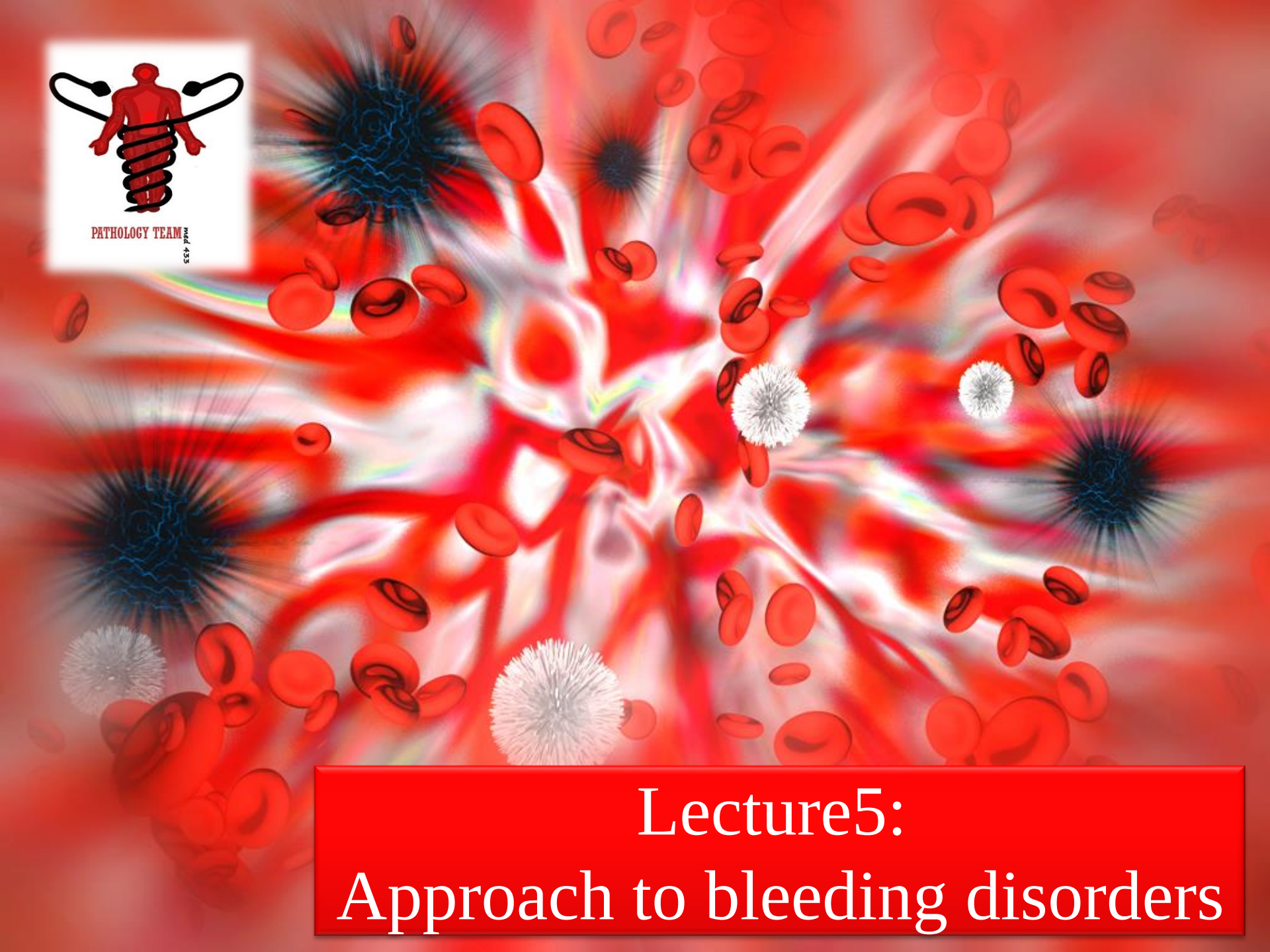
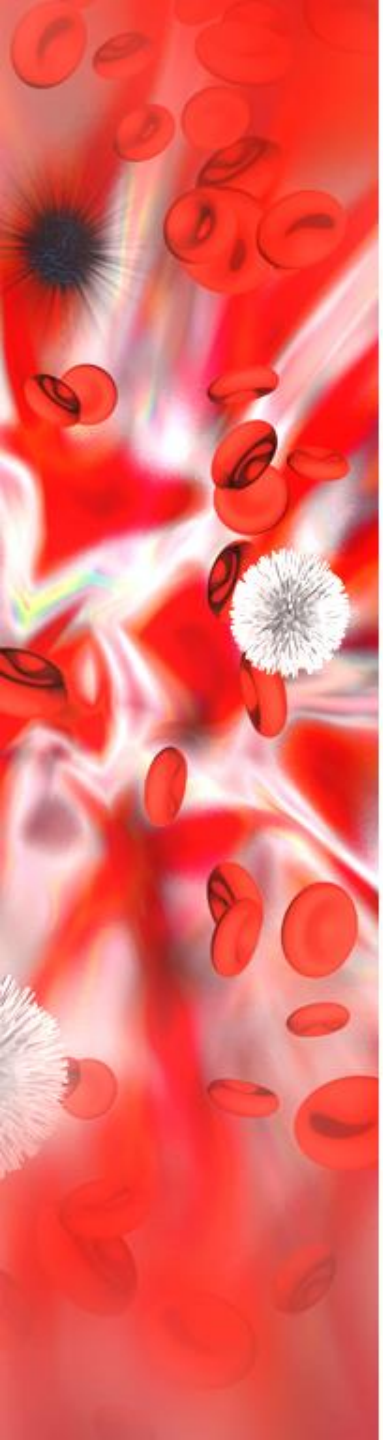


