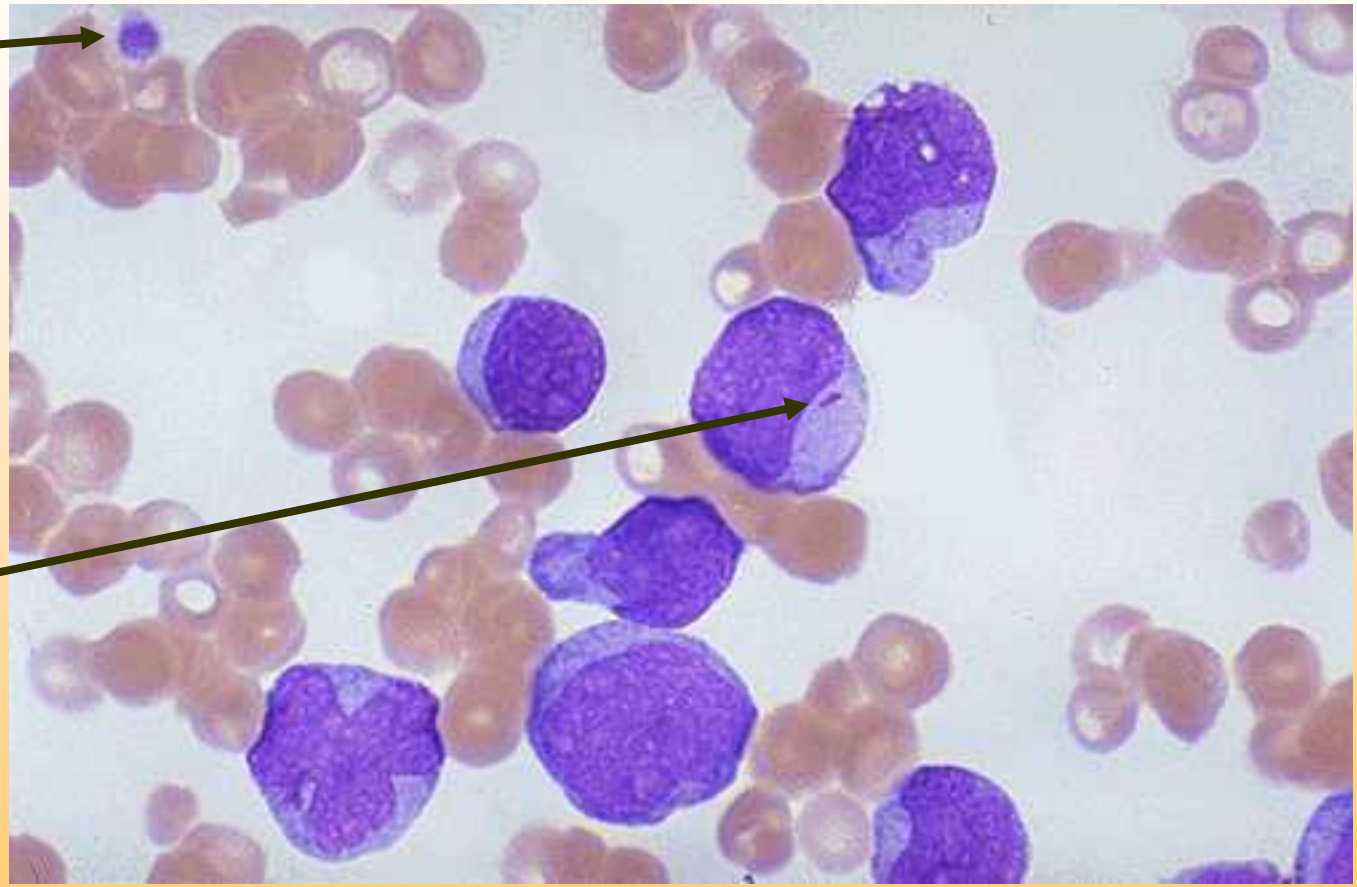


Leukemia (AML-M4)

