17/4/25

HLS
Platelet disorders

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PLATELET DISORDERS

- The platelets arise from the fragmentation of the cytoplasm of megakaryocytes in the bone marrow and circulate in blood as disc-shaped anucleate particles for 7-10 days.

- Platelet disorders lead to defects in primary hemostasis and produce signs and symptoms different from coagulation factor deficiencies (disorders of secondary hemostasis).

- Isolated thrombocytopenia is associated with a bleeding tendency and normal coagulation tests.

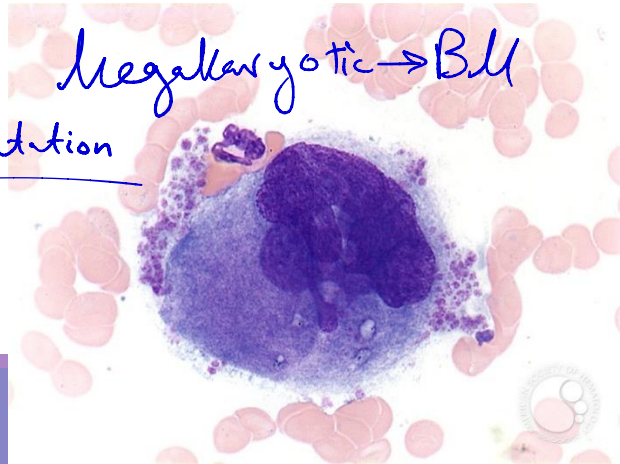
deficiency

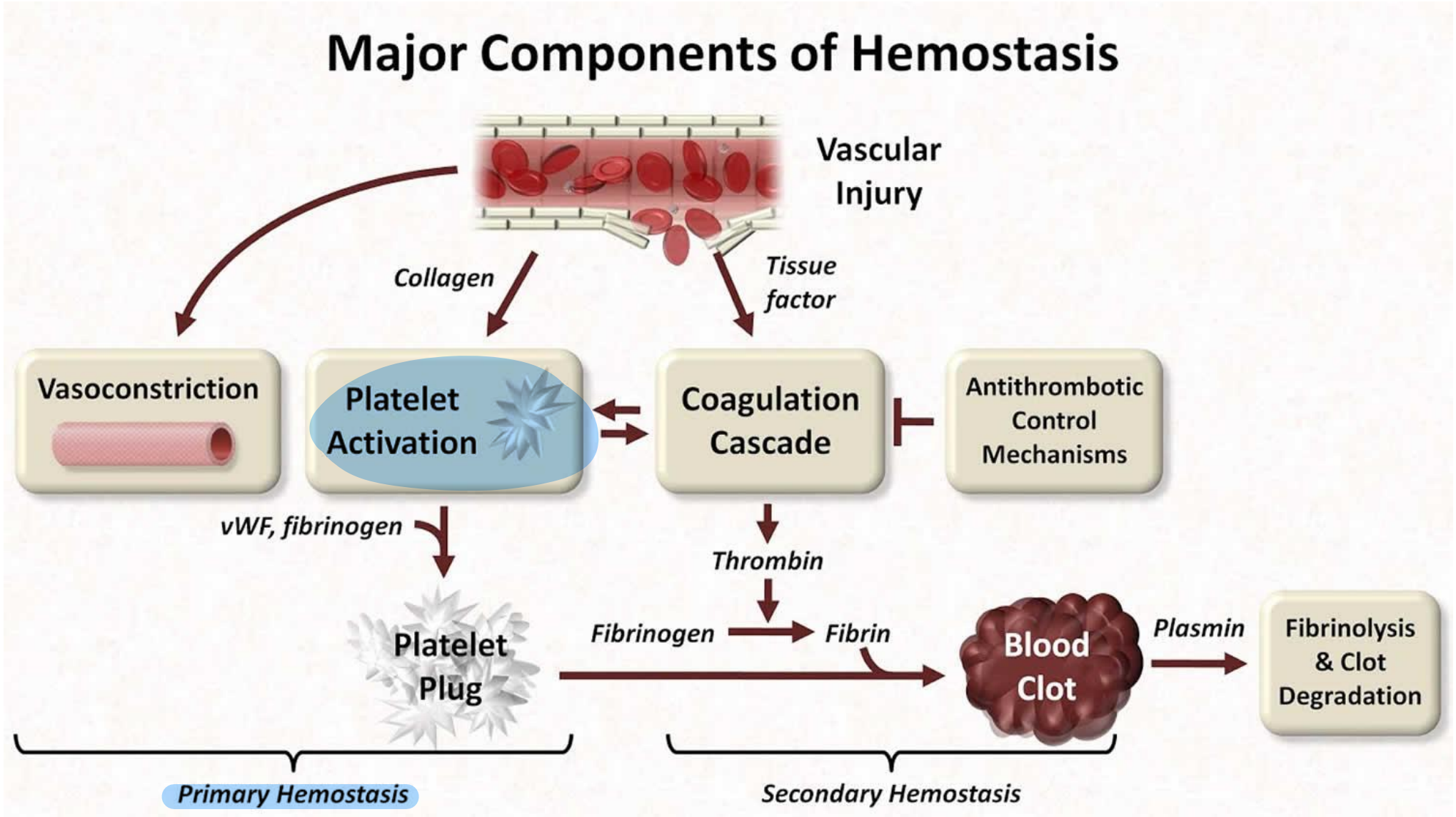
CBC → platelet count.

