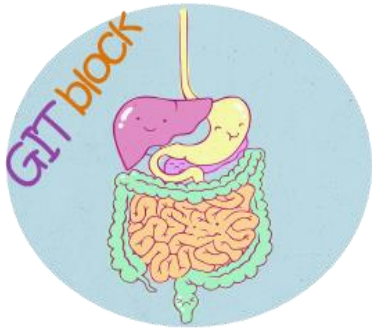


APPROACH TO BLEEDING DISORDERS

To understand you should study coagulation cascade 1st

You should know only the diseases in red color

Color coding

- important
- Extra info
- Notes from lecturer

دعاء فبل المذاكرة :

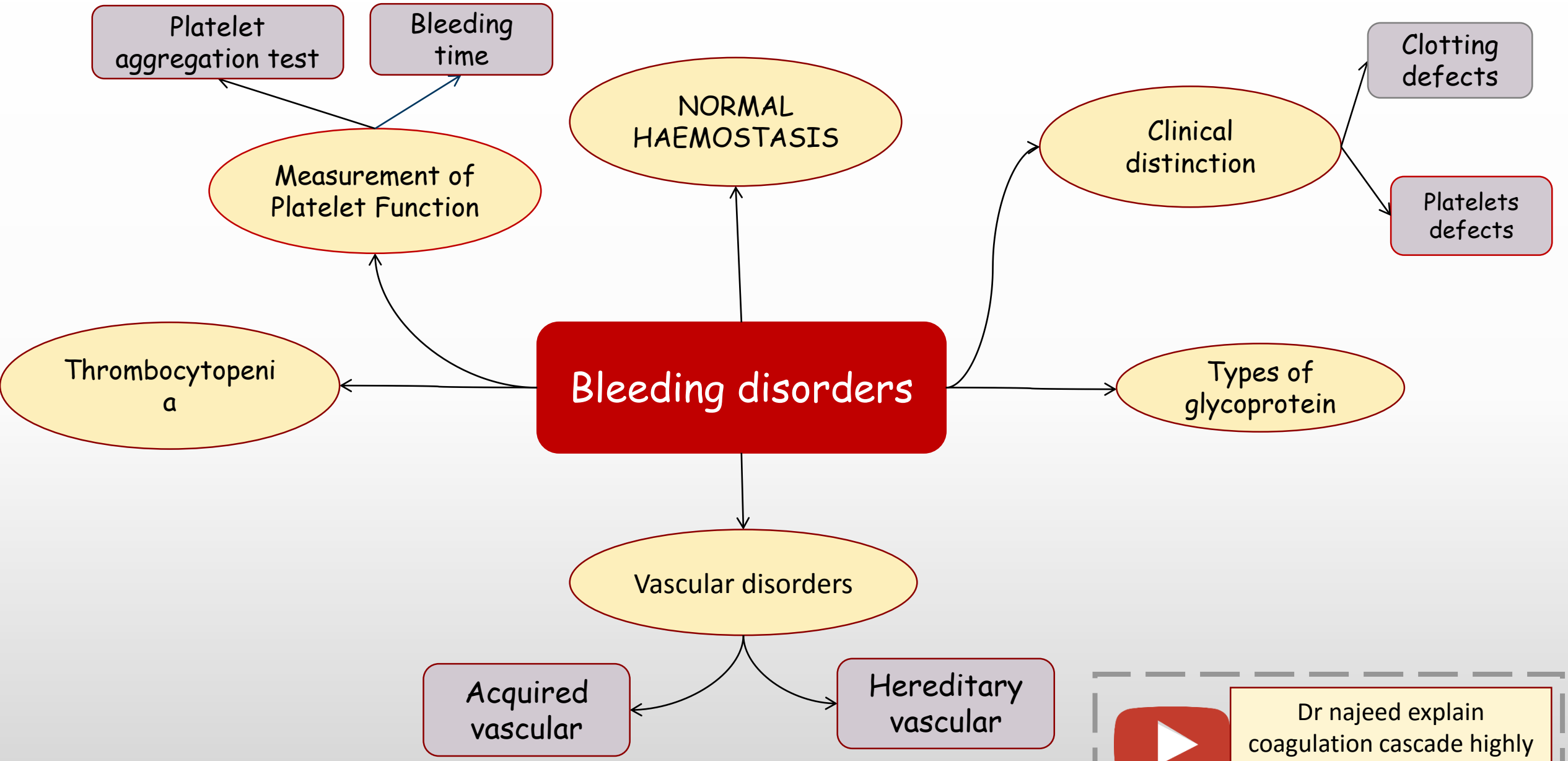
(اللهم أني أسالك فهم النبين و حفظ الملرسلين و الملائكة المقربين اللهم اجعل السنتنا عامرة بذكرك و قلوبنا بخشيتك، أنك على كل شيئا قدير و حسبنا الله نعم الوكيل)

