# Haematology

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Lec. 1

## Haemostasis & Coagulation disorders

### Objectives:

- Define haemostasis and what are the major components involved in haemostasis?
- How to assess the coagulation status?
- List the main causes of bleeding?
- List causes of bleeding due to vascular disorders?
- List causes of thrombocytopenia?
- -What is the meaning of immune thrombocytopenia purpura? Cause, pathogenesis,diagnosis?
- Define post-transfusion purpura?

**Haemostasis:** refers to the process whereby blood coagulation is initiated and terminated in a tightly regulated fashion, together with the removal (or fibrinolysis) of the clot as part of vascular remodeling.

The **five major** components involved in haemostasis are:

**1.Blood vessels:**The endothelial cell forms a barrier between platelets and plasma clotting factors and the subendothelial connected tissues . Also they produce substances that have important role in coagulation.

**2.Platelets:** The main function of platelets is 1)-the formation of the primary haemostatic plug. 2)- release of platelet activating and procoagulant molecules.

**3. Coagulation factors :** include coagulation factors : ( I) fibrinogen ,(II) thrombin ,V,VII,VIII,IX,X,XI,XII,XIII& von Willebran Factor (VWF). Most coagulation factors are synthesized by hepatocytes.An exception is von Willebran Factor (VWF)which is synthesized by endothelial cells & megakaryocytes.

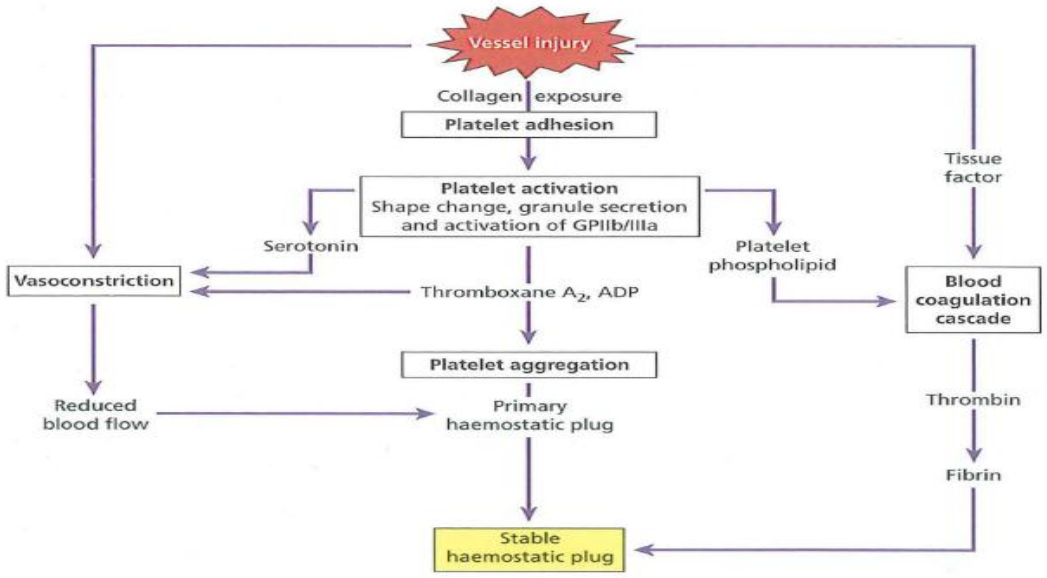
The central event in the coagulation pathways is the production of thrombin, which acts upon fibrinogen to produce fibrin and thus the fibrin clot. This clot is further strengthened by the crosslinking action of factor XIII, which itself is activated by thrombin.

