# BLEEDING DISORDERS (HAEMORRHAGIC DIATHESIS)

- Bleeding disorders or haemorrhagic diatheses are a group of disorders characterised by defective haemostasis with abnormal bleeding.
- Bleeding may be spontaneous in the form of small haemorrhages into the skin and mucous membranes (e.g. petechiae, purpura,ecchymoses)
- excessive external or internal bleeding following trivial trauma and surgical procedure (e.g. haematoma, haemarthrosis etc).

# CAUSES

- Vascular abnormalities
- Platelet abnormalities
- Coagulation disorders
- Fibrinolytic defects
- Disseminated intravascular coagulation (DIC).

# Investigation of Disordered Vascular Haemostasis

1. BLEEDING TIME
2. HESS CAPILLARY RESISTANCE TEST (TOURNIQUET TEST)

# BLEEDING TIME

- Based on the principle of formation of haemostatic plug following a standard incision on skin.
- Three methods:

1. Duke's method: ear lobe puncture
2. Ivy's method: 2-3 punctures on volar aspect of forearm with a lancet ( Cutting depth- 2-2.5mm) under standardized venous pressure of 40mm Hg.
3. Template method: Larger cut, 6-9mm long and 1mm deep.

- The time the incision takes to stop bleeding is measured.
- Normal range is 3-8 minutes.

A prolonged bleeding time may be due to following causes:

i) Thrombocytopenia.

ii) Disorders of platelet function.

iii) von Willebrand's disease.

iv) Vascular abnormalities (e.g. in Ehlers-Danlos syndrome).

v) Severe deficiency of factor V and XI.

# HESS CAPILLARY RESISTANCE TEST (TOURNIQUET TEST)

- This test is done by tying sphygmomanometer cuff to the upper arm and raising the pressure in it between diastolic and systolic for 5 minutes.
- After deflation, the number of petechiae appearing in the next 5 minutes in 3 $cm^2$ area over the cubital fossa are counted.
- Presence of more than 20 petechiae is considered a positive test.
- The test is positive in

❖ increased capillary fragility

❖ thrombocytopenia.

# Investigation of Platelets and Platelet Function

# Investigation of Platelets and Platelet Function

1. SCREENING TESTS

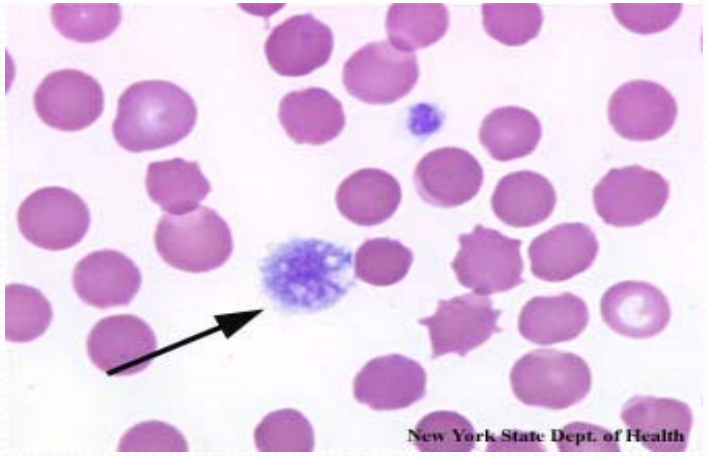
- Skin bleeding time
- Peripheral blood platelet count.

  Thrombocytopenia (<1.5lakhs/cumm)

- Hematological malignancies
- Ingestion of certain drugs
- DIC
- ITP
- Anaemia- Megaloblastic anaemia, aplastic anaemia.

Thrombocytosis (>4.5lakhs/cumm)

- Inflammation
- Following haemorrhage
- Myeloproliferative disorders




- Fresh blood film examination to see the morphologic abnormalities of platelets.
- Giant platelets in myeloproliferative disorder and Bernard Soulier syndrome.

# SPECIAL TESTS

- Platelet adhesion test:
- Whole blood is made to pass over a column of non-siliconised glass beads.
- Proportion of platelets retained are assessed from platelet count done before and after the passage of blood.
- Less than 25% retention is usually observed in Von willebrand disease.