DON’T FORGET to check our editing file : haematology edit

Please don’t hesitate to contact us on:Haematology434@gmail.com

	Male	Female
Hemoglobin(g/dL)	13.5-17.5	11.5-15.5
Hematocrit (PCV) (%)	40-52	36-48
Red Cell Count ($\times 10^{12}$)	4.5-6.5	3.9-5.6
Mean Cell Volume (MCV) (fL)	80-95	
Mean Cell Hemoglobin (MCH) (pg)	30-35	
MCHC %	31 - 37	
Platelet count	140-450x10^3/L	
NORMAL PLATELET SIZE MPV	7.2-11.1 fl	
NORMAL PLATELET DIAMETER	1-2.5 µ	
WBC	4000-11,000 /L	
Segmented (neutrophils)	1.8-7.8	
Eos	0-0.45	
Baso	0-0.20	
Lymphs	1.0-4.8	
Monos	0-0.80	

A Good Doctor Knows normal CBC



Dr najeed explain coagulation cascade highly recommended

NORMAL HAEMOSTASIS:

The cessation of bleeding following trauma to blood vessel is result from three process:

1. The contractions of vessel walls.
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.

Investigations of Bleeding Disorders

- Clinical Features:
- Complaints
- Full Clinical Examinations
- History of Bleeding
- Family History of Bleeding
- If bleeding present, what is the pattern of bleeding episodes

	Range
PLATELET COUNT	140-450x10^3/L
PLATELET SIZE MPV	7.2-11.1 fl
PLATELET DIAMETER	1-2.5 µ
PLATELET LIFE SPAN	7-10 days

PLATELET FORMATION IS BY SEGMENTATION OF THE CYTOPLASM OF THE MEGAKARYOCYTE IN THE BONE MARROW.

M for platelet **M**other **M**egakalocyte

Which produces 1000-5000

Clinical distinction

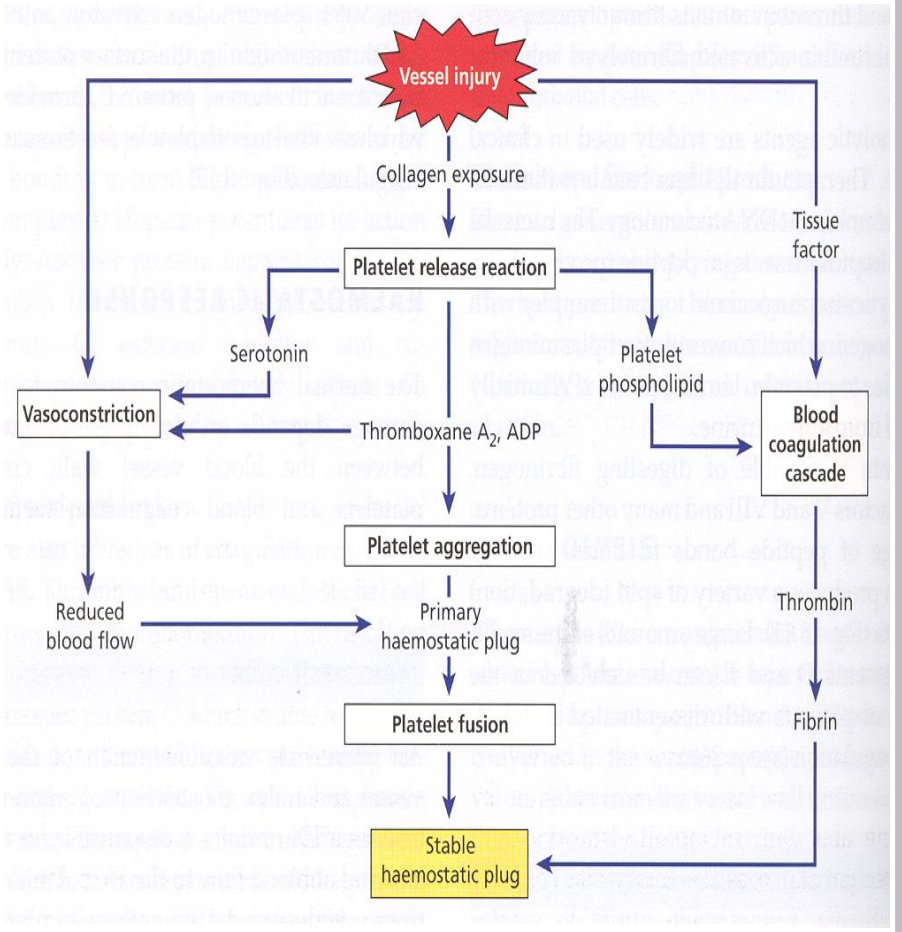
Bleeding due to :

- Platelets defects:

usually present with superficial bleeding into the skin (purpura) and from epithelial surfaces of organs. This is called mucocutaneous bleeding

- Clotting defects:

usually present with bleeding into deep tissue and muscles (haematomas) and joints (haemarthrosis) this is called musculoskeletal bleeding.



