Haemostatic abnormalities

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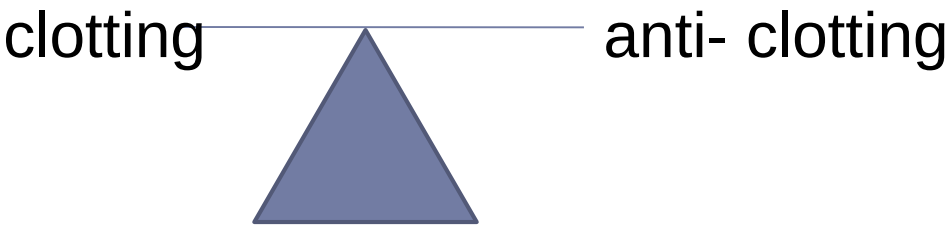
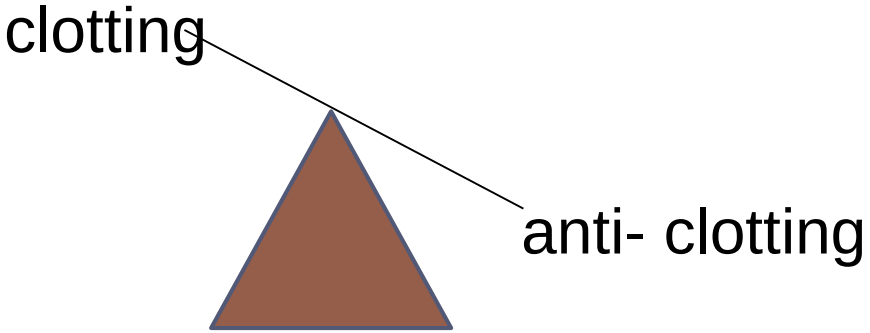
Lecture objectives

- What are abnormalities of haemostasis?
  - Thrombosis
  - Bleeding and clotting disorders
- What are the causes and presentations of thrombosis and bleeding?
- Common examples of bleeding disorders
- How do we investigate a bleeding disorder?

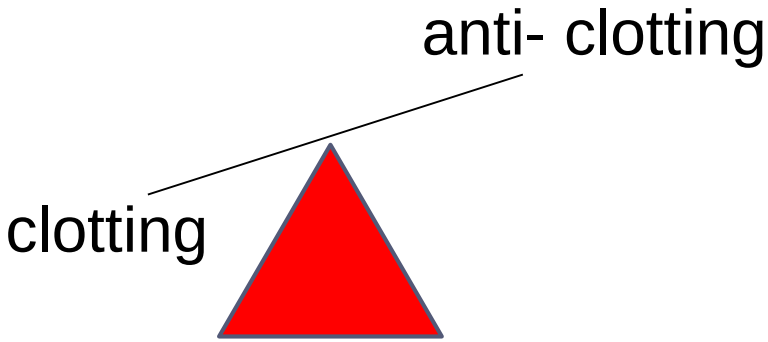
Haemostasis



Abnormalities of haemostasis



BLEEDING



THROMBOSIS
(clotting inside blood vessels)

Thrombosis

- Due to:

↑ activation of clotting pathway OR ↓ anti-clotting pathway activity

- What causes thrombosis?
  - **Accumulation of activated clotting factors** – sluggish flow
  - **Vascular damage and exposure of collagen**
    - Intima damage due to atherosclerotic plaques
  - **Increased tissue thromboplastin generation**
    - Damaged tissues (DIC)

  - Congenital **absence of protein C**
  - Mutations in **protein S, antithrombin III**

How do patients' present?