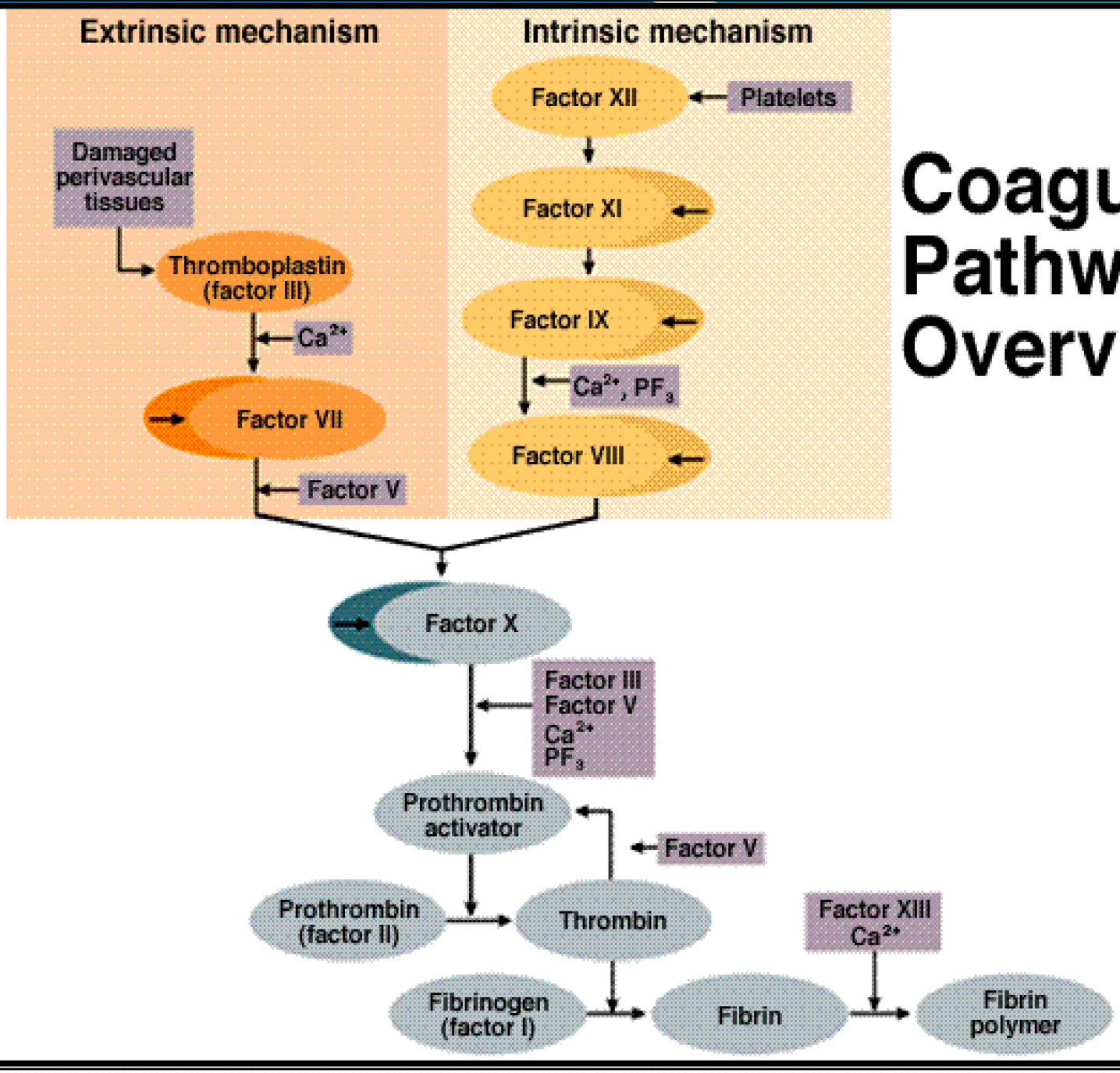
- Aggregation test:
- Special instrument called aggregometer is used.
- Platelet aggregation agent or agonist is added to the platelet rich plasma
- Change in light transmission due to aggregation is recorded with photometer.
- Various agonists: ADP, epinephrine, collagen, arachidonic acid and ristocetin.

- Aggregation response is deficient with ADP, epinephrine, collagen in Glanzmann's thrombasthenia ( Absence of platelet receptor GpIIb-IIIa, necessary for fibrinogen binding during aggregation).

- Defective aggregation with ristocetin but not with other – Von Willibrand disease and Bernard- Soulier syndrome as Ristocetin binds to vWF/GPIb/IX complex and results in agglutination