Lecture5:
Approach to bleeding disorders



Normal Haemostasis

The cessation of bleeding following trauma to blood vessel results from three processes :

1. The contraction of vessel wall.
2. The formation of the platelets plug at the site of the break in the vessel wall.
3. The formation of a fibrin clot within and around the platelet aggregates.

- **Normal plate count = 150-400x10^9/L**
- Normal Plate Size Mpv = 7.3-11.1 Fl
- Normal Platelet Diameter = 1-2.5 µ

Platelet Formation Is By Segmentation Of The Cytoplasm Of The Megakaryocyte(1) In The Bone Marrow.

Clinical distinction :

bleeding due to:

1. **platelet defects (in number or function) or blood vessel wall defects called mucocutaneous bleeding**

Patient presents with : superficial bleeding into the skin (purpura) and from epithelial surfaces of organs.

2. clotting defects (coagulation defects) called musculoskeletal bleeding.

presents with bleeding into deep tissue and muscles (*haematomas*) and joints (*haemarthrosis*)

(1) Megakaryocyte : origin of platelets

Vascular disorders :

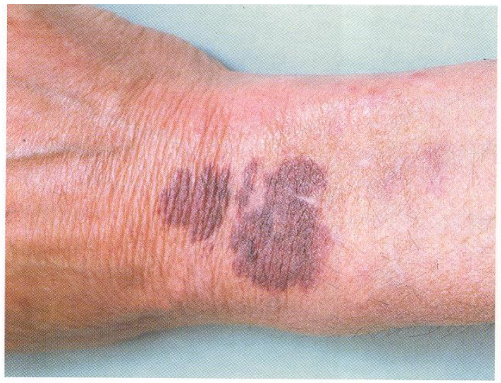
Hereditary vascular disorders :

E.g. Hereditary Haemorrhagic Telangiectasia (Rendu-weber-osler syndrome)

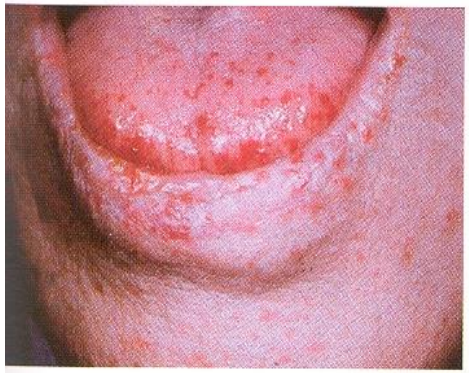
Acquired vascular Disorder:

E.g. Allergic purpura (Henoch-Schonlein purpura)