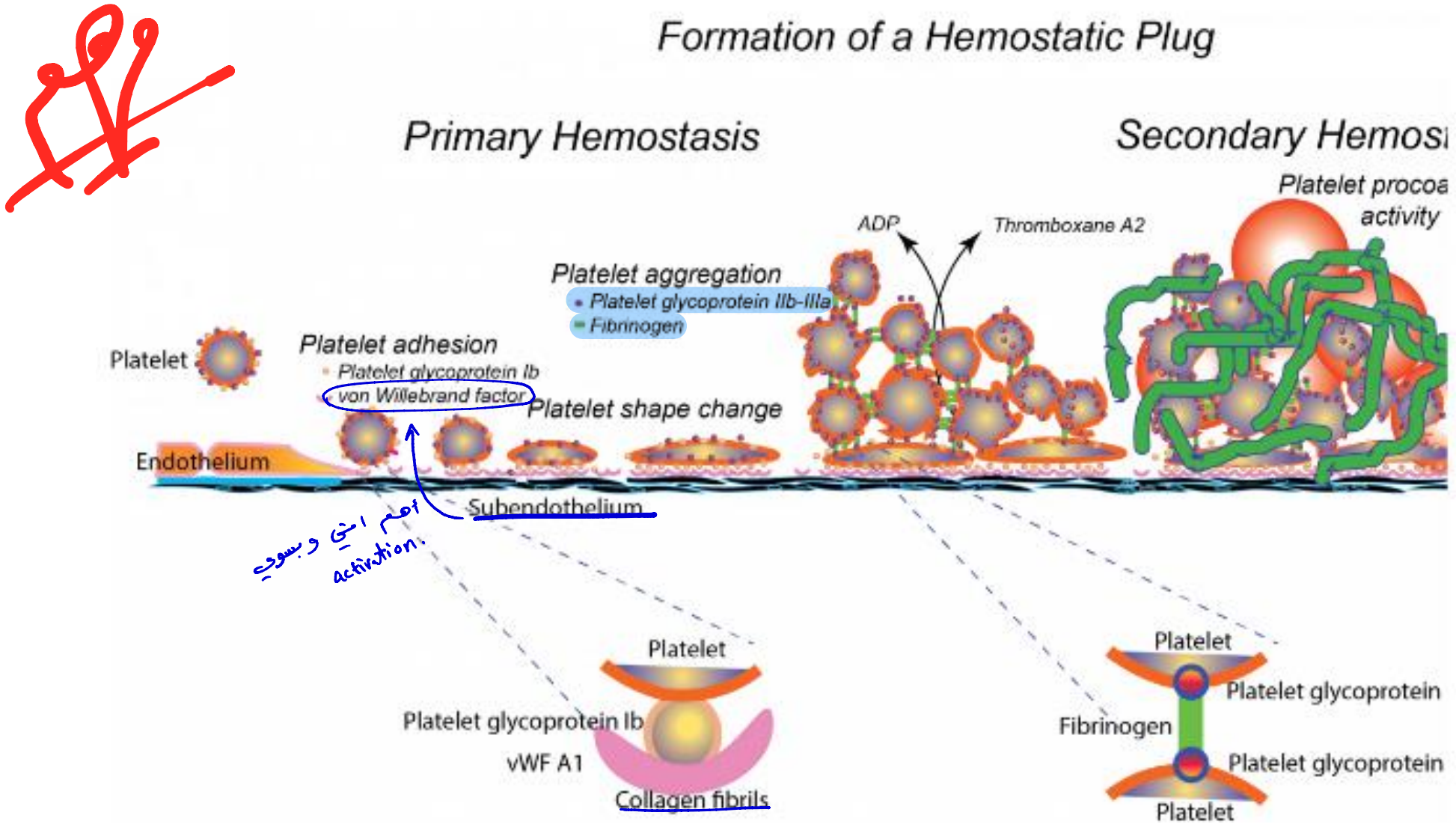
To produce cells.

← Fragmentation

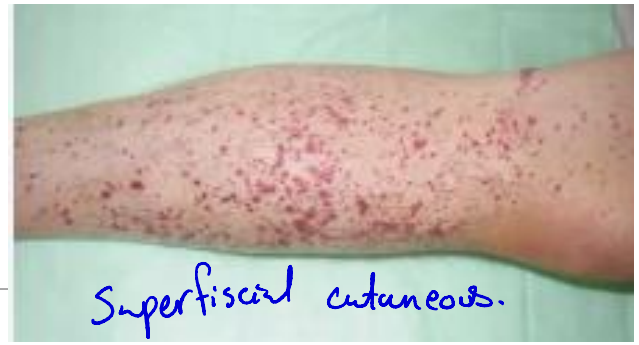
Megakaryotic → BM




Major Components of Hemostasis
Vascular Injury
Collagen
Tissue factor
Vasoconstriction
Platelet Activation
Coagulation Cascade
Antithrombotic Control Mechanisms
vWF, fibrinogen
Thrombin
Platelet Plug
Fibrinogen
Fibrin
Blood Clot
Plasmin
Fibrinolysis & Clot Degradation
Primary Hemostasis
Secondary Hemostasis