# Investigation of Blood Coagulation

# Coagulation Pathways — Overview



# Investigation of Blood Coagulation

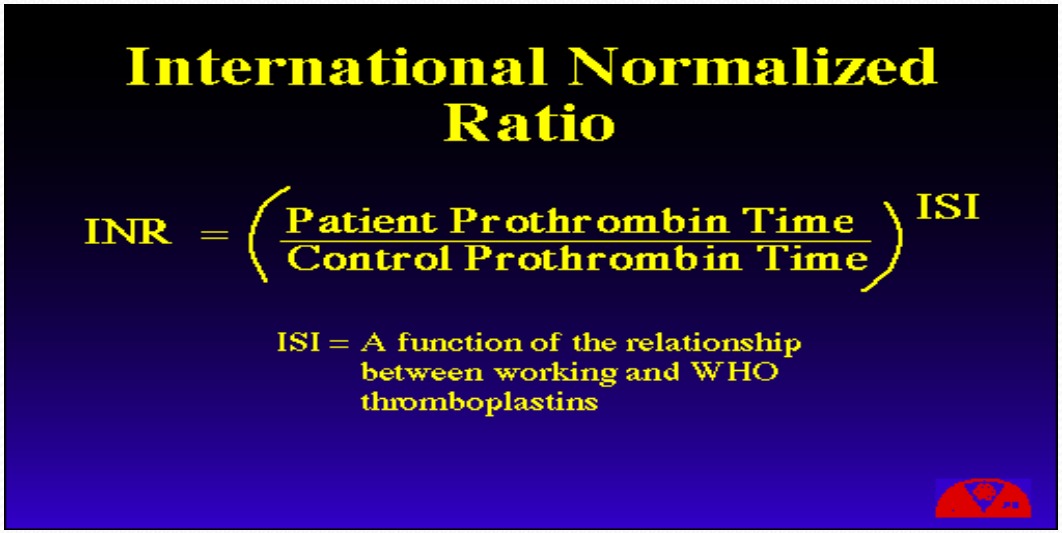
1. **SCREENING TESTS**

- **Whole blood coagulation time**
  - done by various capillary and tube methods
  - limited value, since it is an insensitive and nonspecific test.
  - Normal range is 4-9 minutes at 37°C.
- **One-stage prothrombin time (PT)**
- **Activated partial thromboplastin time (APTT) or partial thromboplastin time with kaolin (PTTK)**
- **Measurement of fibrinogen**

# One-stage prothrombin time (PT)

- Extrinsic and common pathway
- Tissue thromboplastin and calcium are added to platelet poor plasma.
- Clotting time of mixture is noted.
- Commercial tissue thromboplastin is prepared from rabbit brain or lung.
- Normal values depend upon the thromboplastin used
- With most rabbit thromboplastins the range of PT **11-16 sec**

- To ensure uniformity of anticoagulation therapy the results should be reported as INR-international normalized ratio.




- International sensitivity index-determined for each thromboplastin reagent-specific for manufacturer
- Indicated the responsiveness of the particular lot of reagent compared to the international reference thromboplastin

- The common causes of prolonged one-stage PT are as under:

i) Administration of oral anticoagulant drugs.

ii) Liver disease, especially obstructive liver disease.

iii) Vitamin K deficiency.

iv) Disseminated intravascular coagulation.

# Activated partial thromboplastin time (APTT)

- Monitor intrinsic and common pathway
- Platelet poor plasma is incubated with an activator- Kaolin, celite and silica.
- Phospholipid or partial thromboplastin and calcium are then added.
- Normal range is **30-40 sec**.

The common causes of a prolonged PTTK (or APTT) are as follows:

i) Parenteral administration of heparin.

ii) Disseminated intravascular coagulation.

iii) Liver disease.

iv) Inherited def of F VIII or F IX

# Thrombin time

- Thrombin reagent is added to platelet poor plasma.
- Time required for clot formation is noted.
- Normal range is **8-12 sec.**
- Prolongation occurs in

i) Disorder of fibrinogen: afibrinogenaemia, dysfibrinogemaemia.

ii) Chronic liver disease

iii) Increased level of fibrin degradation products.

# SPECIAL TESTS

## 1. Coagulation factor assays:

- PT or APTT is performed using mixture of patient's plasma and factor deficient plasma ( contain all coagulation factors, except one to be assayed).
- The unknown level of the factor activity is compared with a standard control plasma with a known level of activity.
- Results are expressed as percentage of normal activity.
- Normal level for all coagulation factors is 50-150%

**2. Quantitative assays**.

The coagulation factors can be quantitatively assayed by immunological and other chemical methods.

# Investigation of Fibrinolytic System

**SCREENING TEST**

1. Estimation of fibrinogen.
2. Fibrin degradation products (FDP) in the serum.
3. Ethanol gelation test.
4. Euglobin or whole blood lysis time.

# Latex Agglutination test

- A suspension of latex particles coated with anti fibrinogen antibodies or with anti FDP is mixed with serum on a glass slide.
- Agglutination of latex particles- positive test.

# Specific tests

- Functional assays
- Immunological assays by ELISA
- Chromogenic assays of plasminogen activators, plasminogen and FDP.