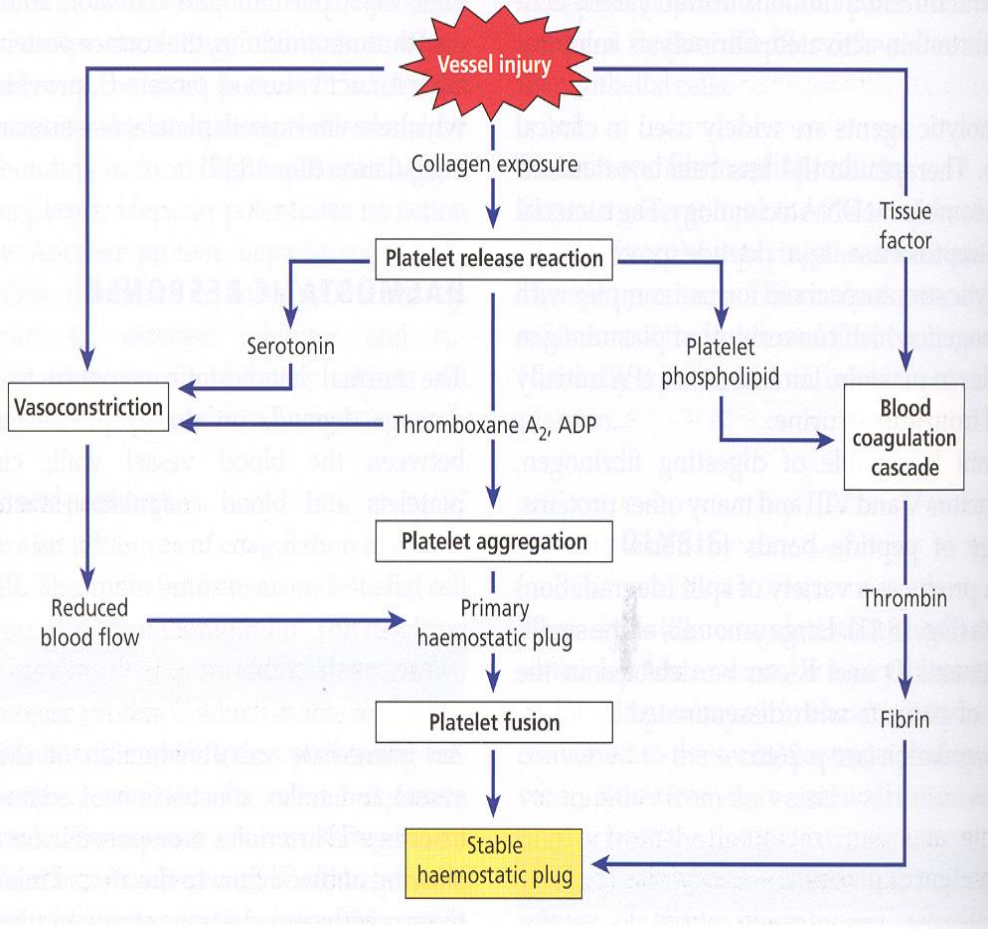
And Senile purpura (in Older)



Senile purpura



Purpura: a small hemorrhage in the skin or mucous membrane



Storage areas in platelets :

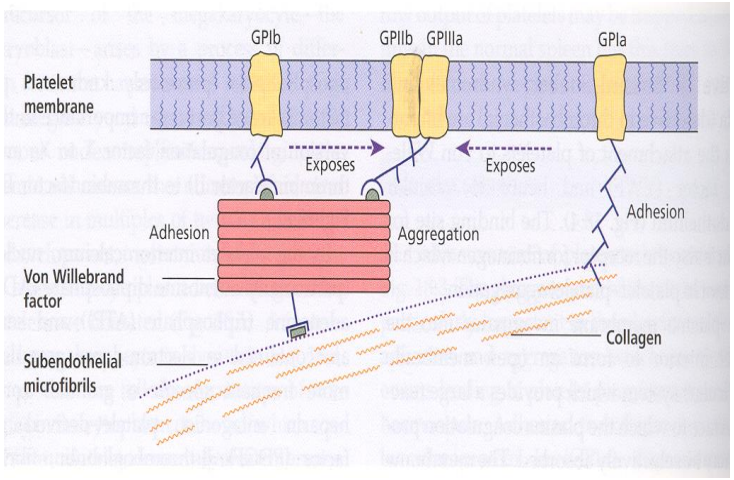
Storage areas	Contents
Deans body	Nucleotides ADP, Serotonin, Calcium
α - granule	Fibrinogen, vWF, Other proteins
lysosome	