Formation of a Hemostatic Plug
Primary Hemostasis
Secondary Hemosi
Platelet procoa
activity
ADP
Thromboxane A2
Platelet aggregation
Platelet glycoprotein IIb-IIIa
Fibrinogen
Platelet
Platelet adhesion
Platelet glycoprotein Ib
von Willebrand factor
Platelet shape change
Endothelium
Subendothelium
Platelet
Platelet glycoprotein Ib
vWF A1
Collagen fibrils
Platelet
Platelet glycoprotein
Fibrinogen
Platelet glycoprotein
Platelet

Relationship Between Platelet Count and Bleeding



- Normal range 150-450X10^3 per µl.
- Levels above 60x10^3/µl will not cause bleeding under normal conditions.
- Levels below 20x10^3/µl will cause:
  - Petechiae, mucosal bleeding.
  - Post-operative bleeding, CNS bleeding.
- Levels around 5x10^3/µl can lead to fatal CNS or GI hemorrhage.
- Levels between 20 and 60x10^3/µl may cause bleeding (depending on platelets functional status).

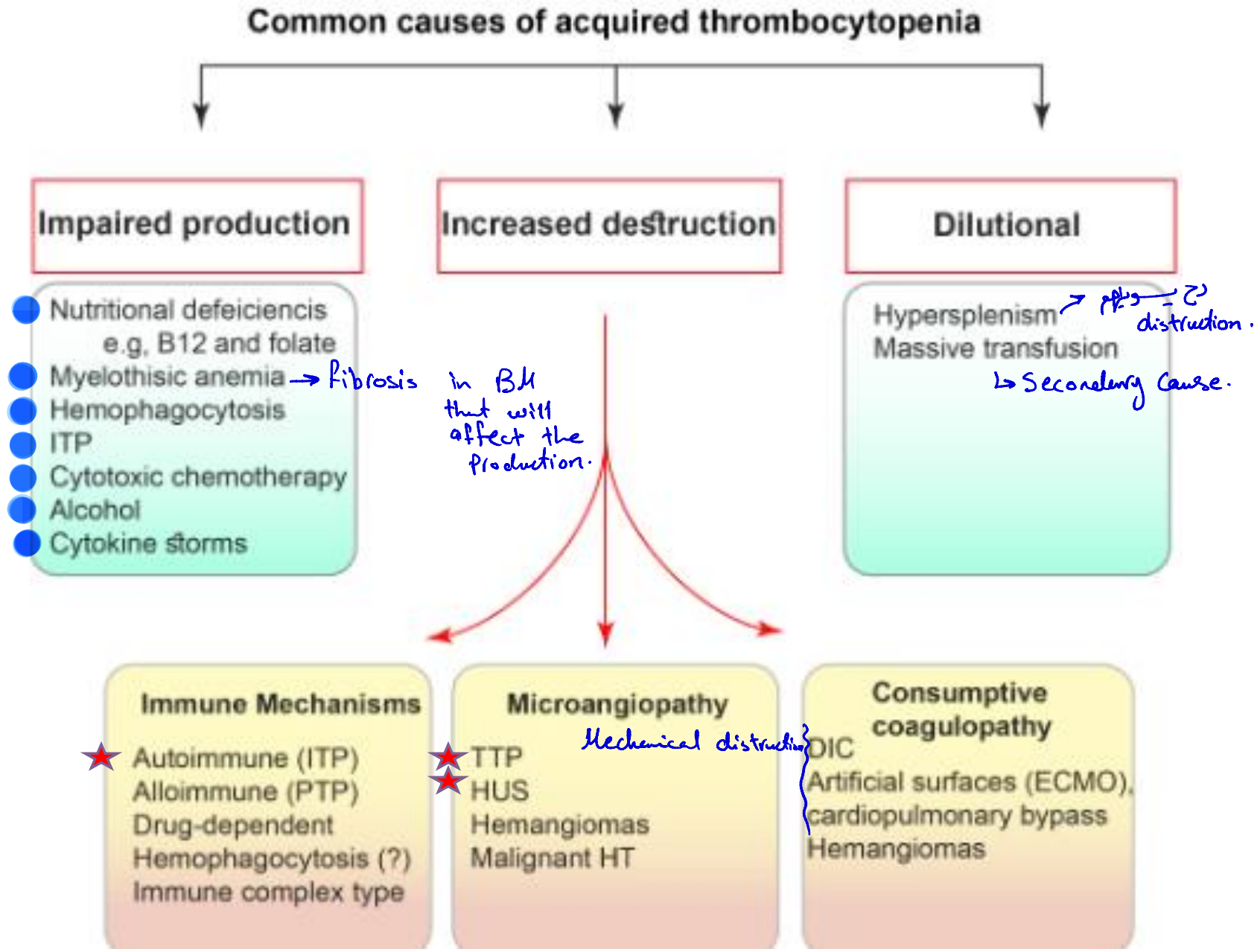

Common causes of acquired thrombocytopenia
Impaired production
Increased destruction
Dilutional
Nutritional defeiciencis
e.g. B12 and folate
Myelothisic anemia → fibrosis in BM that will affect the production.
Hemophagocytosis
ITP
Cytotoxic chemotherapy
Alcohol
Cytokine storms
Hypersplenism → ppl → ↑ distruction.
Massive transfusion
↳ Secondary Cause.
Immune Mechanisms
Autoimmune (ITP)
Alloimmune (PTP)
Drug-dependent
Hemophagocytosis (?)
Immune complex type
Microangiopathy
Mechanical distruction
TTP
HUS
Hemangiomas
Malignant HT
Consumptive coagulopathy
DIC
Artificial surfaces (ECMO), cardiopulmonary bypass
Hemangiomas