Platelet

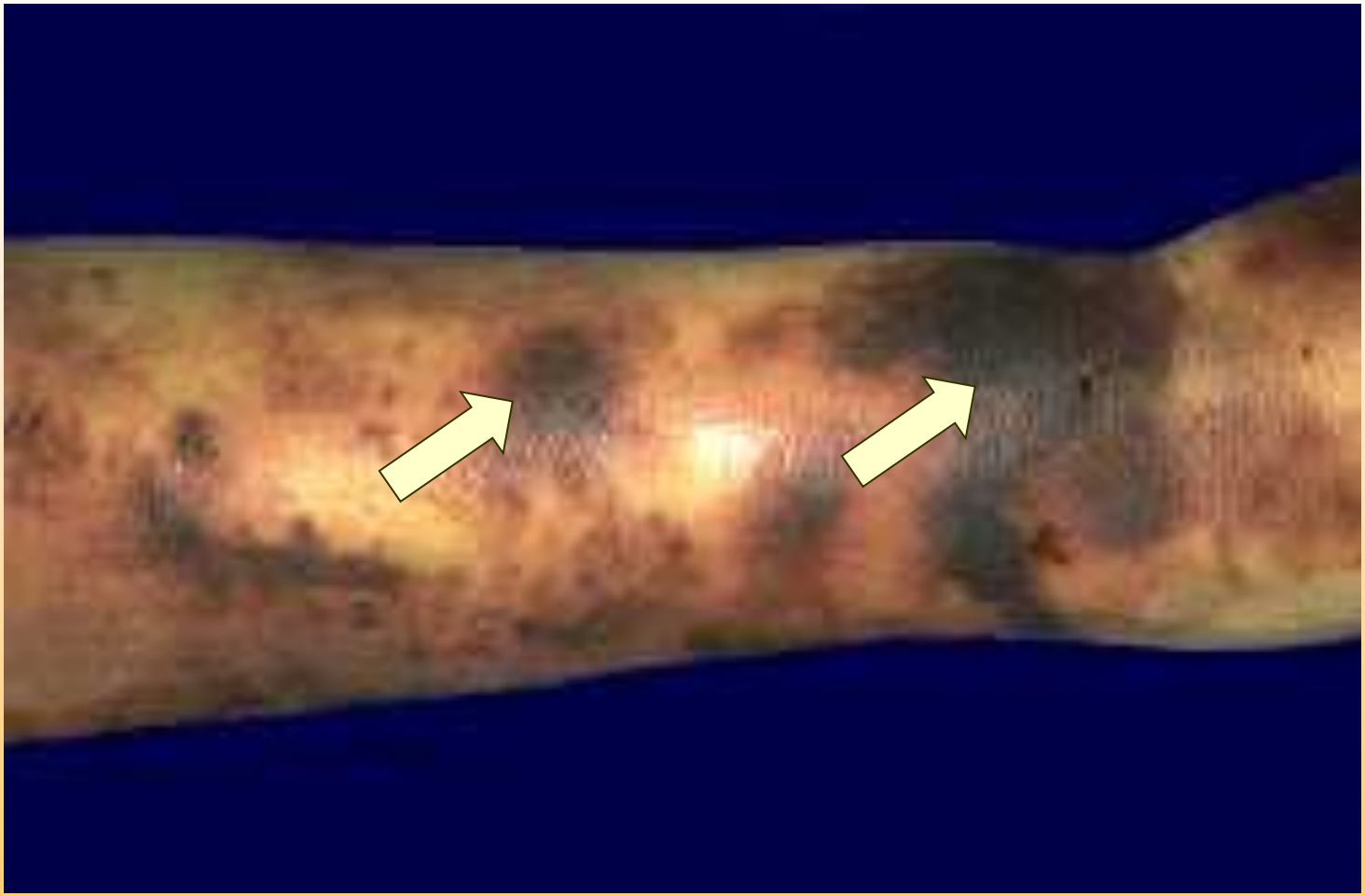
Myeloid Blasts

Auer Rod



Petechiae & Echymoses -↓Plt

Petechiae & Echymoses -↓Plt



Bleeding-Coagulation disorder

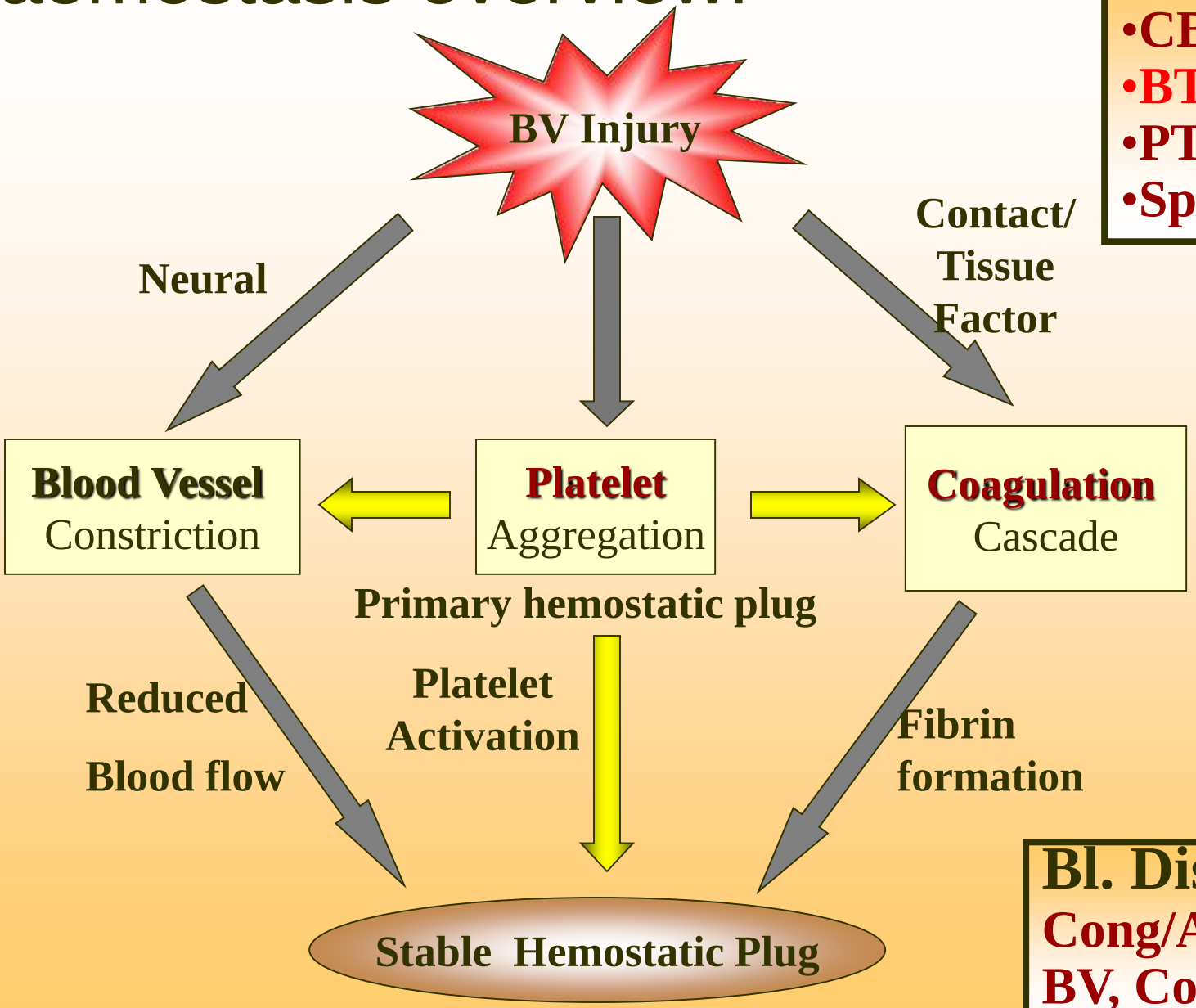
- Deep bleeding
- Haematoma
- Joint bleeds
- Haemophilia

Sub Conjuctival Haemorrhage

Low PLT

Dengue – Hemorrhagic fever ↓Plt

Haemostasis overview:



Lab Tests

- CBC-Plt
- BT,(CT)
- PT, PTT,TT
- Special tests

Bl. Disorders:

Cong/Acqured

BV, Coag, PLT