Glycoproteins in platelet membrane :

Without Glycoprotein the platelets can not adhere to subendothelial microfibrils:

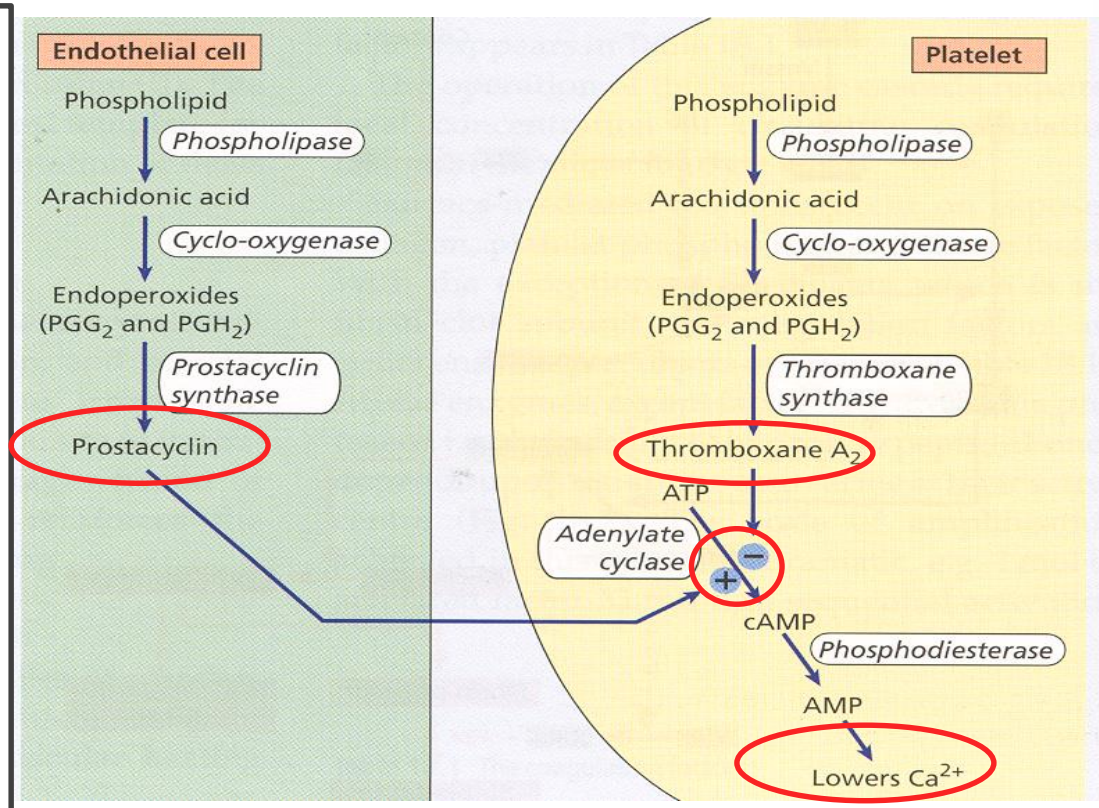
Glycoprotein	
Gp Ia	Direct Adhesion
Gp Ib	Need von willebrand factor
Gp IIb	Need von willebrand factor

- Gp Ib deficiency is associated with BernardSoluier syndrome.
- Gp IIb/IIIa deficiency is associated with Glanzmann's Thrombasthenia disease.
(very important)



- Prostacyclin from endothelial cell stimulates ATP to cAMP conversion "inhibits aggregation"
- thromboxane A2 from platelets inhibits ATP to cAMP conversion "stimulates aggregation "

