# Bleeding disorders

by Ahmed Gamal

The doctor said no need to know about the drugs used and no details about the management

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**Objectives:**

- Overview of Hemostasis.
- Congenital Bleeding Disorders.
- Acquired Bleeding Disorders.
- Platelet Disorders (Number & Function).
- Approach to the bleeding Pt.
- Management of Bleeding Pt.

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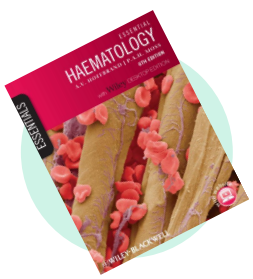
**References:**
**Slides - Black**
**Doctor's notes - Red**
**Step up / davidson - Blue**
**Extra explanation - Grey**

**Optional:**




Chapter 25

Editing file

## Introduction

- In this lecture we will briefly talk about the physiology of bleeding, how it happen? and how it gets controlled? in addition to common bleeding disorders that comes if any of physiological hemostasis steps get disturbed.
- Hemostasis is The process through which bleeding is controlled at a site of damaged or disrupted endothelium.
- Hemostasis can be divided into Primary & Secondary hemostasis.
- Primary hemostasis is concerned with the interaction between platelets and endothelial cells which ultimately resulting in the formation of **PLATELET PLUG**
- knowing that the platelet plug is weak and not strong enough to stop the bleeding. So, needing of a secondary hemostasis is a must!
- Secondary hemostasis is acting like اسمنت that will stabilize and strengthen the weak platelet plug and make it a strong! It is composed of plasma proteins which almost all of them made by liver. It also called “Coagulation Cascade”
- When the secondary hemostasis “Coagulation Cascade” starts it will end up by forming **FIBRIN** which cross linked platelets creating the **platelet-fibrin thrombus!**
- After that, this platelet-fibrin thrombus must be limited to the site of injury to avoid thrombosis and here comes the **FIBRINOLYTICS** to degrade the excess thrombus and make it limited to the site of injury
- Coming to this stage the bleeding normally stops within 2-7 minutes.
- Now, within coming slides we’ll cover common **bleeding disorders** that can disturb the hemostasis (Primary OR secondary)!

## Overview of Hemostasis

**The process through which bleeding is controlled at a site of damaged or disrupted endothelium.**
It is a dynamic interplay between
A) Cellular Components:
- platelets & Endothelium.

B) Plasma Proteins Components: 3 protein systems
- Blood Coagulation (Clot Formation)
- Fibrinolysis (Clot Lysing)
- Anticoagulant (Regulating)

## Hemostatic Phases:

| Primary Hemostasis: | Secondary Hemostasis: |
|---|---|
| 1. Endothelium Injury<br>2. Platelet<br>3. Von Willebrand Factor | 1. Clotting Factors<br>2. Soluble Protein Fibrinogen converted to insoluble Fibrin |
| Bleeding is superficial:<br>Epistaxis, gingival, petechiae, purpura, mucosal surfaces such as the gums, vaginal bleeding | Bleeding is deep:<br>joints and muscles |

**Now, Suppose there is endothelial injury (eg:trauma). The following steps will start**

| Vascular Phase (1) | Platelet Phase (2) | Plasma Coagulation Phase (3) | Fibrinolysis Phase (4) |
|---|---|---|---|
| Release of locally active vasoactive agents (Endothelin, Thromboxane A2, Fibrinopeptides) -> Vasoconstriction at the site of injury -> reduced blood flow | Platelet Adhesion & Aggregation (via VWF, ADP, TXA2) -> formation of platelet Plug ضعيفة لو نفختها طارت | Propagation of the clotting process by the coagulation cascade, formation of Fibrin Clot. Strong (لا يقدر عليها بعد الله اللى plasminogen) | Termination of clotting by antithrombotic control mechanisms & removal of the clot |

## Platelets

- Produced in the Bone Marrow by fragmentation of the cytoplasm of megakaryocytes, each rise from 1000 to 5000 platelets.
- Extremely small & discoid (3 x 0.5 µm in diameter)
- Time interval from differentiation of the human stem cell to the production of Platelets (~ 10 days).

! The major regulator of Platelet production is Thrombopoietin via c-MPL receptor. It is produced by Liver & Kidney and it regulates the production of platelets by stimulating the production and differentiation of megakaryocytes.