Table 12.13 Causes of Thrombocytopenia

Decreased Production of Platelets
Generalized Bone Marrow Dysfunction
Aplastic anemia: congenital and acquired
Marrow infiltration: leukemia, disseminated cancer
Selective Impairment of Platelet Production
Drug-induced: alcohol, thiazides, cytotoxic drugs
Infections: measles, HIV infection
Ineffective Megakaryopoiesis
Megaloblastic anemia
Paroxysmal nocturnal hemoglobinuria
Decreased Platelet Survival
Immunologic Destruction
Autoimmune: ITP, systemic lupus erythematosus
Isoimmune: posttransfusion and neonatal
Drug-associated: quinidine, heparin, sulfa compounds
Infections: infectious mononucleosis, HIV infection, cytomegalovirus infection
Nonimmunologic Destruction
Disseminated intravascular coagulation
TTP
Giant hemangiomas
Microangiopathic hemolytic anemias
Sequestration
Hypersplenism
Dilutional
Multiple transfusions (e.g., for massive blood loss)

Autoimmune Thrombocytopenia's

- Immune thrombocytopenia.
- Thrombocytopenia in pregnancy
- Posttransfusion purpura
- Thrombocytopenia and COVID-19.
- Neonatal alloimmune thrombocytopenia
- Drug-induced thrombocytopenia.
- Thrombotic thrombocytopenic purpura
- Hemolytic-uremic syndrome

1. Immune thrombocytopenia (ITP)

- Immune thrombocytopenia (ITP) is one of the most common autoimmune disorders.

- ITP is caused by autoantibodies to platelets. The antigenic target is platelet GP IIb/IIIa complex.

- These antibodies may be directed toward viral antigens and then :

Virus + Platelets → Cause Thrombocytopenia

- cross-react with platelet antigens then they trapped in the spleen, and efficiently removed by splenic macrophages.

Or:

- react with the developing megakaryocytes in the bone marrow, leading to ineffective thrombopoiesis.

ITP

- Primary (idiopathic) or secondary
- Acute (self limiting) or chronic.

Acute ITP (Idiopathic/Childhood)

- Usually Affects children.
- Develops acutely with 1-2 week duration.
- Presented as Bruising and petechia
- Preceded by infection or vaccination in 75% of cases.
- Initial Platelet .count <20,000.
- Self limited, Spontaneous remission in >90% of cases.
- Severe cases benefit from steroids or IV immunoglobulins.

Chronic Immune Thrombocytopenic Purpura (ITP)

- High incidence in women of child bearing age (20-50).
- NO recent history of drug or recent infection.
- Mostly idiopathic, secondary causes include SLE, HIV, CLL, Hodgkin's disease, drugs (uncommon).
- Autoantibodies against GP IIb/IIIa, or Ib/IX (30% of cases).
- Platelets lifespan reduced to hours.
- Megakaryocytes increased. → for feedback كعملية توازن.
- Petechial bleeding, easy bruising, menorrhagia.

Diagnosis

* On CBC:

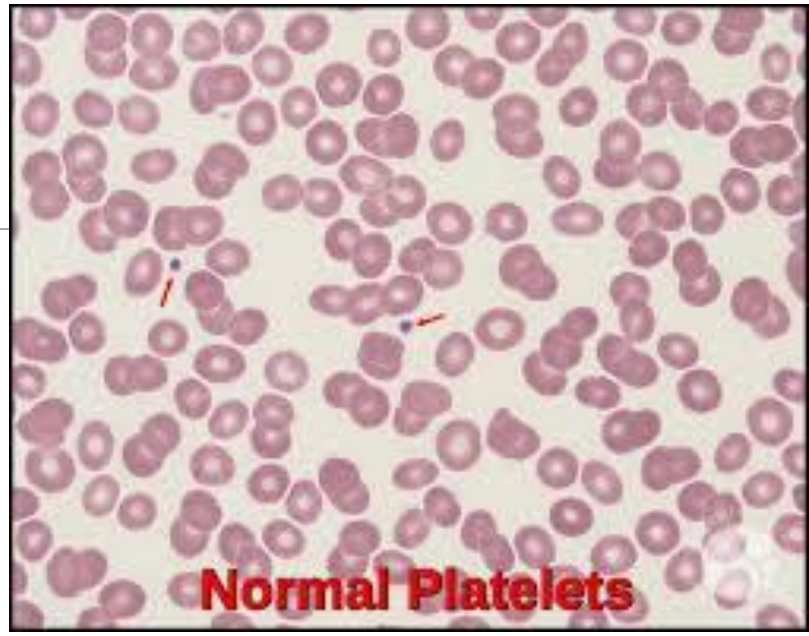
Decreased platelet count (10-50x109/l), normal Hb and WBCs.