Vascular disorders

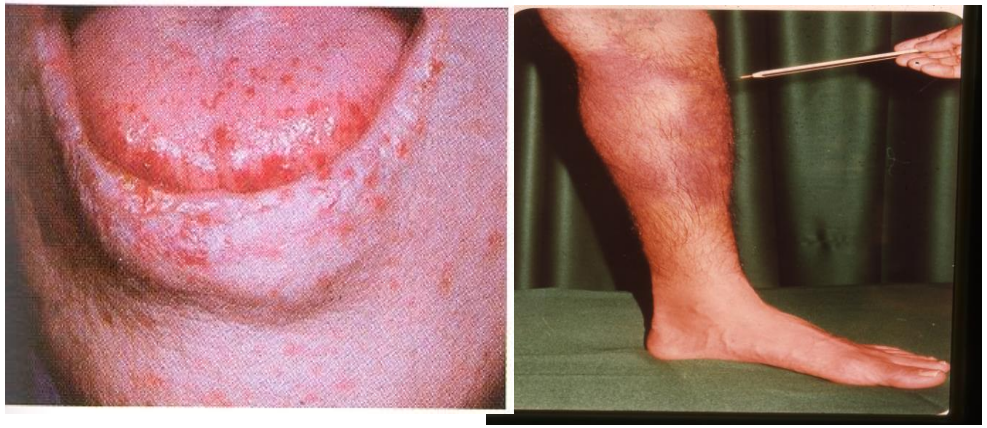
And they can hereditary or acquired

Hereditary vascular disorders:

* More in lips and mouth *

- Hereditary Haemorrhagic Telangiectasia

(Rendu weber-osler syndrome) the common one

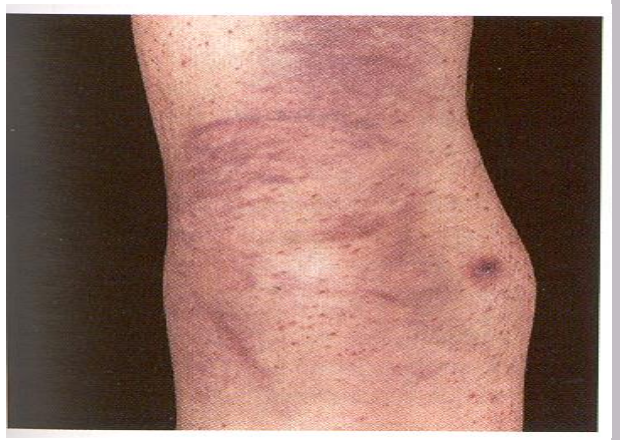


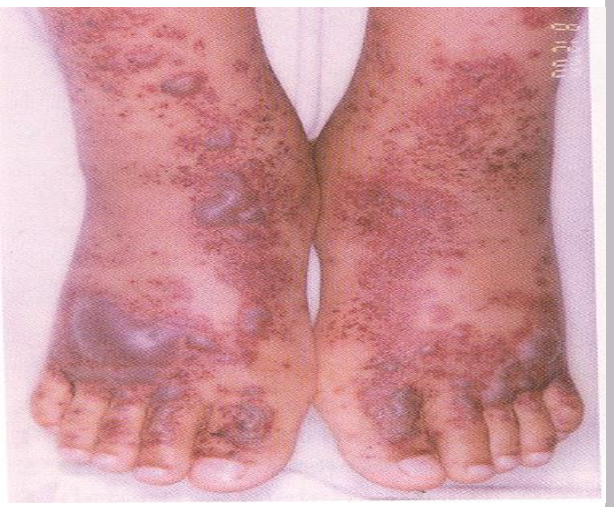
Acquired vascular Disorder.

- Allergic purpura (Henoch-Schonlein purpura)
- Paraproteinemia and amyloidosis.
- Senile purpura

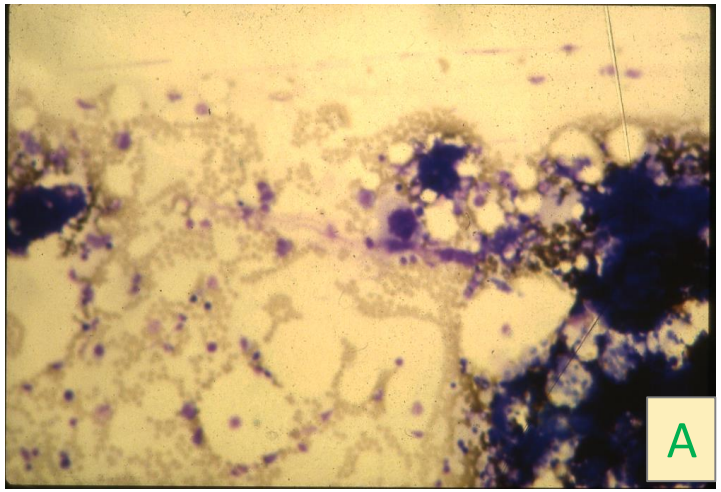
(dark blue normal in old people more in hands)