- Normal counts (150 – 400 x $10^9$), up to 20 thousand is considered safe platelet count and it's rare to bleed, unless there is qualitative platelet destruction.
- Normal Lifespan (7 – 10 days). It could be less than that in abnormal situations. Refractoriness to platelet transfusion is often multifactorial and can be separated into non-immune and immune causes.

**PLTs Ultrastructure**
Storage pool for many enzymes and under certain situations like vascular injury, it will be released and stimulate platelet aggregation and adhesion.

**3 types of storage granules**
**α- Granules**
- VWF von willebrand factor
- Clotting Factors
- PDGF
- ILGF1

**Dense Granules (δ Granules) H-SAC**
- Serotonin
- ADP & ATP
- Ionized Ca
- Histamine

**Lysosomes**
- Hydrolytic enzymes

! Where vWF comes from?
- ***α- Granules* of platelets.**
- **Weibel-Palade bodies in the endothelial cells.**

**What is the function of the platelets?**

**1. Adhesion** (platelet – Vessel Wall)

- Via vWF through glycoprotein Ib/IX/V it is synthesized in endothelial cells & megakaryocytes. It also Binds the factor VIII coagulant protein and protects it from degradation.
- Stored in storage granules of endothelial cells & α granules of platelet
- Rise with stress, exercise, adrenaline, infusion of DDAVP= desmopressin).

Desmopressin increase factor XIII activity

**2. Aggregation** (cross linking of PLT – PLT)

vWF & Fibrinogen through GP IIb/IIIa receptors.

**3. Release Reaction & Amplification** (aggregation formation & stabilization)

A. Release of α granules contents, & ADP from dense granules.

B. Formation of Thromboxane A2 by various agonists induces intracellular signaling.

**Why they usually don't stake to the vessels wall, what inhibit their effect?**

| **Prostacyclin ($PGI_2$)** | **Nitric Oxide (NO)** |
|---|---|
| • synthesized by vascular endothelial cells, potent inhibitor of PLT aggregation & causes vasodilation by rising cAMP<br>• prevents platelets deposition on normal vascular endothelial | released from endothelial cells, macrophages, & platelets<br>inhibit platelets activation & promotes vasodilatation |

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## Fibrinolysis:

Fibrinolysis is the breakdown of a fibrin clot. Plasmin is the enzyme that breaks down fibrin. It is activated from inactive plasminogen by tissue plasminogen activator (t-PA).

the major player in plasminogen is tissue plasminogen activator

I gave anticoagulation to prevent the propagation, but I leave the plasminogen to resolve the clot. if I want to interfere I will give tissue plasminogen activator.

(The table was not in the slides)

| Antiplatelet | Anticoagulant | | fibrinolytic |
|---|---|---|---|
| MCQ **Aspirin** | **Heparin** | **Warfarin** | **tissue plasminogen activator (tPA), streptokinase (SK), and urokinase (UK).** |
| **Delay clot formation by inhibiting the platelet aggregation. It works by irreversibly inhibit the synthesis of** Thromboxane A2 | Bind to antithrombin III and accelerate its action (inactivate factors IIa, IXa, Xa, Xia and XIIa) | Interfere with vit-K synthesis Decreases factors II,VII,IX and X | |
| **Measured by** bleeding time. | measured by **PTT** | measured by **PT** | |

# Congenital and Acquired Bleeding Disorders

## Hemophilia

an inherited bleeding disorder caused by deficiency of coagulation factor.

- **Congenital:** genetic mutation in F8 & F9 located on the long arm of X chromosome.
  It is X-linked recessive disorder so observed commonly in males due to their hemizygous state and rarely in females due to (Heterozygous females as result from nonrandom X chromosome inactivation, skewed Lyonization, or the presence of other genetic abnormalities (Turner Syndrome or X autosomal translocations).
- **Acquired:** development of autoantibodies most commonly directed against factor VIII – As. with pregnancy, malignancy, advanced age. Its qualitative defect you have the factor 8 but it's not working due to autoantibody.

**Type is based on the affected factor:**

A. hemophilia *A* – Inherited deficiency of factor VIII.
B. Hemophilia *B* – Inherited deficiency of factor IX also called **Christmas Disease**
C. Hemophilia C – Inherited deficiency of factor XI also called **Rosenthal Syndrome** an **autosomal recessive disorder**. Rarely, heterozygotes may have bleeding

(autosomal dominant transmission, due to heterodimer binding). especially common in Ashkenazi Jews. Extremely rare)

**Characterized based on the residual or baseline factor activity level or "factor level"**

Factor levels typically correlate with the degree of bleeding Symptoms.