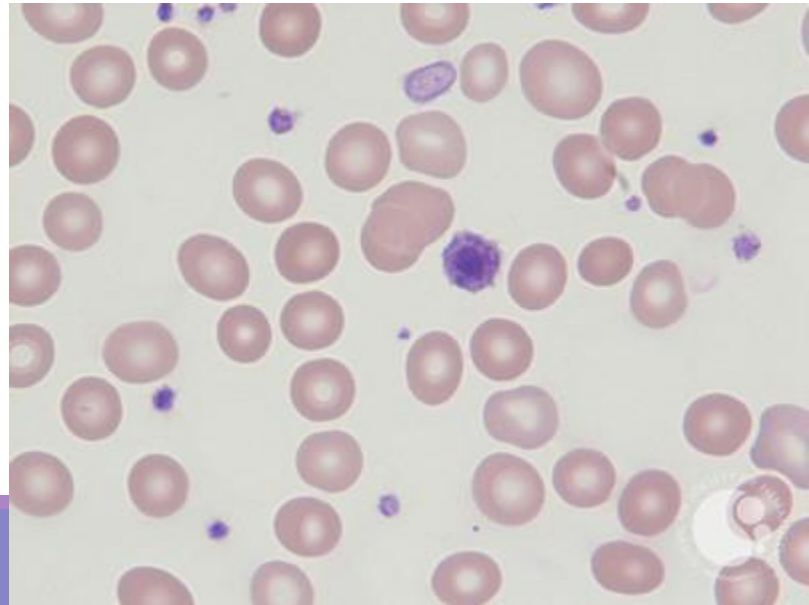
* Peripheral blood: large platelet.

* Bone marrow: Increased Megakaryocytes numbers.

* Bleeding time: : Mild prolongation.

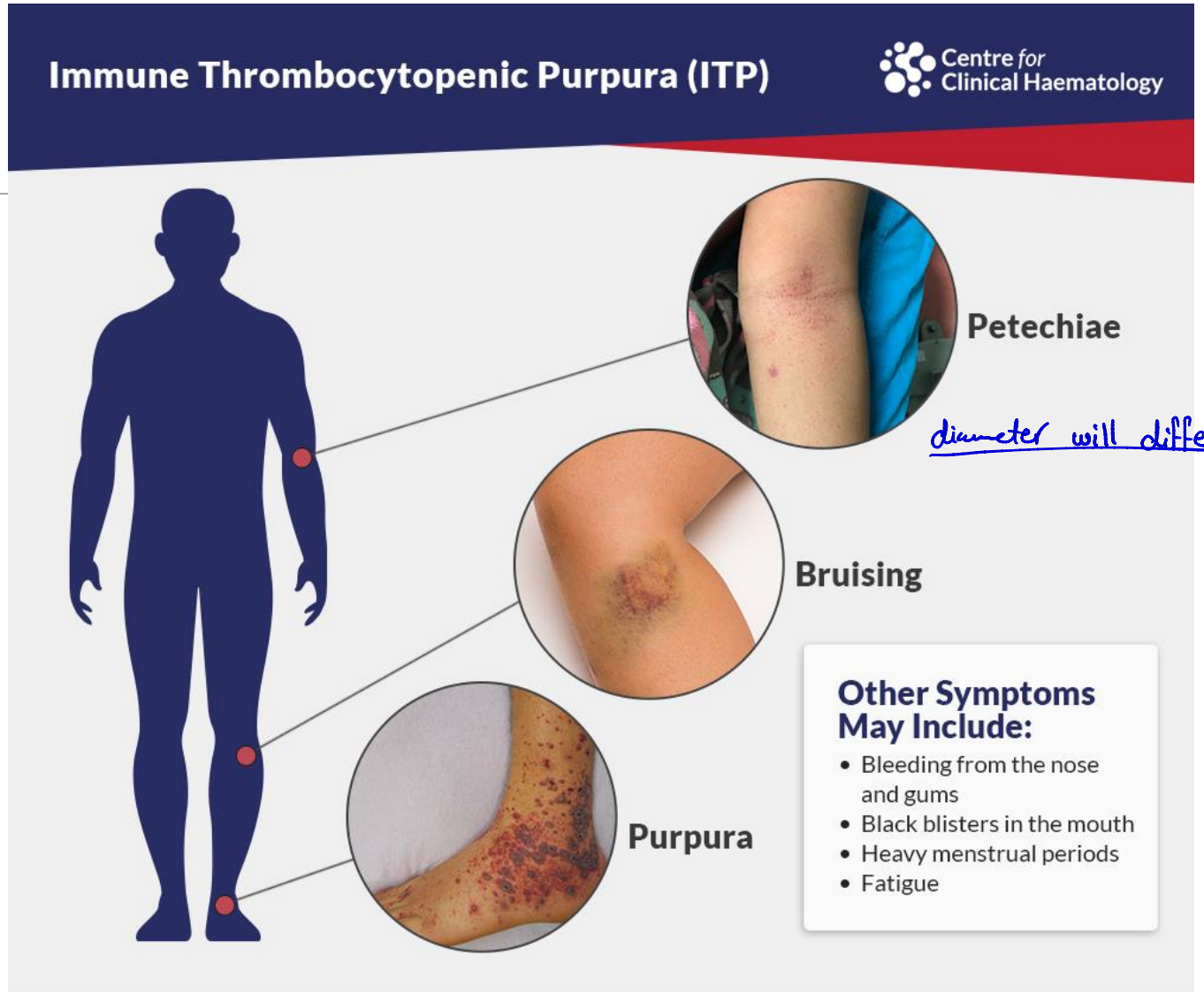
* Assay for Antiplatelet antibodies.