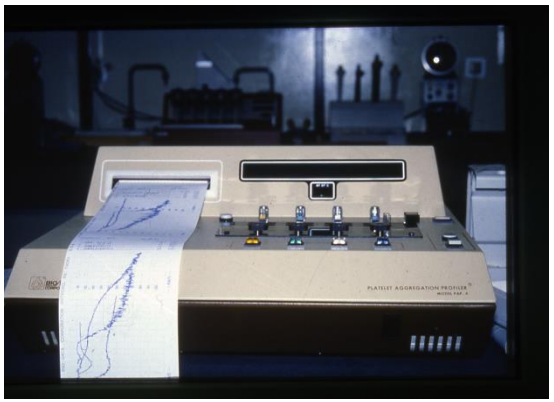
* cAMP is important to decrease the Ca++ in platelet (this step is important to prevent platelets aggregation)



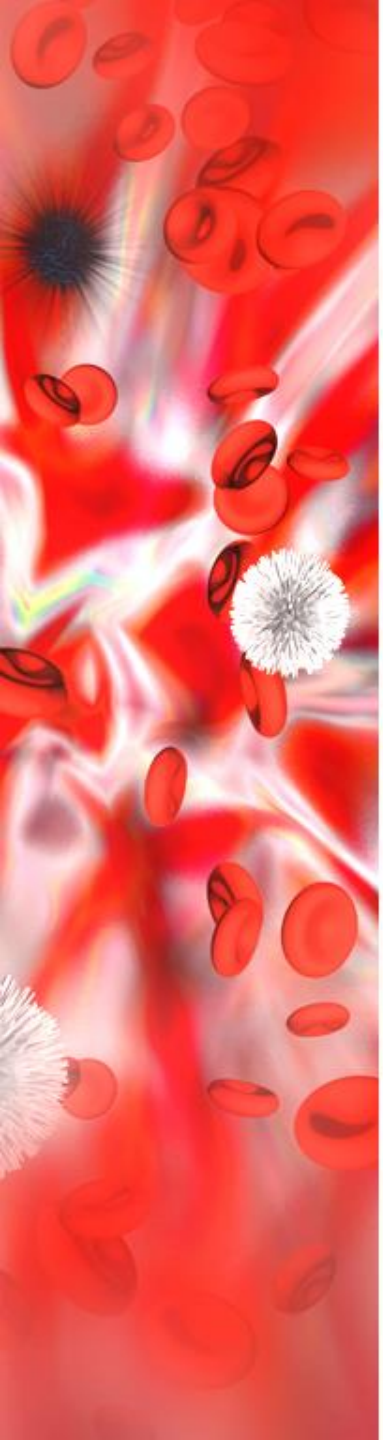
Measurements of platelet function :

1. **Bleeding Time (by simplate) :**
   Normal : 3 – 8 min.

2. **Platelet aggregation test.**



Platelet aggregation test.



Hereditary Platelet Disorders

❖ Inherited disorders of platelet function :

Membrane abnormalities

- Bernard – Soulier syndrome
- Thrombasthenia
- Platelet factor–3 deficiency

Intracellular abnormalities

Storage-pool (dense body) deficiency

- Hermansky – Pudlak syndrome
- Wiskott – Aldrich syndrome
- Chediak – Higashi syndrome
- Thrombocytopenia with absent radii
- Idiopathic storage – pool disease

α- granule deficiency

- Gray platelet syndrome

Combined deficiency of dense bodies and α granules

Defects of thromboxane synthesis

- Cyclo-oxygenase deficiency
- Thromboxane synthetase Deficiency
- Defective response to thromboxane

Miscellaneous

- Epstein's syndrome
- May-Hegglin anomaly

❖ Causes of acquired platelet dysfunction :

- Uraemia
- Myeloproliferative disorders
- Drugs
- Scurvy
- Sever Burns
- Valvular and congenital heart disease
- Acute leukaemias and pre-leukaemic states
- Liver disease
- chrinic hypoglycemia
- Dysproteinaemias