- Severe Hemophilia defined as <1 % factor activity (<0.01 IU/mL).
- Moderate Hemophilia – defined as a factor activity level ≥1 % of normal and <5 % of normal (≥0.01 - <0.05 IU/mL).
- Mild Hemophilia – defined as a factor activity level ≥5 % of normal and <40 % of normal (≥0.05 - <0.40 IU/mL).

More than 1% bleeding risk is rare and interfere if the patient is going to have an operation.

**Clinical features:**

1. hemarthrosis: the most common clinical manifestation

Knees are the most common site, but any joint can be involved.
Progressive joint destruction can occur secondary to recurrent hemarthrosis.

2. Intracranial bleeding. (second most common cause of death after AIDS due to past history of transfusion [before screening was initiated]).
3. Hematomas (Intramuscular, Retroperitoneal)
4. Hematuria or hemospermia.
5. bruising
6. bleeding (mucosal, GI, GU)

! Mixing study: Mix patient's plasma with normal plasma, if PTT:
- Corrected (not becoming prolonge) → that means there is a real deficiency in the factor
- NOT corrected(still prolonge) → that means the problem related to autoantibody that inhibiting the factor

**Diagnosis :**

- high aPTT.
- Decrease Factor Level.
- Mixing study (corrected) hemophilic Patients are treated with infusions of either plasma-derived or recombinant factor VIII. However, some patients develop inhibitory antibodies (inhibitors) to infused factor VIII which render it ineffective.to detect the inhibitor If normal plasma is mixed with plasma from a hemophiliac patient, **PTT becomes normal.** If **PTT fails to normalize**, this is diagnostic of the **presence of a factor VIII inhibitor.**

A **Bethesda unit** (BU) is a measure of blood coagulation inhibitor activity. It is the amount of inhibitor that will inactivate half of a coagulant during the incubation period.One Bethesda unit is defined as that amount of inhibitor that results in 50% residual FVIII coagulant activity activity of a defined test mixture.



- Normal levels of VWF & PT.

**Treatment:**

- Replacement of the deficient coagulation Factor (recombinant or plasma derived) + Adjunctive therapy (Desmopressin (DDAVP).
- Antifibrinolytic agents (Tranexamic Acid, Aminocaproic Acid).
- Recombinant factor VIIa with inhibitors.

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## Von Willebrand Disease

It is the most common bleeding disorder (affects 1% to 3% of population), Autosomal dominant and rarely recessive disorder characterized by deficiency or defect of vWF, also known as factor VIII- related antigen.

Rarely acquired disease caused by:

- Autoantibodies against vWF immune complex formation,
- vWF binding to cancer cells.
- Congenital Heart Disease.
- Aortic Stenosis.
- Angiodysplasia = vascular malformation in the gut

There are three major subtypes with varying severity.
a. Type 1 (most common form)—decreased levels of vWF.
b. Type 2 (less common)—exhibits qualitative abnormalities of vWF.
c. Type 3 (least common form)—absent vWF (very severe disease).

**Clinical features:**
1 Cutaneous and mucosal bleeding—epistaxis, easy bruising, excessive bleeding from scratches and cuts, gingival bleeding.
2 Menorrhagia (affects more than 50% of women with von Willebrand Disease [vWD]).
3 GI bleeding is possible.
In many patients vWD is mild, and is not diagnosed until surgery or trauma. In general bleeding in vWD is much milder than in hemophilia. Spontaneous hemarthrosis do not occur.

**Diagnosis:**

- Normal aPTT in **Type 1 & 2.**

- prolonged aPTT in **Type 2N, 2B, & 3.**
- Low factor VIII assay **in 2N & 3.**
- Low Platelet in **2M**.
- For the differentiation of subtypes: immunological assays of vWF, vWF:Ag, vWF Ristocetin Cofactor, vWF:RCo and vWF multimers.