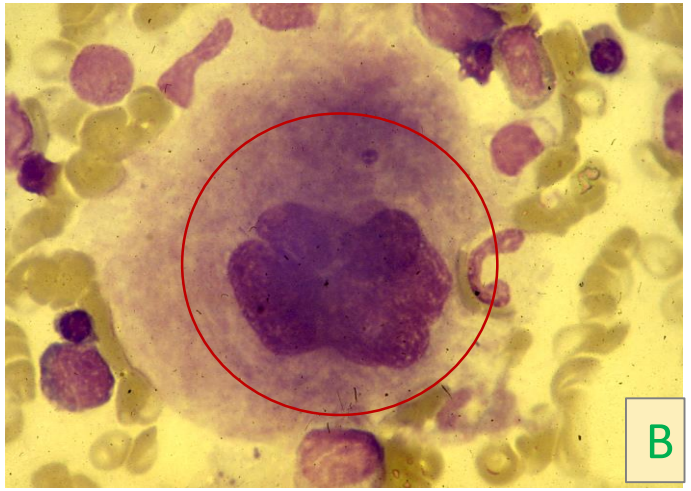
- Drug-induced vascular purpuras (Steroid therapy, sulfonamides, iodides, aspirin, digoxin, methyldopa).
- Vitamin C Deficiency (Scurvy)
- Purpura simplex (Easy brusability)
- Psychogenic purpura
- Purpura associated with infections.

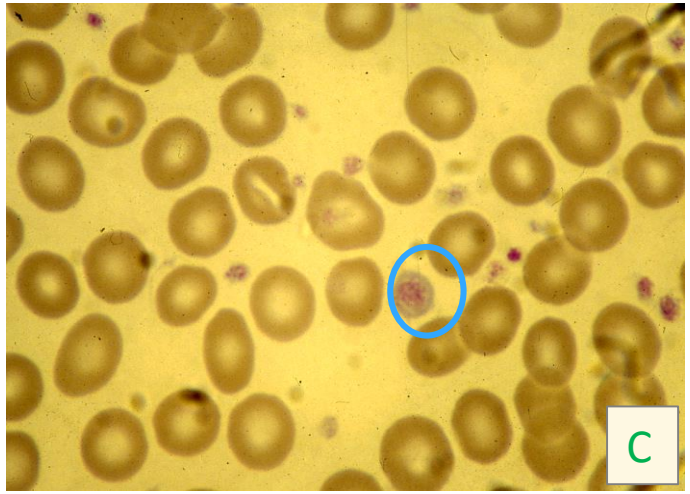




Blood smear film shows:



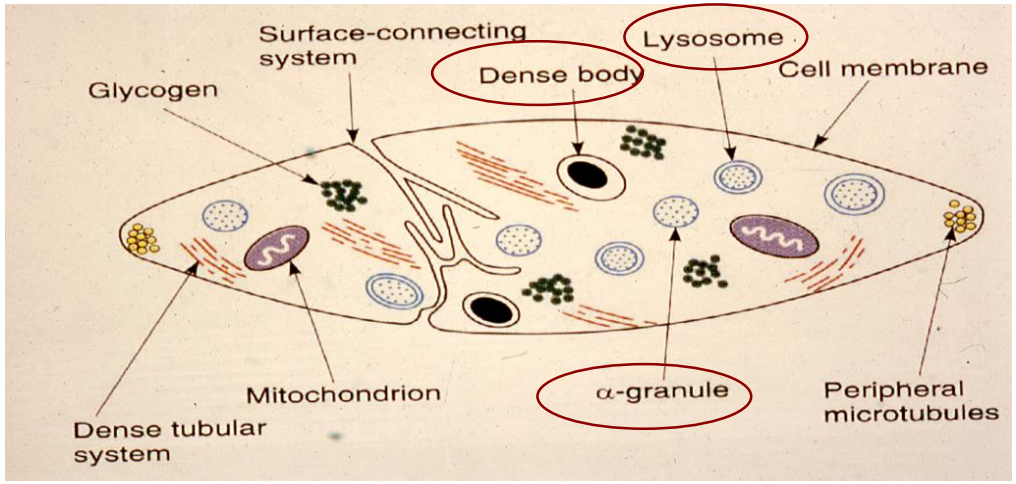




A) Bone marrow

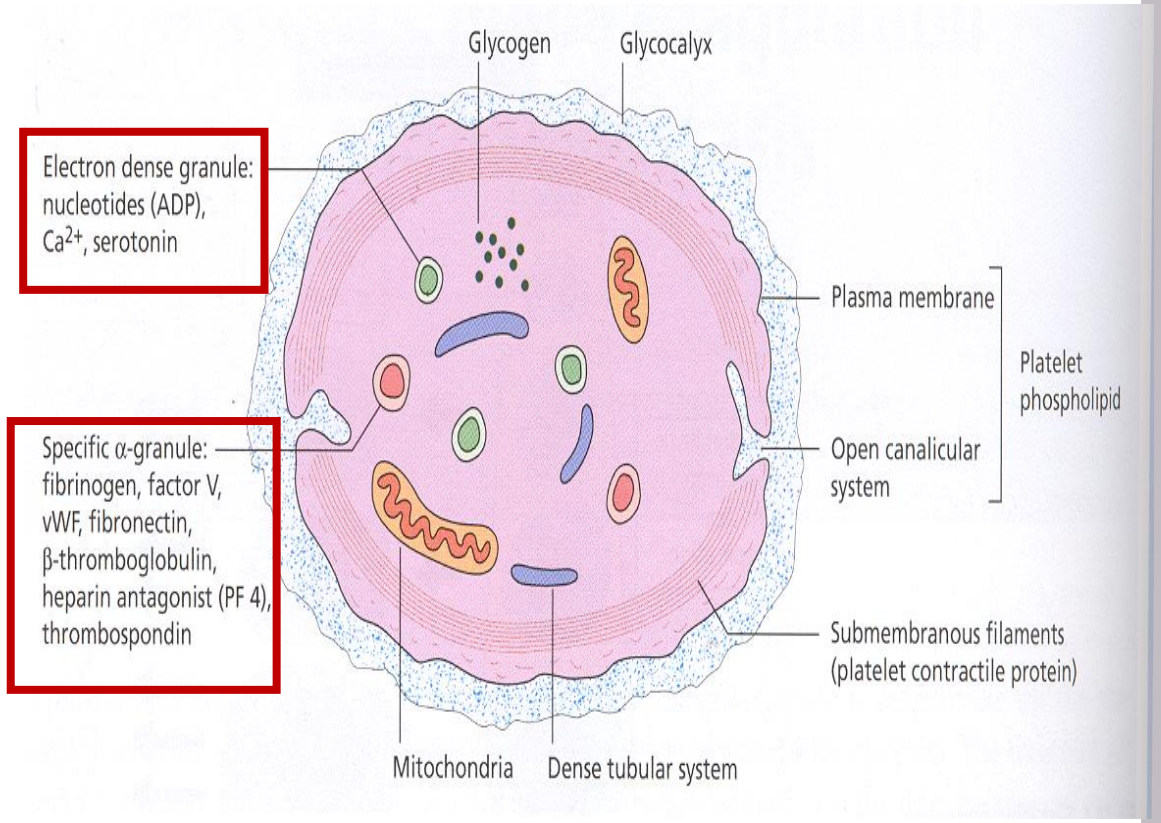
B) Megakaryocyte in the bone marrow has abundent purble cytoplasm which later fragmentate and gives the platelets
(one megakaryocyte gives 1000 - 5000platelets).

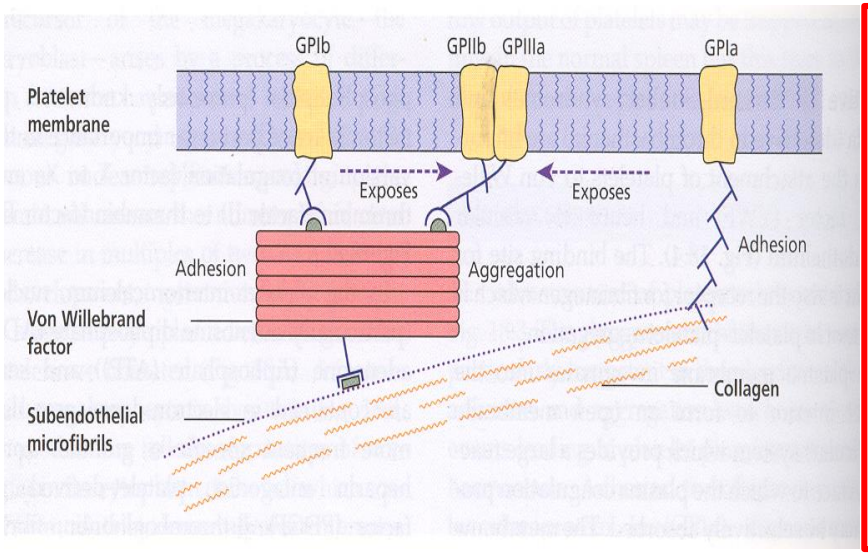
C) Platelets appear in the peripheral blood film as small purple dots.