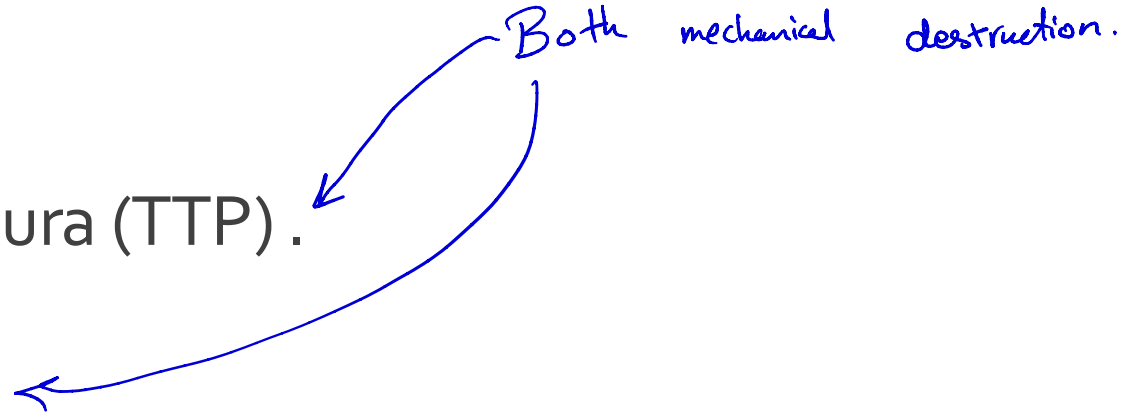
Treatment

- Steroids.
- Splenectomy (long term Rx.).
  - ↳ spleen normally engulf the platelets
- High dose IV immunoglobulins.
- Immunosuppressive therapy.



2. Microangiopathic Thrombocytopenia TTP/HUS

The term thrombotic microangiopathies encompasses a spectrum of clinical syndromes that include :



- Thrombotic thrombocytopenic purpura (TTP) .
- Hemolytic uremic syndrome (HUS).

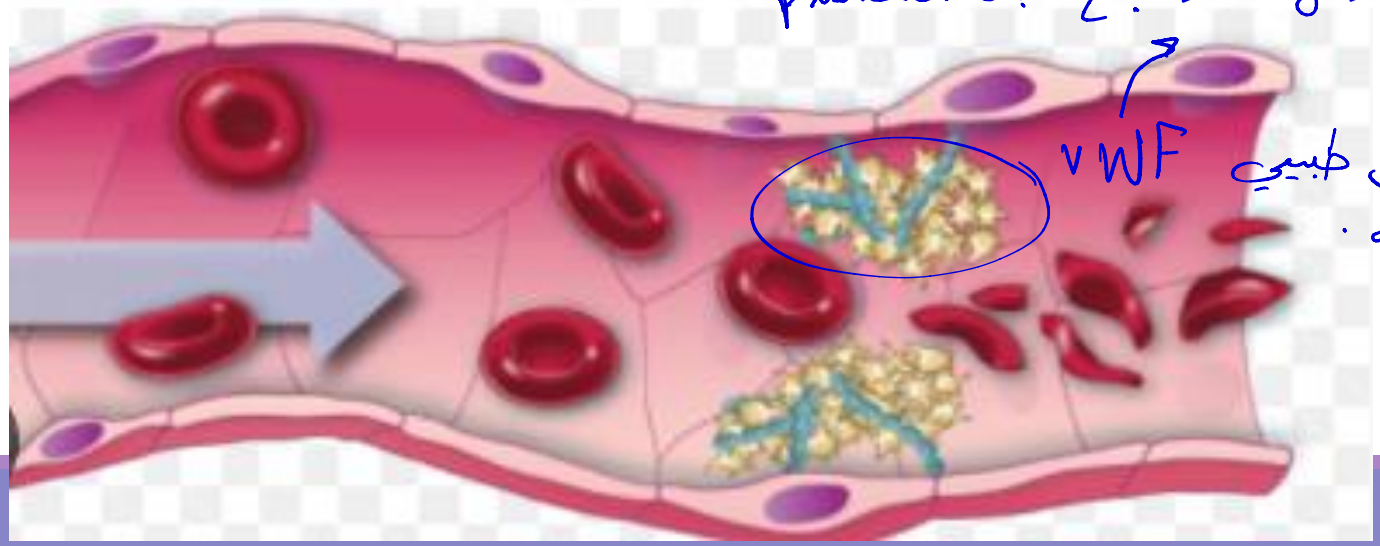
Thrombotic thrombocytopenic purpura (TTP)

- Thrombotic thrombocytopenic purpura (TTP) is a rare blood disorder characterized by clotting in small blood vessels (thromboses), resulting in a low platelet count.