**Treatment:**

1. Replacement of exogenous vWF concentrate
2. DDAVP (desmopressin)—induces endothelial cells to secrete vWF. (first line treatment)
    a. Treatment of choice for type 1 vWD (the most common type).
    b. Some patients with type 2 vWD may respond to DDAVP, but it is not effective in type 3 vWD.
3. Factor VIII concentrates (containing high-molecular-weight vWF).
    a. Give to all patients with vWD (any type) after major trauma or during surgery.
    b. Recommended for type 3 vWD (and type 2 patients not responsive to DDAVP).
4. Antifibrinolytic agents (Tranexamic Acid, Aminocaproic Acid).
5. Conjugated Estrogens & oral contraceptive Agents (for menorrhagia).
6. in acquired type you need to treat the underlying cause.



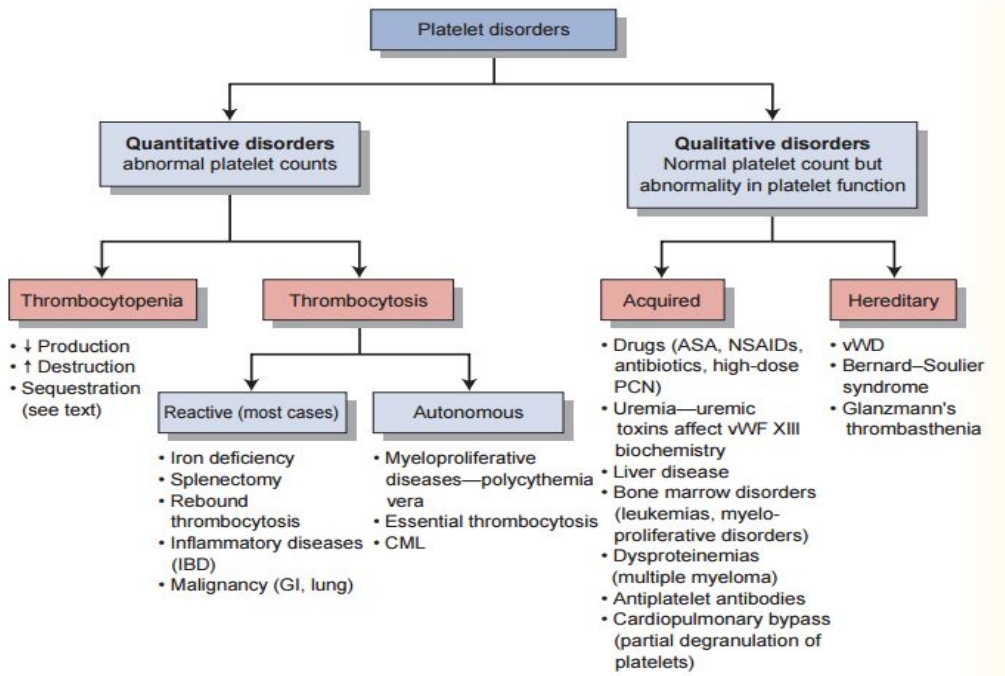
**Other diseases:** not in the slides

## Other congenital bleeding disorders:

| | Coagulopathy liver disease | Vitamin K Deficiency |
|---|---|---|
| **General characteristics** | All clotting factors are produced by the liver except vWF.<br>The liver must be severely diseased in order to show effect so the prognosis is poor | -Vit K deficiency mostly due to TPN and antibiotic use.<br>-Decreased liver synthesis of Vit-K dependent clotting factors (factors II, VII, IX, and X; proteins C and S) |
| **Clinical features** | • Abnormal bleeding-GI is the most common.<br>• Prolong PTT and mostly PT | • Hemorrhage<br>• Initially PT prolongation followed by PTT. |
| **Treatment** | FFP = fresh frozen plasma<br>Vit-K in cholestasis.<br>Cryoprecipitate if there is fibrinogen deficiency. | Vit-K replacement |

# Platelets disorders

- The abnormality is in the platelets themselves with preserved coagulation factors
- Abnormality could be either QUANTITATIVE or QUALITATIVE
- Clinical features include:- Mucosal & skin bleeding [Superficial]
- Ex of Mucosal bleeding: Epistaxis, Gums bleeding, hematuria,hemoptysis AND GI + intracranial bleeding in severe cases
- Ex of skin bleeding: Petechiae, Purpura, Ecchymoses
- Platelets <50K symptoms initially may start!