Storage granules include:

- Dense body : ADP / Ca++ / serotonin
- lysosomes
- α-granule: Fibrinogen / factor V / vWF / fibronectin / B thromboglobulin / heparin antagonist /thrombospordin





There are 4 glycoprotein:

Without Glycoprotein the platelets can not adhere to subendothelial microfibrils

- GPIa : direct adhesion the subendothelial
- GPIIb / GPIIIa : indirect adhesion (Von Willebrand factor) deficiency is associated with Glanzmann's Thrombasthenia disease.
- GPIb :indirect adhesion via
- (Von Willebrand factor) deficiency is associated with BernardSoluier syndrome.

Measurement of Platelet Function by:

- Bleeding time test :

Normal range from 3-8 min.

- Platelet aggregation test:

is specific for platelets and performed by adding some substances (e.g. collagen, ADP, Arachidonate, Ristocetin) to the platelets and the result of the reaction comes on graph.

Factors:

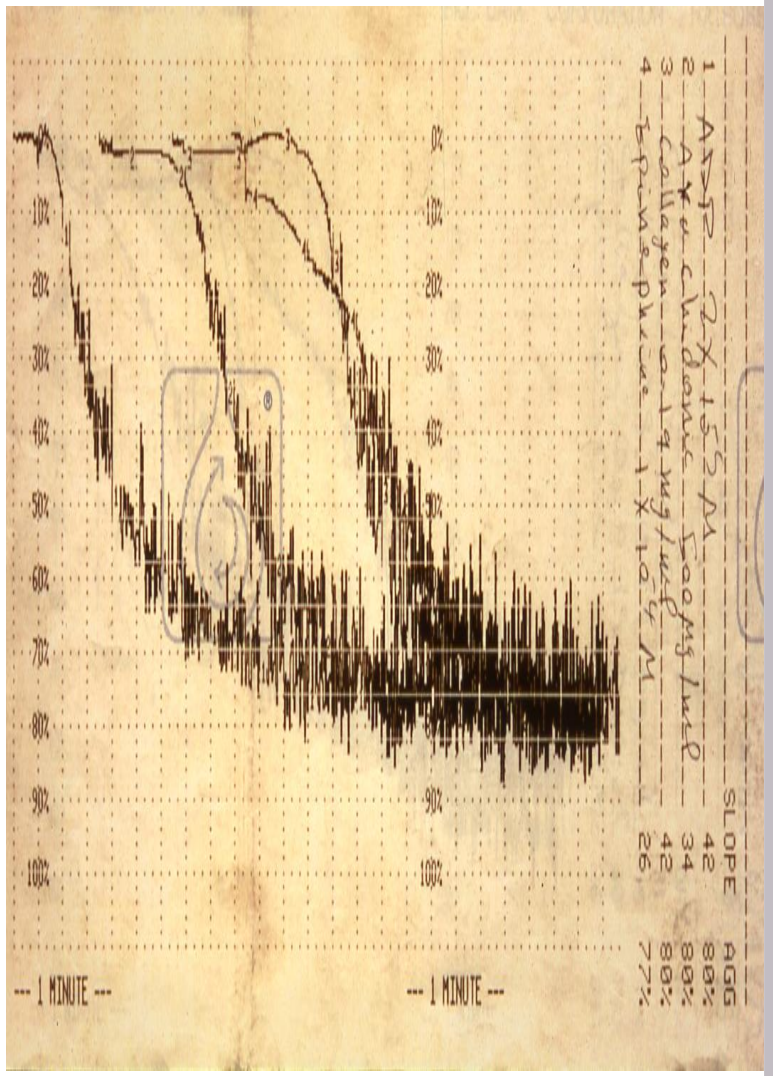
ADP Bio/Data

Arachidonic

Adrenaline

Collagen

Ristol 1.5 mg/ml



Inherited disorders of platelet function

A defect in function is suspected if there is prolonged bleeding time with or without skin or mucosal hemorrhage in the presence of normal platelet count.

A) Membrane abnormalities :Bernard – Soluier syndrome /Thrombasthenia /Platelet factor – 3 deficiency

B) Intracellular abnormalities

1) Storage-pool : (dense body) deficiency : Hermansky / Pudlak syndrome Wiskott / Aldrich syndrome /Chediak / Higashi syndrome / Thrombocytopenia with absent radii Idiopathic storage - pool disease

2) α- granule deficiency : Gray platelet syndrome / Combined deficiency of dense bodies and α granules