- Occlusion of arterial supply causing ischaemia
  - E. g. myocardial infarction/ stroke
- Pain and oedema due to venous obstruction
  - E.g. Deep vein thrombosis
- Embolism
  - E. g. pulmonary embolism

Bleeding

- Due to:

↓ activation of clotting pathway OR ↑ fibrinolytic pathway activity

Haemostasis

- Vascular contraction
- Formation of a temporary platelet plug
- Formation of a fibrin clot – clotting pathway

Abnormalities

- Vascular abnormalities
- Abnormalities of platelets
  - deficiency
  - dysfunction
- Abnormalities in clotting pathway

BLEEDING DISORDERS

1. **Due to defective vascular response**

- Abnormality is either in the vessel itself or in perivascular tissue

- Bleeding time is prolonged but clotting time remains normal.

  eg. Scurvy due to vitamin C deficiency

2. Due to platelet defects

Thrombocytopenia or platelet function defects

- Bleeding time is prolonged but clotting time remains normal.

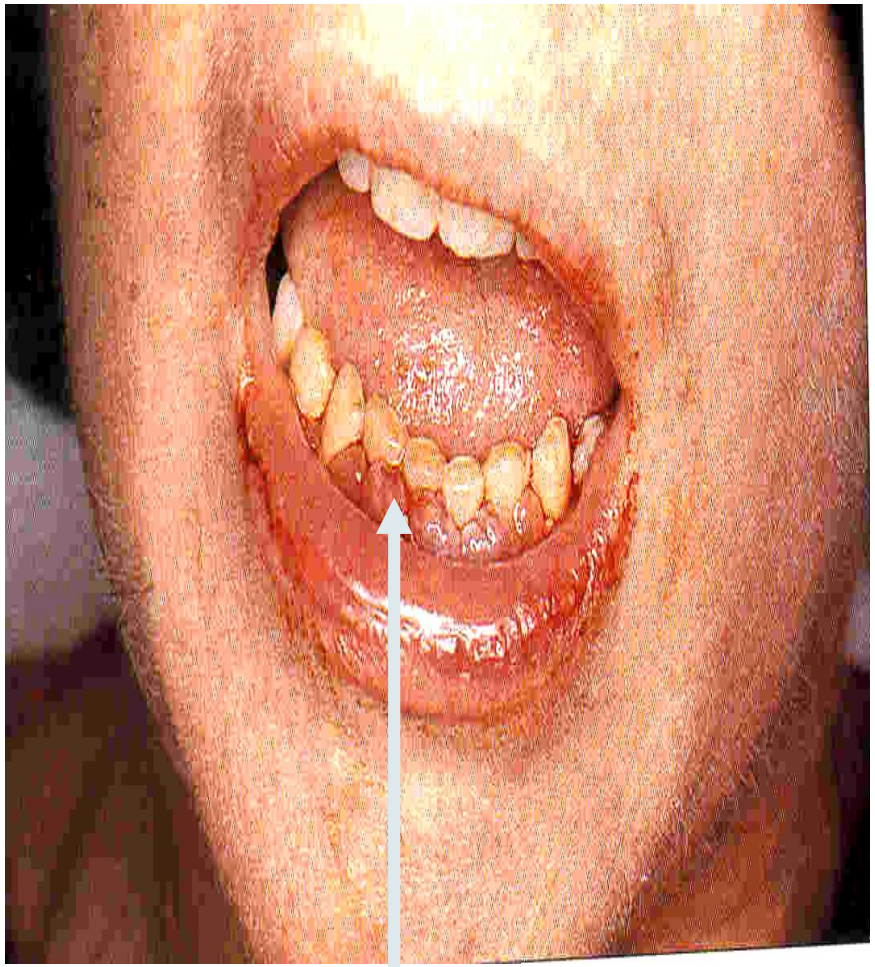
  eg. Dengue haemorrhagic fever

  Idiopathic Thrombocytopenic Purpura (ITP)