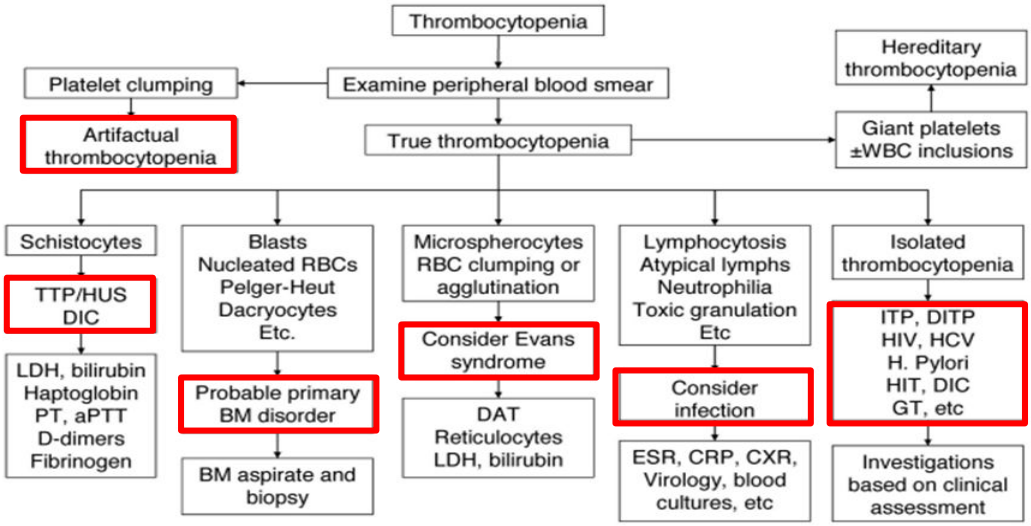



| Causes of Thrombocytopenia | |
|---|---|
| **a. Decreased production** | • Bone marrow failure: acquired (aplastic anemia), congenital (Fanconi syndrome), congenital intrauterine rubella<br>• Bone marrow invasion: tumors, leukemia, fibrosis<br>• Bone marrow injury: drugs (ethanol, gold, cancer chemotherapy agents, chloramphenicol), chemicals (benzene), radiation, infection |
| **b. Increased destruction** | • Immune: infection, drug-induced(e.g.Chemotherapy), immune thrombocytopenic purpura (ITP), SLE, heparin-induced thrombocytopenia (HIT) type 2, HIV-associated thrombocytopenia<br>• Nonimmune: disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP), HIT type 1 |
| **c. Sequestration** | • Splenomegaly |
| **d. Dilutional** | • After transfusions or hemorrhage |
| **e. Pregnancy** | • Usually an incidental finding (especially third trimester) but can also occur in setting of preeclampsia or eclampsia (remember HELLP syndrome) |

**HELLP** syndrome: is a life threatening pregnancy complications characterized by:
**H**emolysis
**E**levated liver enzymes
**L**ow **P**latelets count

## Approach to Thrombocytopenia

- It's very important to ask for peripheral blood smear: to see any additional abnormal cells
- Platelet clumping: in vitro condition in which the device count 2 PLTs as one. So, it's better to do manual PLTs counting




A- **Quantitative**

### 1- Immune Thrombocytopenic Purpura (ITP)

Roll out to know the diagnosis (Diagnosis of Exclusion)

This results from autoimmune antibody formation against host platelets. These antiplatelet antibodies (IgG) coat and damage platelets, which are then removed by splenic macrophages (reticuloendothelial system binds self immunoglobulins attached to the platelet)

1) Primary: isolated thrombocytopenia due to immune Plt destruction & ↓ production (auto-Antibodies to megakaryocytes) (بدون سبب)
2) Secondary: disease/drug exposure → Viral (HIV, HCV, HBV, EBV, CMV, Parvovirus), SLE, antiphospholipid syndrome (APLS), H. Pylori Infection, Chronic Lymphocytic Leukemia (CLL), Hodgkin Lymphoma,autoimmune hemolytic anemia ( AIHA)

### Clinical features

1. Petechiae and ecchymoses on the skin—many patients will have only very minimal bleeding symptoms despite extremely low platelet counts (<5,000/mL)
2. Bleeding of the mucous membranes
3. No splenomegaly

**Diagnosis**: Dx of exclusion, no robust clinical or Lab parameters, Typically CBC (Isolated ↓ PLT < 100.000), 10% have ITP + AIHA (Evans Syndrome), PBS (Large Plts), Anti-Plt AB (not useful)