لأنه جمعهم بمكان وسكرت عليهم .

- The classic histologic lesion is one of bland thrombi in the microvasculature of affected organs. These thrombi consist predominantly of platelets, with little fibrin and red cells compared with thrombi that occur secondary to intravascular coagulation.

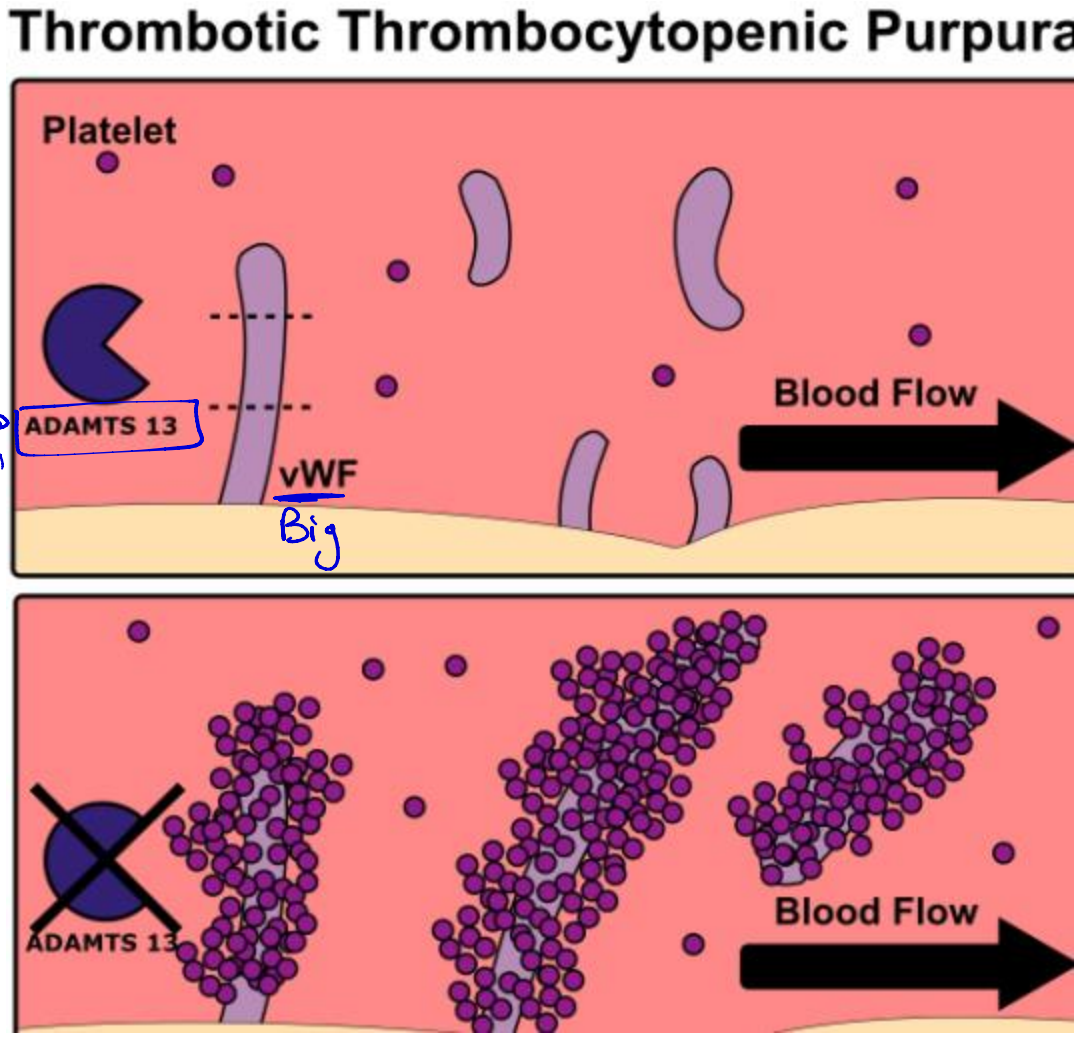
صار Big وتجمع بال platelet .



شكل طبيعي .

- Patients with TTP have unusually large multimers of von Willebrand factor (vWF) in their plasma.
- they have functional deficiency of a plasma protease (designated ADAMTS13) that is responsible for the breakdown of these ultralarge vWF multimers.
- The accumulation of ultralarge vWF multimers on the endothelial surface results in platelet aggregation and eventually thrombus formation

Cause of
- Thrombus.
- Thrombocytopenia.



- TTP can affect any organ system, but involvement of the peripheral blood, the central nervous system, and the kidneys causes the clinical manifestations

- In its full-blown form, the disease consists of the following pentad:

- Microangiopathic hemolytic anemia
- Thrombocytopenic purpura
- Neurologic abnormalities
- Fever
- Kidney disease

haptoglobin, bilirubin will be asked for lab.