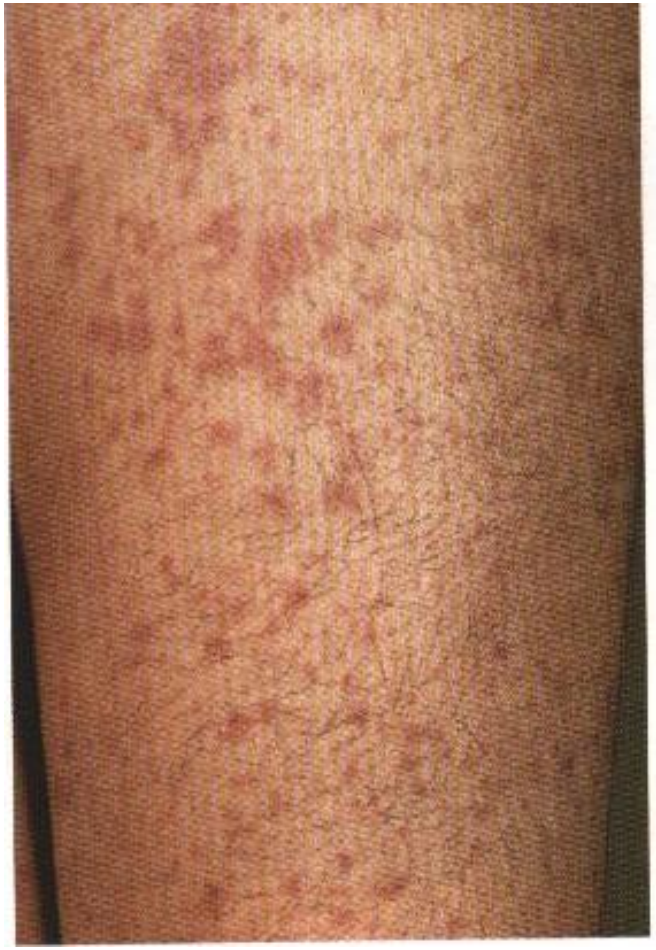
  Viral infections

- Some patients have positive Hess test

  eg. Dengue haemorrhagic fever



Gum bleeding due to thrombocytopenia



Purpura & petechiae due to dengue haemorrhagicc fever

3. Due to coagulation factor deficiency

(I) Hemophilia A and B

- Hemophilia is the most common hereditary disorder of blood coagulation
- Transmitted genetically as a X-linked recessive trait
- Males are affected and females are carriers
- Clotting time and APTT are prolonged
- Bleeding time and prothrombin time are normal

- Hemophilia A is due to factor VIII deficiency and constitute 85% of Hemophiliac patients

- Treated with factor VIII

  e.g. factor VIII concentrate, cryoprecipitate, fresh frozen plasma

- Hemophilia B is due to factor IX deficiency and constitute 15% of Hemophiliac patients

- Is treated with fresh frozen plasma

Haemarthrosis due to Hemophilia A

Haematoma formation due to Hemophilia A

Ecchymoses

(II) von Willebrand disease

- Associated with abnormal platelet adhesion with reduced factor VIII activity
- Inherited as a autosomal dominant disorder
- Primary defect is reduced synthesis of von Willebrand factor (vWF).

- vWF factor promotes platelet adhesion and it is carrier molecule for factor VIII protecting it from premature destruction

- Bleeding time, APTT and clotting time are prolonged.

III. Disseminated Intravascular Coagulation (DIC)

(An acquired bleeding disorder)