**Clinically**: insidious onset of mucocutaneous bleed, more common in female. F:M(3:1)

**Treatment**: rarely indicated if PLT > 50.000 unless bleeding, trauma/surgery, anticoaglants, comorbidities.
1st line: Steroids, IVIG =intravenous immunoglobulin
2nd line: Splenectomy, TPO(Thrombopoietin) agonists (Romiplostim, Eltrombopag)

## 2- Thrombotic Thrombocytopenic Purpura (TTP) / Hemolytic Uremic Syndrome (TTP/HUS)

- The doctor only talked about it briefly
- Very important emergency. Curable but has 90% mortality if not diagnosed.
- On peripheral blood smear we will see schistocytes.

### A. General characteristics

1. TTP is a rare disorder of platelet consumption. Patients with TTP lack functional ADAMTS13, a protease that cleaves von Willebrand factor (vWF). Ultralarge vWF multimers build-up in the blood as a result of this deficiency.
2. Microthrombi (mostly platelet thrombi) occlude small vessels leading to microangiopathic hemolytic anemia—any organ may be involved. They cause mechanical damage to RBCs (schistocytes on peripheral smear)
3. This is a life-threatening emergency that is responsive to therapy. If untreated, death occurs within a few months.

### B. Clinical features

1. Hemolytic anemia (microangiopathic)
2. Thrombocytopenia
3. Acute renal failure (mild)
4. Fever
5. Fluctuating, transient neurologic signs—can range from mental status change to hemiplegia

### C. Treatment

1. Plasmapheresis (large volume).
a. Begin as soon as diagnosis is established (delay in treatment is life-threatening).
b. Response is usually good (monitor platelet count, which should increase).
2. Corticosteroids and splenectomy—may be of benefit in some cases.
3. Platelet transfusions are contraindicated.

## 3- Disseminated Intravascular Coagulation (DIC)

- DIC is characterized by abnormal activation of the coagulation sequence, leading to formation of microthrombi throughout the microcirculation. This causes consumption of platelets, fibrin, and coagulation factors. Fibrinolytic mechanisms are activated, leading to hemorrhage. Therefore, bleeding and thrombosis occur simultaneously
- Most common in critically ill patients (in ICU), but can occur in healthy patients as well
- Can be acute (and fatal), or more gradual

**Etiology :** Trauma, shock, infection, malignancy (esp APML= acute promyeloid leukemia), Obstetric complications.

**Pathogenesis :**

- **massive activation of coagulation that overwhelms control mechanisms → thrombosis**
- **Acute consumption of coagulation factors & Plts → bleeding**

### Clinical features

1. Bleeding tendency (more common in acute cases)
    a. Superficial hemorrhage (ecchymoses, petechiae, purpura)
    b. Bleeding from GI tract, urinary tract, gingival or oral mucosa
    c. Oozing from sites of procedures, incisions, and so on
2. Thrombosis—occurs most often in chronic cases. End-organ infarction may develop; all tissues are at risk, especially the CNS and kidney

**Diagnosis:**

- ↑ PT, ↑ aPTT, ↑ LDH
- ↓ Fibrinogen (may be N b/c acute phase), ↓ PLT, ↓ Haptoglobin
- +ve D-Dimer/FDP, +ve Schistocytes

**Treatment:**

**1- Treat underlying process**

**2- FFP, Cryoprecipitate (Goal Fibrinogen > 100 mg/dL), PLT Tx**

| B- Qualitative: The doctor didn't explain it | |
|---|---|
| **ACQUIRED PLT FUNCTIONAL DISORDERS** | **INHERITED DISORDERS OF PLT FUNCTION** |
| 1.**Liver Disease**<br>2.**Cardiopulmonary Bypass**<br>3.**Uremia**<br>4.**Dysproteinemia ( Multiple Myeloma or Waldenstrom Macroglobulinemia )**<br>5.**Myeloproliferative Disorders (MPDs)**<br>6.**Diabetes Mellitus**<br>7.Acquired Glanzmann's Thrombasthenia | 1.**Giant platelet disorders** includes Plt GP abnormalities (eg, **Bernard-Soulier Syndrome**, **Deficiency of Platelet Alpha granules (eg, Gray Platelet Syndrome)**, Deficiency **May-Hegglin Anomaly** (which also involves the presence of abnormal neutrophil inclusions (ie, Döhle-like bodies)), & some kindreds with type 2B vWD (**Montreal Plt Syndrome**)<br>2.**Wiskott-Aldrich syndrome**<br>3.**Storage Pool Disorders** such as **Hermansky Pudlak Syndrome (HPS)** (Deficiency of Dense Granules)<br>4.**Glanzmann thrombasthenia**<br>5.**Platelet release disorders**<br>6.**Glycoprotein VI defects**<br>7.**Sticky platelet syndrome**<br>8.Congenital Deficiency of the ADP receptor $P2Y_{12}$<br>9.**Scott syndrome** |