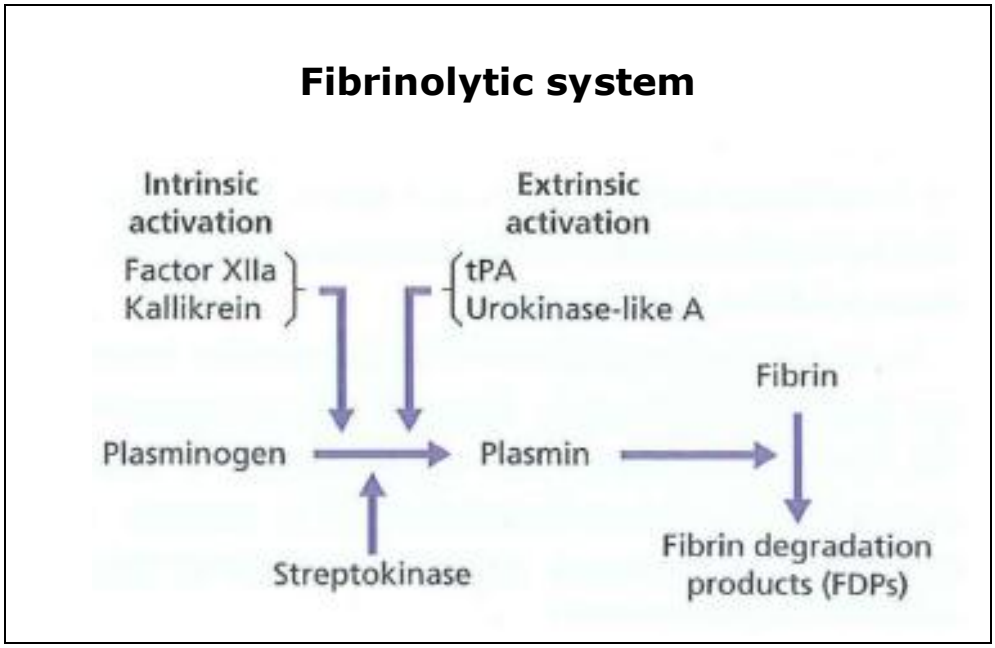
**4. Coagulation inhibitors :**Coagulation is normally localized to the site of injury &is controlled by a number of naturally occurring anticoagulant proteins ,which are activated during

haemostasis.These include :Tissue factor pathway inhibitor(TFPI), Protien C , Protien S , Antithrombin.

**5. Fibrinolysis** : Fibrinolysis (like coagulation) is a normal haemostatic response to vascular injury. Plasminogen is converted to plasmin by tissue plasminogen activator (tPA) & urokinase (uPA). Plasmin acts on fibrinogen &fibrin. **Cleavage of peptide bonds in fibrin and fibrinogen produces fibrin degradation product s FDP** .

**The involvement of blood vessels, platelets and blood coagulation in haemostasis**






**Assessment of Coagulation Status**:
**1.**Clinical assessment.
**2.**Labroratory assessment.

***Clinical Assessment*:** includes:
**-** A personal history.
**-** A family history.
**-** A drug history.
**-** Physical examination: should look for evidence of haemorrhage ,including the presence of petechiae,ecchymoses or bruises .

***Purpura* :** bleeding into the skin &mucous membranes.
***Petechia*:** pinpoint cutaneous haemorrhages,a form of purpura.
***Ecchymosis*:** Large cutaneous haemorrhage,a form of purpura.
***Bruise* :** Bleeding into subcutaneous tissues

***Laboratory assessment of Coagulation:***
Tests used to evaluate different aspects of hemostasis are the following:
•***Bleeding time:*** Prolongation generally indicates a *defect in platelet numbers or function.*
•***Platelet counts:*** The reference range is 150 to 400 × $10^9$/L.

•***Prothrombin time (PT):*** This assay tests the *extrinsic* and common coagulation pathways. *A prolonged PT can result from*

*deficiency or dysfunction of: factor VII, factors X, V, prothrombin, or fibrinogen.*

•***Partial thromboplastin time (PTT**):* This assay tests the *intrinsic* and common clotting pathways. *Prolongation of the PTT can be due to deficiency or dysfunction of: factors VIII, IX, XI, or XII, factors X, V, prothrombin, or fibrinogen.*

***.Thrombin time (TT):*** is sensitive to a deficiency of fibrinogen or inhibition of thrombin by heparin or FDPs.

. **Others** :

Specific clotting factors assay.
Fibrinogen assay.
Fibrin degredation products (FDP) .
Platelet function tests.

## Bleeding Disorders:

***Excessive bleeding*** can result from:

**1.Vascular disorders.**
**2. Thrombocytopenia or platelets dysfunction.**
**3. Defective coagulation.**
**4. Combinations of these.**

### 1.Vascular disorders:

The abnormality is either in the vessels themselves or in the perivascular connectiveTissues. Usually no serious bleeding problems. Most often, they induce small hemorrhages in the skin or mucous membranes.

***The platelet count, bleeding time, and results of the coagulation tests (PT, PTT) are usually normal***.

-Vascular defects may be inherited or acquired.

**■ Inherited vascular disorders:**

• ***Hereditary haemorrhagic telangiectasia**:* an autosomal dominant disorder characterized by dilated microvascular swellings develop in the skin, mucous membranes and internal organs.

•***Connective tissue disorders*** : In the Ehlers-Danlos syndrome.

**▪Acquired vascular defects:**

• **Simple easy bruising**: is a common benign disorder which occurs in otherwise healthy women, especially those of child-bearing age.