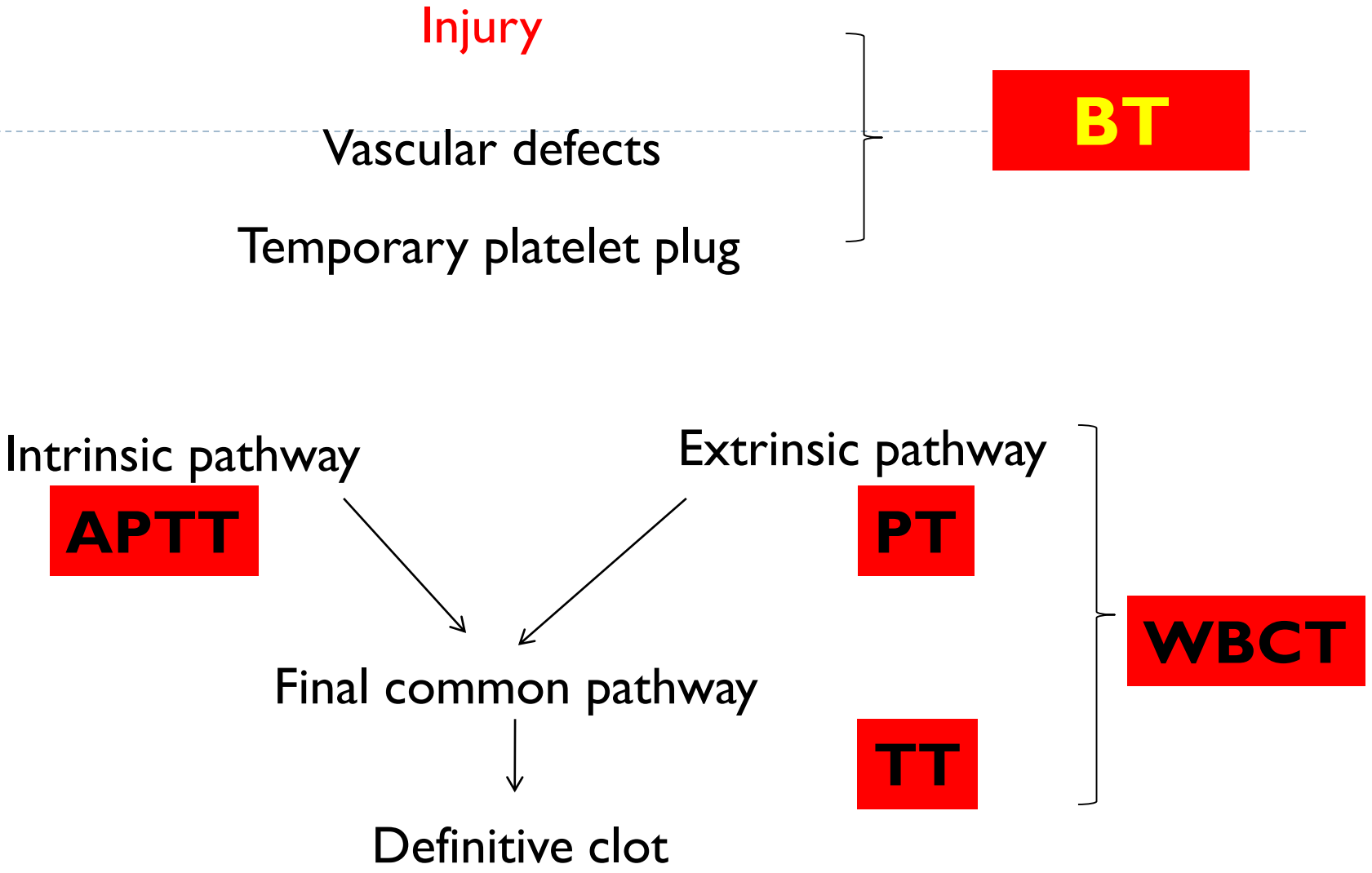
- Patient gets affected due to widespread thrombosis of different blood vessels
- Clotting develops intravascularly
- Due to extensive clotting the clotting factors are exhausted
- So the haemostatic mechanism fails and even venepuncture can cause uncontrolled bleeding

- Intense fibrinolysis is stimulated by thrombi on vessel walls

- The release of Fibrinogen Degradation Products (FDPs) inhibits fibrin polymerization contributing to coagulation defect

- Excessive bleeding can also occur in,
  - Chronic liver diseases
  - Vitamin K deficiency
  - Drugs

Basis of tests used to detect bleeding disorders


Injury
Vascular defects
Temporary platelet plug
BT
Intrinsic pathway
APTT
Extrinsic pathway
PT
WBCT
Final common pathway
TT
Definitive clot

Activated Partial Thromboplastin Time (APTT)

- Citrated plasma
- Add
  - Kaolin (activates factor XII)
  - PL (phospholipids, acts as platelet substrate)
  - Ca^{2+}
- Initiate the intrinsic pathway

Prothrombin time (PT)

- Citrated plasma
- Add
  - Tissue thromboplastin from brain extract
  - Ca^{2+}
- Initiate the extrinsic pathway