**Bernard-Soulier Syndrome: A genetic GPIb deficiency → Impaired platelets adhesion**
**Glanzmann thrombasthenia: A genetic GPIIb/IIIa deficiency → Impaired platelets aggregation**

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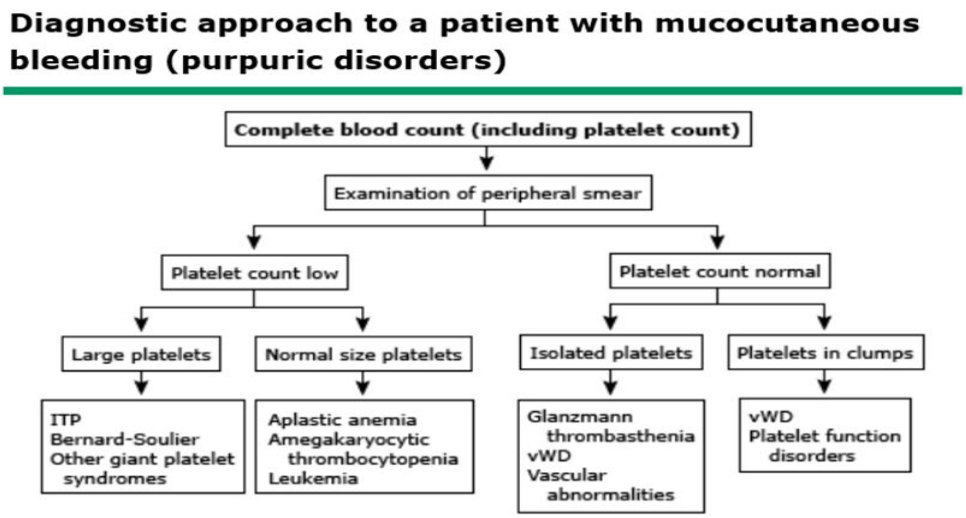
## Diagnostic Approach to PLTs Disorders



## Approach to Pt with potential bleeding (very important)

**I. Detailed Pt & Family Medical History** (Crucial & Vital regardless of the prior Lab testing)
>> establish likelihood of a bleeding disorder
>> guide laboratory Testing

- Early in the newborn period (circumcision)
- After hemostatic Challenges ( delivery, injury, trauma, surgery, invasive dental procedure, menstruation)
- Frequency & pattern
- Duration
- Onset ( congenital vs. acquired )
- Time required for cessation

Sites of bleeding (specific or multiple)

! **Sites of bleeding (specific or multiple)**
- Mucocutaneous Bleeding: Easy bruising, Epistaxis, Menorrhagia → Primary Hemostasis Defects ( PLT or vW Factor )
- Deep Tissue Bleeding: Joints, Muscles, Central Nervous System → Secondary Hemostasis Defects (Clotting Factors Deficiencies )

- Current use of medications or herbal supplements
- Use of Bleeding Assessment Tools (differentia bleeding phenotypes, require validation by prospective studies)

**II. Laboratory Testing**
- Screening Tests (not sensitive to all abnormalities)

I.CBC (Platelet count)
II.Prothrombin Time (PT) >> measures F VII, X, V, II, I - (N Time 10-14 secs)
III.International Nmalized Ratio (INR) >> the ratio of a pt's PT to a normal (control) sample, raised to the power of the ISI= international safety index value for the control sample used.
IV.Activated Partial Thromboplastin Time (aPTT or PTT) >> measures F XII, XI, IX, VIII, X, V, II, I - (N Time 30 – 40 secs)
V.Thrombin (Clotting) Time (TT) >> sensitive to deficiency of Fibrinogen or inhibition of thrombin - (N Time 14 – 16 secs)
VI.Bleeding Time >> (3-8 secs) (not sensitive – not specific )

