Hematology

- Histology
- Biochemistry
- **Pathology**
- Pharmacology
- Physiology
- Microbiology

- Handout
- **Slide 3**
- Sheet

- Dr. name :
  Dr Tareq Aladily
- lecture number :
  3- Platelet Disorders
- Done BY :

By: Amer Abu Shanab

Platelets / clotting factors diseases

Hemophilia A

- Etiology (factor VIII)
- Mode of inheritance
- Family history (70%)
- Intrinsic pathway: prolonged partial thromboplastin time (PTT)

Pathogenesis

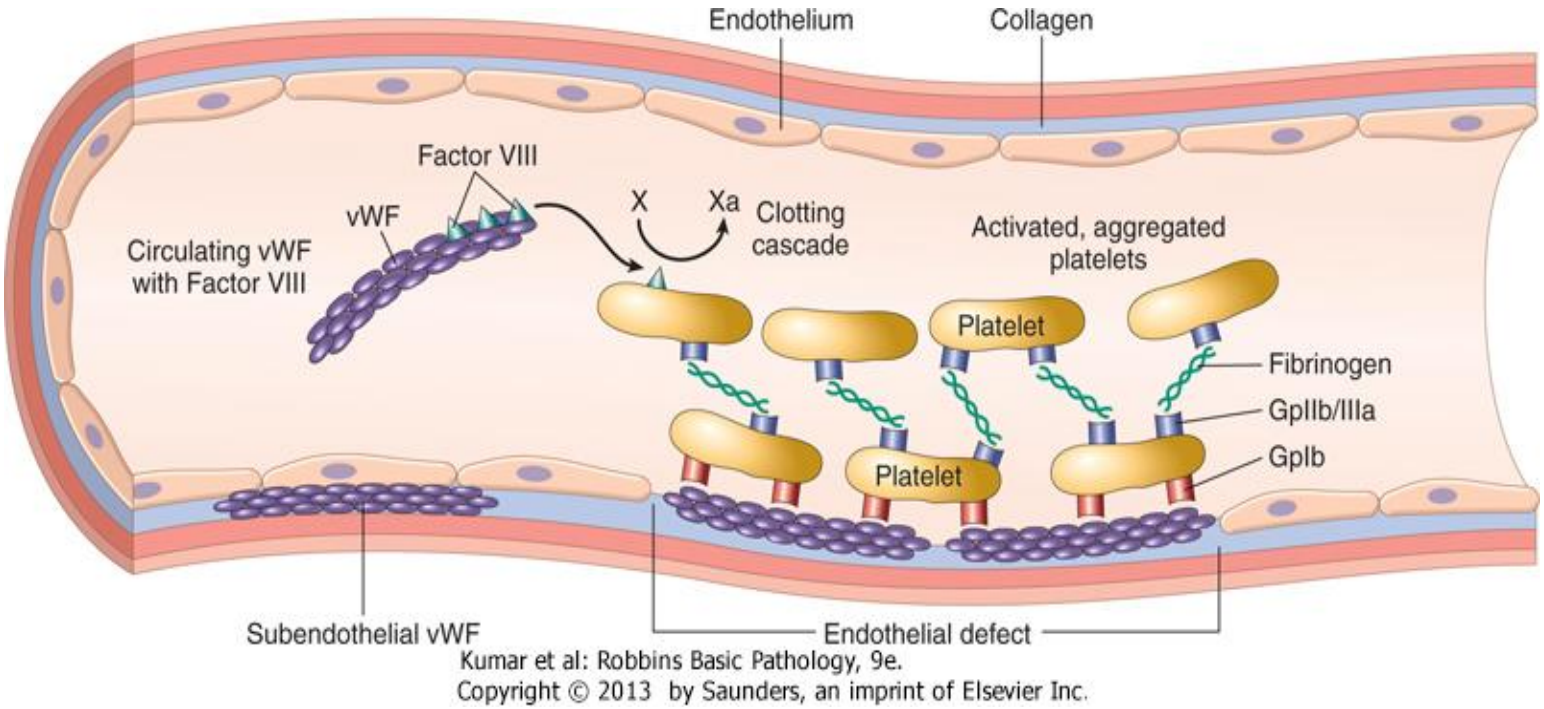
- Quantitative deficiency (90%)
- Normally, large reserve of factor VIII
- Bleeding secondary to minor trauma (10%)
- Spontaneous bleeding (1%)
- Hematoma in deep organs, oral and nasal cavities, joints (deformity)
- Manifests early in life

Hemophilia B

- Etiology: factor IX
- Mode of inheritance
- Family history
- Clinically similar to hemophilia A
- Prolonged PTT
- Corrected by mixing study
- Specific factor assay