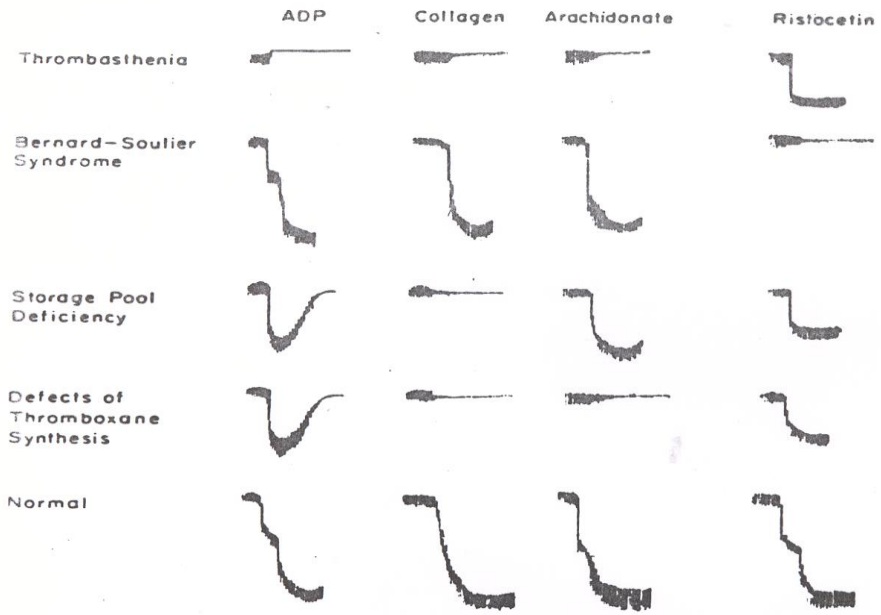
*You should know only the diseases in red colour

1- What Bernard-Soulier syndrome
2- What Thrombasthenia
3- What Gray platelet syndrome
4- What May-Hegglin anomaly

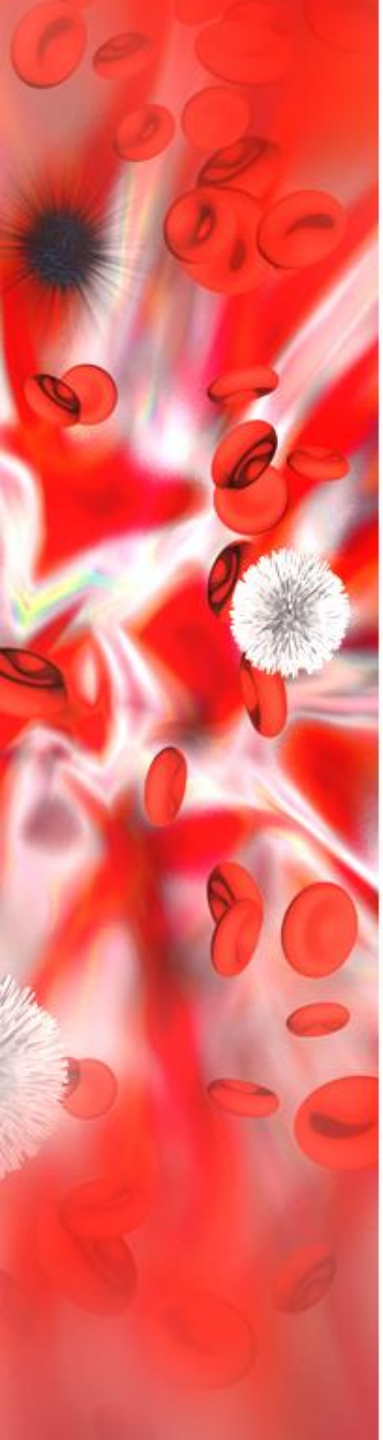
Inherited disorders of platelets function In Platelets aggregation test

	ADP	collagen	arachidonate	Ristocetin
normal	reaction	reaction	reaction	reaction
Thrombasthenia	no reaction (linear)	no reaction (linear)	no reaction (linear)	reaction
Bernard – Soluier syndrome	reaction	reaction	reaction	no reaction (linear)
Storage-pool deficiency	reaction	no reaction (linear)	reaction	reaction
Defects of thromboxane synthesis	reaction	no reaction (linear)	no reaction (linear)	reaction

Important . especially Bernard – Soluier syndrome and Thrombasthenia



Aggregation patterns in platelet disorders.