• **Senile purpura**: caused by atrophy of the supporting tissues of cutaneous blood vessels is seen mainly on dorsal aspects of the forearms and hands

•. **Many bacterial, viral or rickettsial infections** may cause purpura from vascular damage by the organism or as a result of immtme complex formation (e.g. measles, or meningococcal septicaemia).

• **The Henoch-Schonlein syndrome**:

- usually seen in children ,often follows an acute upper respiratory tract infection.

-It is an immoglobulin A (IgA)-mediated vasculitis.

- It is characterized by a purpuric rash, usually most prominent on the buttocks and ,extensor surfaces of the lower legs and elbows. *colicky abdominal pain* (presumably due to focal hemorrhages into the gastrointestinal tract), *polyarthralgia,* and acute *glomerulonephritis.*

- It is usually a self limiting condition but occasional patients develop renal failure.

•**Scurvy**. In vitamin C deficiency, perifollicular petechiae.

• **Steroid purpura**. is caused by defective vascular supportive tissue.

## *2. Thrombocytopenia*

***Thrombocytopenia*** *can be defined as* platelet count of **100× $10^9$ /L or less** .

It is characterized by spontaneous skin purpura and mucosal haemorrhage and prolonged bleeding after trauma .

-***A prolonged bleeding time****, and a normal PT and PTT.*

-Spontaneous bleeding becomes evident when counts fall below 20× $10^9$ cell/L

## -According to mechanism causes of thrombocytopenia are :

**1-Failure of platelet production**

**-2Increased destruction of platelets**

**3-Abnormal distribution of platelets**
**4-Dilutional loss**

## ■1.Failure of platelet production :

**This is the most common cause of thrombocytopenia and is usually part of a generalized bone marrow failure.**

- **Causes include:Cytotoxic drugs , radiotherapy ,aplastic anaemia, blood malignancies like Leukaemia , marrow infiltration ( e.g. carcinoma, lymphoma ),megaloblastic anaemia , HIV infection**

**Selective megakaryocyte depression may result from drug toxicity or viral infection.**

**Rarely it is congenital e.g.**

- **Wiskott–Aldrich syndrome (WAS) :**thrombocytopenia with eczema ,immune deficiency and small size platelets

**Bernard–Soulier syndrome** -

Autosomal recessive disease with thrombocytopenia , large platelet and platelet dysfunction.

## ■ 2. Increased destruction of platelets:

***A)Immunologic destruction:***

***- Autoimmune***: immune thrombocytopenic purpura(ITP) , systemic lupus Erythematosus (SLE)

-***Alloimmune***: post-transfusion and neonatal.

***-Drugs*:** heparin

***B ) Nonimmunologic destruction:***

-Disseminated intravascular coagulation (DIC).

-Thrombotic thrombocytopenic purpura (TTP).

## ■3.Abnormal distribution of platelets:

***-- Splenomegaly*** Thrombocytopenia , may develop in any patient with marked splenomegaly , Up to 90% of platelets may be sequestered in the spleen whereas normally the spleen contains one third of bodys 'platelets.

■ 4.**Dilutional loss**:-

Massive transfusions (more than 10 units over a 24-h period) can produce a dilutional thrombocytopenia. Blood stored for longer than 24 hours contains virtually no viable platelets ; thus , plasma volume and red cell mass are reconstituted by transfusion , but the number of circulating platelets is relatively reduced.

## Immune thrombocytopenic purpura (ITP):

Platelet autoantibodies (usually IgG) result in the premature removal of platelets from the circulation by macrophages of the reticuloendothelial system, especially the spleen . The normal lifespan of a platelet is 7-10 days but in ITP this is reduced to a few hours.

▫▫▫ ***ITP may be chronic or acute :-***

- ***Chronic immune thrombocytopenic purpura***

- A relatively common disorder.

- The highest incidence is in adult aged 15-50 years , women more than men.

-Treatment is usually needed.

-It is either: 1. Idiopathic( usually). Or

2. occur in association with other diseases such as systemic lupus erythematosus (SLE) , chronic lymphocytic leukaemia (CLL), lymphoma .

- ***Acute immune thrombocytopenic purpura*:**

**-**Most common in children **,** with equal incidence in boys & girls.

**-**Usually the episode follows vaccination or an infection such as chickenpox or infectious mononucleosis.

-Spontaneous remission is usual & often no treatment is needed.

***Diagnosis of ITP :-***

1.The platelet count is decreased .

2. The blood film shows reduced numbers of platelets.

3. The bone marrow shows normal or increased numbers of megakaryocytes.

4 . Tests to detect autoantibodies.

**Post-transfusion purpura**

Thrombocytopenia occurring approximately 10 days after a blood transfusion due to antibodies in the recipient developing against platelet antigen on transfused platelets (absent from the patient's own platelets).