Von Willibrand Disease

- Synthesized by endothelium and platelets
- Carry factor VIII
- Adhere to collagen, binds platelets by GPIb (hemostatic plug)



Von Willibrand Disease

- Mode of inheritance
- Prevalence: most common
- Type 1: quantitative
- Type 2: qualitative: abnormal binding to platelets, thrombocytopenia
- Factor VIII is lost
- Bleeding in wounds, mucosa, deep organs
- Prolonged PTT, sometimes prolonged bleeding time
- Clinically milder than hemophilia

Idiopathic Thrombocytopenic Purpura

- Etiology
- autoimmune IgG against GP IIb/IIIa
- Prevalence
- Acute setting: children, post viral infection, molecular mimicry
- Chronic: middle age, women, autoimmune diseases, deranged immune system (high TH1 count and function), also with infections of HIV, HCV, H. Pylori
- Bleeding in skin and superficial sites

Pathogenesis and morphology

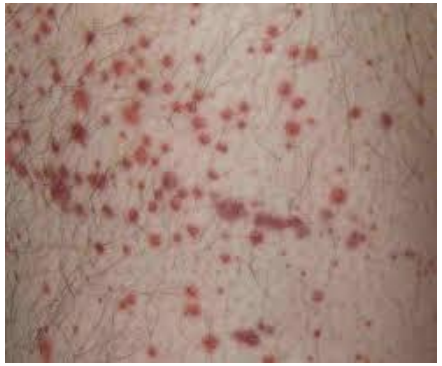
- Molecular mimicry
- Deranged immune system
- High TH1 count and function
- Activation of B-cells in spleen – IgG secretion
- Binding of Fc fragment to its receptor on histiocytes – phagocytosis
- Activation of megakaryopoiesis in BM
- Increased immature platelets production
- Thrombocytopenia, large platelets

Thrombotic Thrombocytopenic Purpura

- Etiology: ADAMTS13 deficiency/ mutation
- 90% Acquired (autoantibody, IgG, temporary)
- 10% inherited (AR)
- Large vWF multimers --ADAMTS13 → vWF
- Large vWF multimers bind many platelets
- Microcirculatory occlusion
- Widespread thrombosis
- Secondary bleeding (thrombocytopenia)

Clinical and laboratory features

- Pentad: anemia, thrombocytopenia, renal failure, neurologic symptoms, fever, purpuric rash
- Life-threatening disease
- Anemia is hemolytic (schitocytes)
- Prolonged bleeding time
- Normal Prothrombin time (PT): extrinsic pathway
- Normal Partial Thromboplastin Time (PTT)



Hemolytic Uremic Syndrome

- Common in children
- 90% follow hemorrhagic diarrhea
- E. Coli infection (serotype O157:H7)
- Shiga-like toxin
- Binds endothelial cells, mainly kidney glomeruli, damage, inflammation,
- Thrombosis, thrombocytopenia, renal failure
- Marked schistocytes
- Prolonged bleeding time, normal PT, PTT

Disseminated Intravascular Coagulation

- Acquired
- Systemic activation of clotting factors
- Widespread thrombosis, thrombocytopenia
- Secondary activation of fibrinolysis, bleeding
- Life threatening
- Prolonged BT, PT, PTT
- High fibrin-degradation product

Causes of DIC

- Carcinoma (mucin)
- Acute Promyelocytic Leukemia (tissue factor)
- Sepsis (TF, endotoxin)
- Severe inflammation (pancreatitis)
- Head trauma (brain tissue)
- Labor (placental tissue)
- Widespread endothelial injury (snake venom, heat, burn)

Acquired bleeding disorders

- Chronic liver disease
- Vitamin K deficiency
- Warfarin
- Aspirin
- Microangiopathic Hemolytic Anemias (DIC, TTP, HUS)

Thrombophilia

- Mostly acquired:
- Thrombocytosis (MPN)
- Polycythemia
- Sickle cell anemia
- PNH
- Antiphospholipid syndrome (auto antibodies against protein C, S, prothrombin activation)
- Pregnancy (high thrombin, fibrinogen)
- Drugs (OCP)

Thrombophilia

- Inherited

Factor V Leiden mutation

- AD
- Resistant to lysis by protein C
- Increased activation of thrombin

Factor II mutation (Prothrombin G20210A)

- Slow degradation of prothrombin mRNA

Protein C deficiency (AD)

Protein S deficiency (AD)

increased activity of factor V

Deep Vein Thrombosis (DVT)

- Lower limbs are favored site for venous thrombosis
- Sluggish blood flow
- Prolonged immobility
- 50% have associated thrombophilia
- Legs appear swollen, red, painful, hot
- Thrombus can detach and cause pulmonary embolism (lung infarction): chest pain, dyspnea, hypoxia, death??