Thrombocytopenia (decreased platelets count)

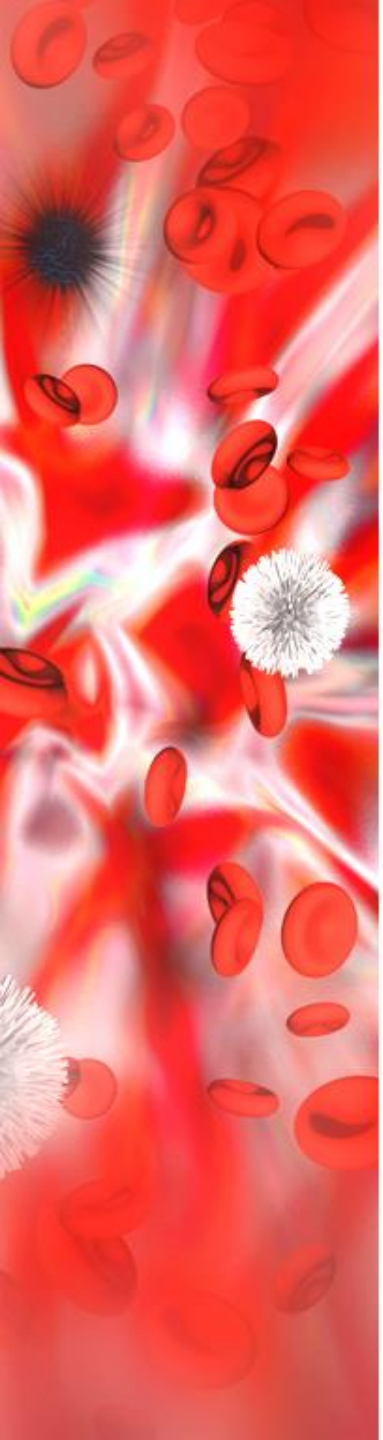
Causes of thrombocytopenia

- Failure of platelet production
- Selective megakaryocyte depression
- marrow infiltration e.g. carcinoma, lymphoma
- cytotoxic drugs
- Radiotherapy
- aplastic anaemia
- megaloblastic anaemia
- multiple myeloma
- Immune
- associated with systemic lups erythematosus
- chronic lymphocytic leukaemia or lymphoma
- infections: HIV, other viruses, malaria
- Heparin
- Thrombotic thrombocytopenic purpura
- myelodysplastic syndromes
- Splenomegaly
- Massive transfusion of stored blood to bleeding patients
- autoimmune (idiopathic)

Briefly: any disease affects the bone marrow or the immune system

1. Thrombocytopenia as a result of drugs or toxins

Bone marrow suppression
Antimicrobials
Diuretics
Anticonvulsants
Antidiabetics
Analgesics



2. Immune thrombocytopenia

Clinical features of immune thrombocytopenia

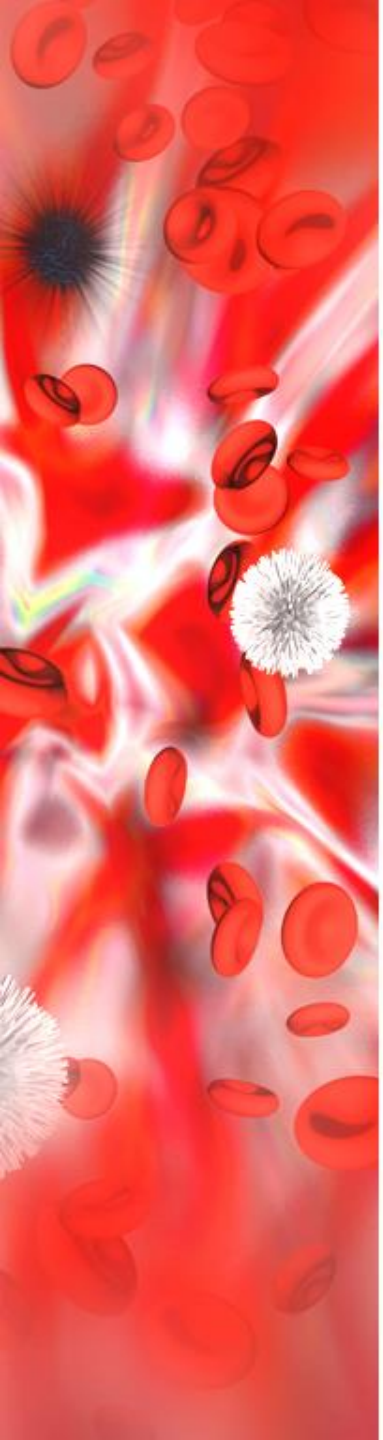
Degree	Symptoms	Physical findings
Mild (>50 000/mm^3)	None	None
Moderate (30-50 000/mm^3)	Bruising with minor trauma	Scattered ecchymoses at trauma site
Severe (10-30 000/mm^3)	Spontaneous bruising menorrhagia	Petechiae and purpura , more prominent on extremities
Marked (<10 000mm^3)	spontaneous brusing, mucosal bleeding, risk for CNS bleeding	Generalized purpura, epistaxis, GU bleeding CNS symptoms