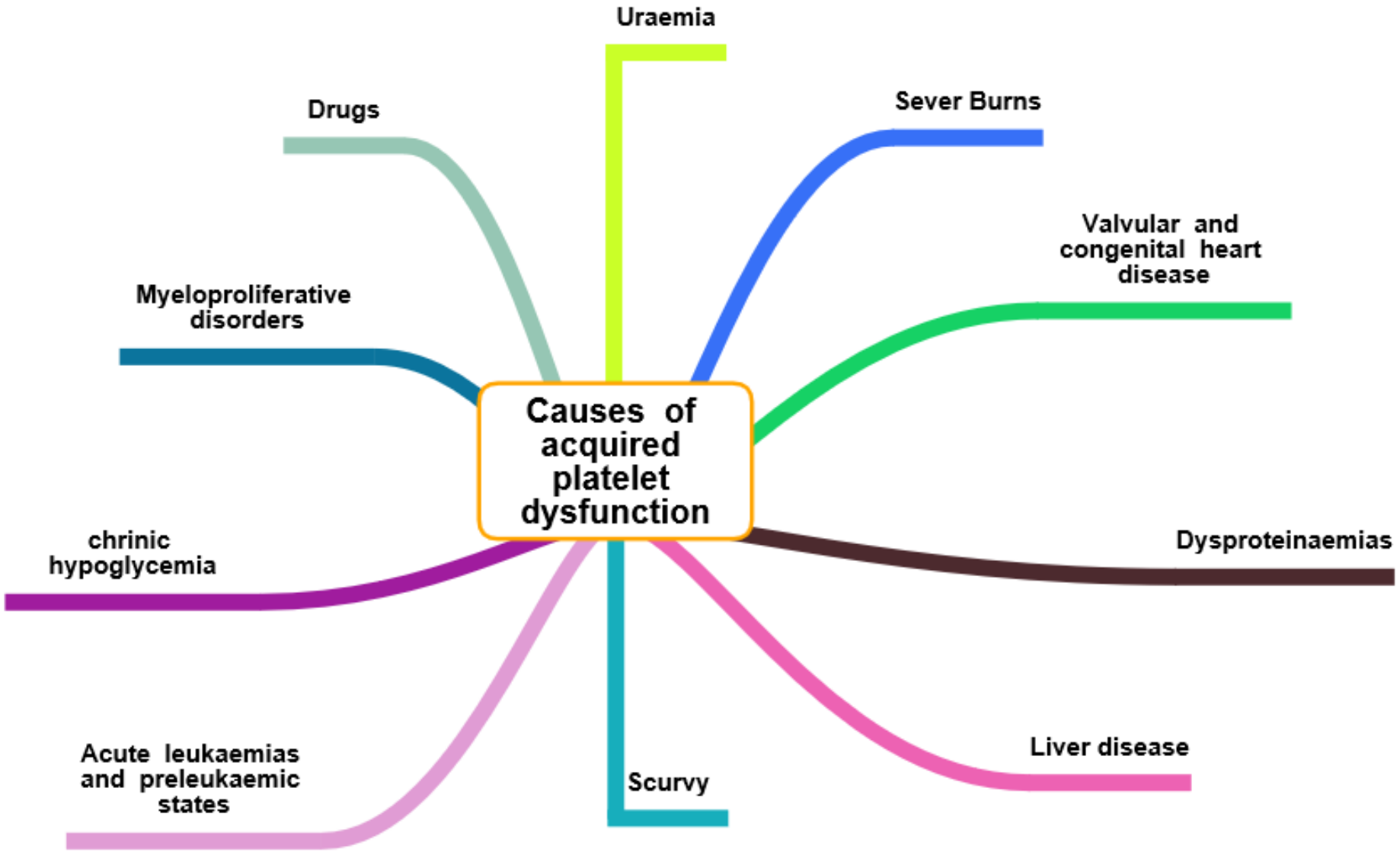
3) Defects of thromboxane synthesis : Cyclo-oxygenase deficiency /Thromboxane synthetase Deficiency /Defective response to thromboxane

C) Miscellaneous : Epstein's syndrome /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
				

Causes of acquired platelet dysfunction :



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)

Thrombocytopenia

❖1. Thrombocytopenia as a result of drugs or toxins

- Bone marrow suppression
- Predictable (dose-related) ionizing radiation, cytotoxic drugs, ethanol.
- Antimicrobials (pencillins, sulphonamides, trimethoprim, rifampicin)
- Diuretics (acetazolamide, chlorathiazides, frusemide)
- Anticonvulsants (dizepam, sodium valproate, carbamazepine)
- Antidiabetics (chlorpropamide, tolbutamide)

❖Analgesics, anti-inflammatory drugs, gold salts.

Thrombocytopenia

2. Immune thrombocytopenia

Clinical features of immune thrombocytopenia

Degree of Thrombocytopenia	Symptoms	Physical findings
Mild (>50 000/mm3)	None	None
Moderate (30 000-50 000/mm3)	Bruising with minor trauma	Scattered ecchymoses at trauma site
Severe (10 000-30 000/mm3)	Spontaneous bruising menorrhagia	Petechiae and purpura , more prominent on extremities
Marked (<10 000mm3)	Spontaneous bruising, mucosal bleeding, risk for CNS bleeding	Generalized purpura, epistaxis, GU bleeding CNS symptoms

❖Laboratory features of immune thrombocytopenia :

- Thrombocytopenia 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.
- 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.