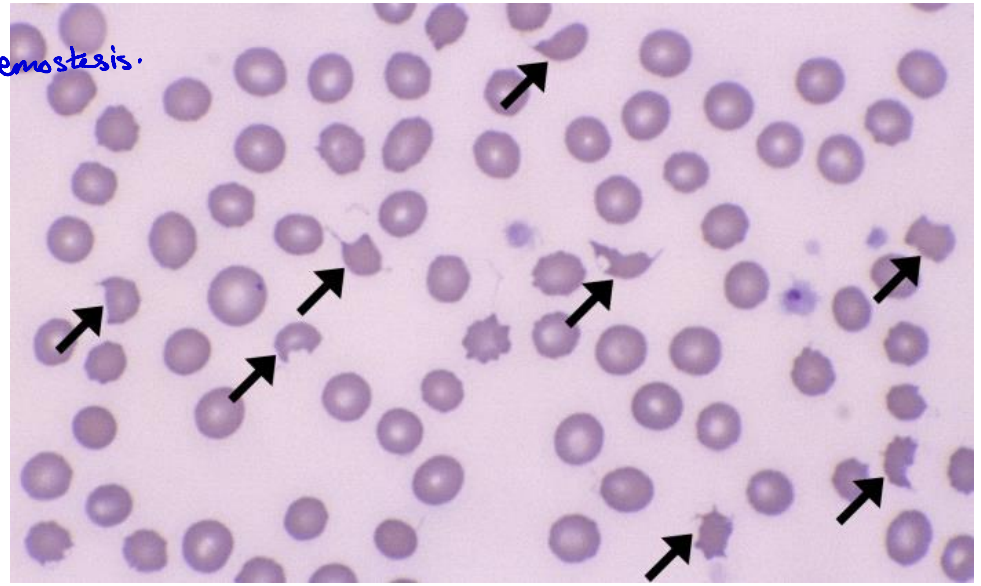
5

Diagnosis and treatment

#Laboratory studies for suspected TTP include:

- *CBC with platelet count.*
- *peripheral blood smear.*
- *coagulation studies(*Normal PT, PTT, D-Dimer but elevated BT).
- **Signs of hemolysis:** Increase LDH, Increase indirect bilirubin Decrease Haptoglobin
- *BUN and creatinine.*
- Measuring ADAMTS13 activity level.

→normal, I didn't use 2ndary hemostasis.



- Treatment:

- The therapy of choice for TTP is plasma exchange with fresh frozen plasma

Hemolytic Uremic Syndrome (HUS)

Hemolytic-uremic syndrome (HUS) is a clinical syndrome characterized by progressive kidney failure that is associated with microangiopathic (nonimmune, Coombs-negative) hemolytic anemia and thrombocytopenia.

HUS is the most common cause of acute kidney injury in children .

* Resemble TTP but:

- More seen in pediatric population
- After viral/bacterial infection
- Pathologic thrombi almost always limited to glomerular capillaries

→ kidney.

Damage to endothelial cells by E. coli O157:H7 toxin is the primary event in the pathogenesis of hemolytic-uremic syndrome (HUS).

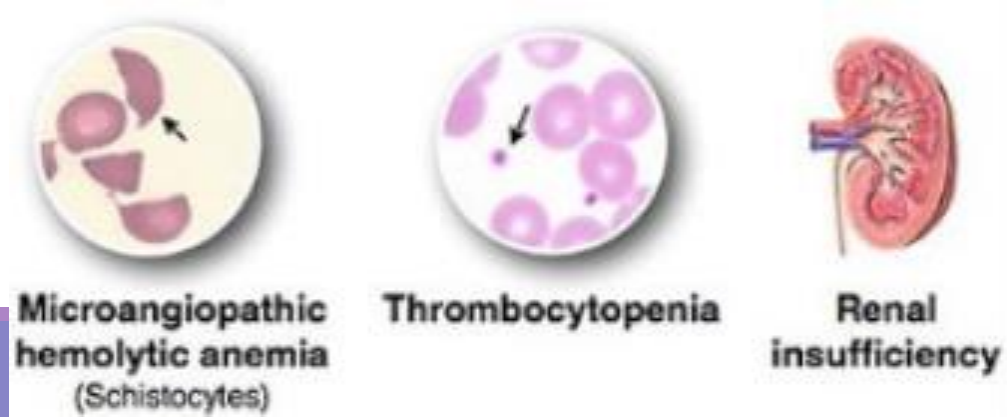
edema, periorbital
↳ toxin damage to endothelial in kidney. } Renal insufficiency.

The cardinal lesion is composed of arteriolar and capillary microthrombi (thrombotic microangiopathy [TMA]) and red blood cell (RBC) fragmentation.

Platelet microaggregate (Hyaline microthrombi) formation, usually limited to the glomerular capillaries.

Lab: Normal PT, PTT, D-Dimer but elevated BT.

Rx: Conservative ما بقدر أعمل اشي.



Thrombocytopenia and COVID-19

- Thrombocytopenia is infrequently seen in mild or asymptomatic cases of COVID-19. Of patients with moderate to severe COVID-19, 5-40% develop thrombocytopenia.

- A meta-analysis suggested an association between thrombocytopenia at admission and increased severity of COVID-19.

- Multiple mechanisms are involved in the pathogenesis of COVID-19–related thrombocytopenia, including:
  - bone marrow suppression.
  - platelet consumption in microthrombi in the lung.
  - platelet destruction by autoantibodies and immune complexes.

due to sever infection.