Laboratory features of immune thrombocytopenia :

- Thrombocytpenia with increased number of large platelets
- Increased number and size of megakaryocytes.
- Reduced intravascular platelet survival.
- Elevated levels of platelet-associated IgG.

Treatment of immune thrombocytopenia :

IV immunoglobulin , corticosteroids and splenectomy



Thrombotic thrombocytopenic purpura (TTP) – Hemolytic uremic syndrome (HUS):

Clinical Features:

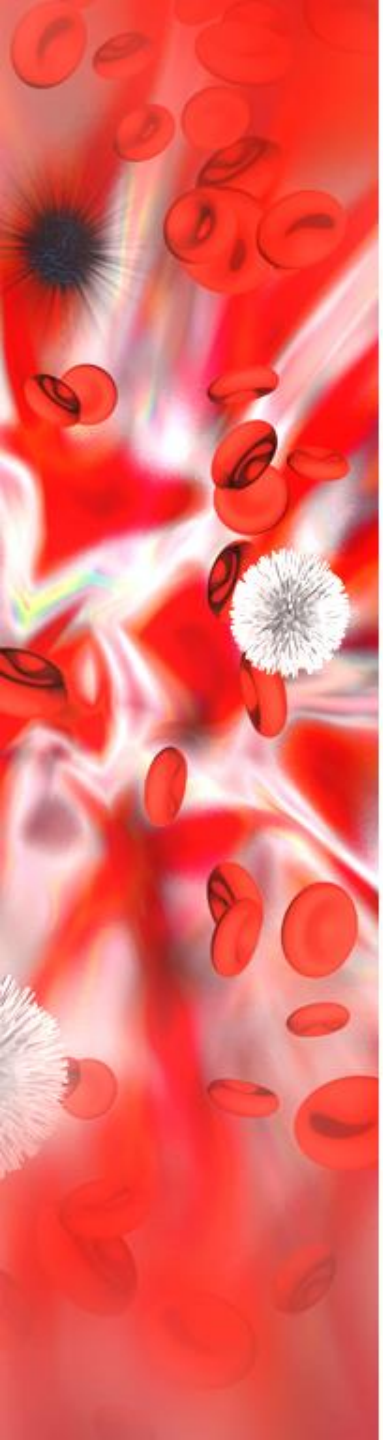
- Fever.
- Thrombocytopenic purpura.
- Hemolytic anemia.
- Neurological symptoms.(more common in TTP)
- Renal dysfunction. (more common in HUS)
- genetic predisposition
- It associates with other condition

Causes:

- Infections (E.coli type 0157, Shigella dysenteriae serotype 1, and viral infection).
- Hypersensitivity.
- Oral contraceptive.
- Autoimmune diseases e.g. SLE and rheumatoid arthritis.
- Chemotherapy.

Treatment of TTP & HUS :

1. Plasma pheresis & FFP
2. Platelets transfusion is contraindicated
3. Renal dialysis
4. Treatment of the cause



Blood count film

IN case of low platelet count

Check out these :

1. Bone marrow examination
2. Platelets antibodies
3. Screen tests for DIC (**disseminated intravascular coagulation)**

IN case of normal platelet count

Check out these :

1. Bleeding time
2. Platelet aggregation
3. Other special platelet tests: nucleotide, pool measurement

4. Factor VII clotting assay: vWF assay , vWF antigen assay

Done by

Yara Abdullah

Revised by

Khalid Alsuhaibani

Team leader: Abdulrahman Al-Thaqib

Contact us:

haematology433@gmail.com

@haematology433