Summary :

Hemostasis is maintained by :	Vessel Wall	Platelets	Coagulation factors
When defected presents with :	Superficial bleeding (Purpura) Mucocutaneous bleeding	Superficial bleeding (Purpura) Mucocutaneous bleeding	Deep (musculoskeletal) bleeding : Hematomas (muscles) Hemarthrosis (joints)
Most common causes	Hereditary: Hereditary Hemorrhagic Telangiectasia Acquired: Allergic (Henoch-Scholein Purpura)	Hereditary : Membrane abnormalities (Bernard-soluier \ Glanzmann thrombasthenia \Factor3 deficiency) Alpha- granules abnormality (Grey platelets syndrome) Acquired: Uremia \ drugs \ Liver diseases (Functional defect) Hereditary : rare Acquired: Infections \ radiation\ drugs\ Leukemia\Anemia\Autoimmune (Count defect)	_____
Tests	_____	CBC(MPV) \ Blood film \ Coagulation profile \Coagulometer	Factors assays (Von willebrand \ factor Vlll)

1) Which of the following causes thrombocytopenia?

A. Aspirin
B. Hyposplenism
C. Heparin
D. paracetamol

2) Which of the following will results in functional defect of Platelets ?

A. Splenomegaly
B. Multiple myeloma
C. Low vitamin C levels
D. MDS

3) Hematomas are most likely associated with :

A. Uremia
B. SLE
C. Vessel wall abnormality
D. Von Willebrand disease

4) The main presentation of Henoch-scholein purpura is :

A. Abdominal pain
B. Bruising
C. Musculoskeletal bleeding
D. Gum hypertrophy

5) The bleeding disorder in which the blood vessels are more fragile than normal, which leads to frequent bleeding episodes is called :

A. Hemorrhagic Telangiectasia
B. Ehlers-Danlos syndrome
C. Allergic purpura
D. Thrombocytopenia

1-C
2-C
3-D
4-B
5-A

6) Which one of the following is NOT a component of dense body ?

A. ADP
B. Fibrinogen
C. Ca++
D. Sertonin

7) Normal bleeding time :

A. 3-8 min
B. 1-3min
C. 3-8 s
D. 1-3 s

8) In clotting factores defect superficial bleeding into the skin

A. True
B. False

9) Deficiency of which of the following will cause Glanzmann's Thrombasthenia disease.

A. GPIa
B. GPIb
C. GPIIIa
D. GPIIIb

1) is c because aspirin effect platelet function while heparin decrease platelets number

6. B
7. A
8. B
9. C

Q1) A 14 years old girl presented with persistent bleeding from nose and bruising .

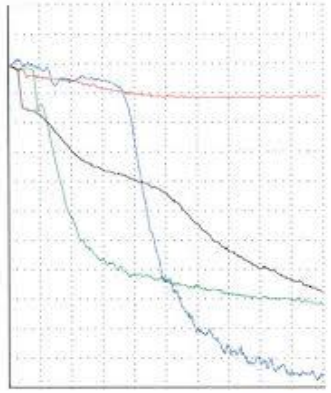
- What tests would you request for her ?

CBC – Blood film – coagulation profile – caogulometer

Q2) In CBC platelets count was low and the blood film shows giant platelets , bleeding time is prolonged .

Platelet aggregation studies in coagulometer (platelets do not aggregate in response to ristocetin but do have normal aggregation in response to adenosine diphosphate, epinephrine, and collagen) What is your most likely diagnosis ?

Bernard–Soulier syndrome (BSS), also called hemorrhagiparous thrombocytic dystrophy, is a rare autosomal recessive coagulopathy (bleeding disorder) that causes a deficiency of glycoprotein Ib (GpIb), the receptor for von Willebrand factor, an important glycoprotein involved in hemostasis.



Red = Ristocetin

Q3)what are Immune thrombocytopenia degress & how treat it ?

Mild (>50 000/mm3)

Moderate (30 000-50 000/mm3)

Severe (10 000-30 000/mm3)

Marked (<10 000mm3)

Treated by : IV immunoglobulin ,Corticosteroids ,Splenectomy.

Thank you for checking our work

Now you can check a lecture out :D

Done by:

Nada Alamri

Alhanouf Almuhanna

Amerah Mansour

Reviewed by:

Hadeel B.Alsulami

Abdullah M. Albasha

دعاء بعد المذاكرة :

(اللهم اني أستودعتك ما قرأت وما حفظت وما تعلمت، فرده لي عند حاجتي اليه أنك على كل شيء قدير، وحسبنا الله ونعم الوكيل)