**III. Specialized Tests**
- ❖ Mixing Study Mentioned before

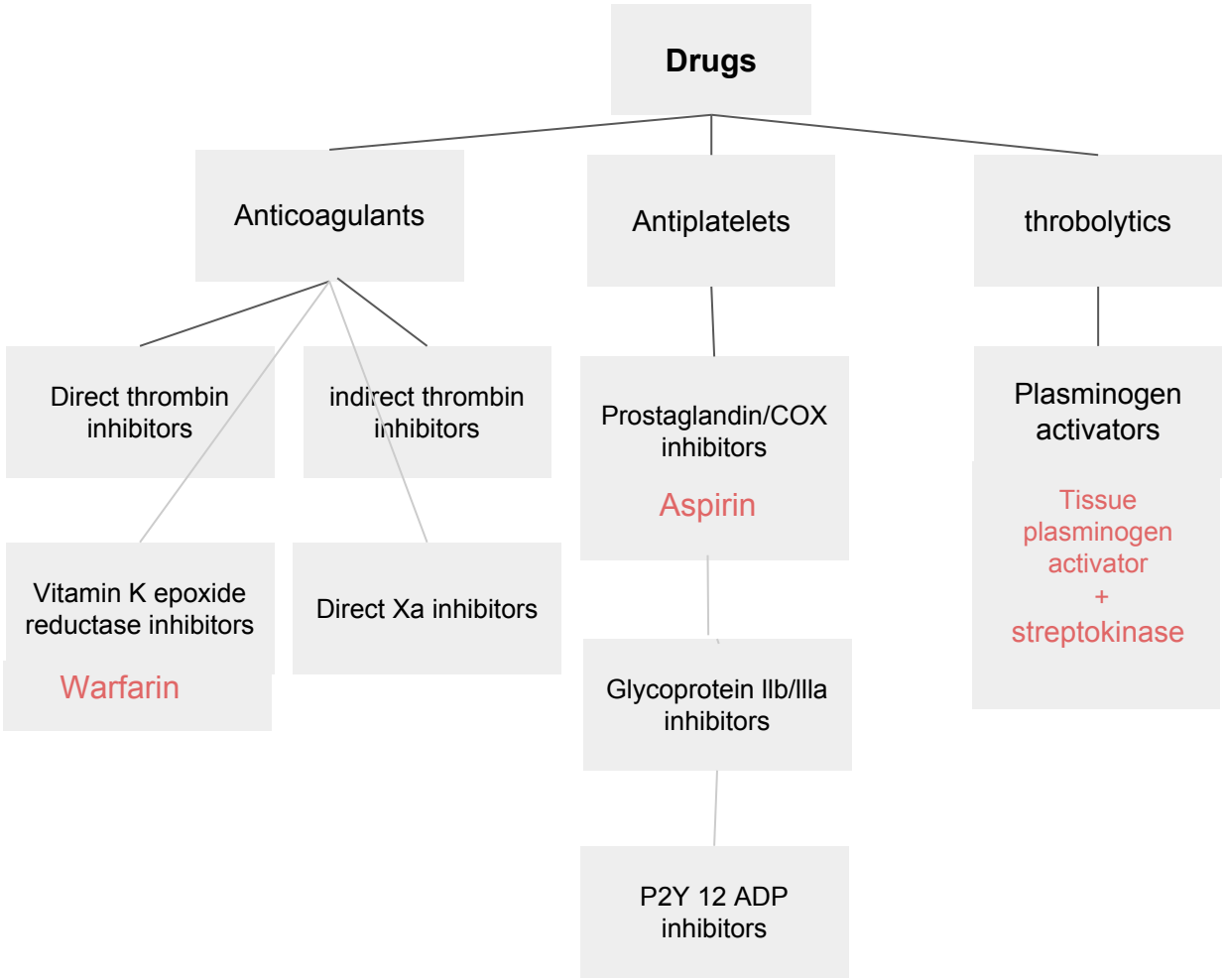
I.PLT Function Assay (PFA - 100): assess PLT function
- *Specificity* : 90 % for severe PLT dysfunction of vWD (vWF plasma levels < 25%)
- *Sensitivity* : 24 – 41 % (low) in mild PLT secretion defect or Storage Pool Disease ( not screening tool )

II.PLT Aggregation Tests: (5 external aggregating factors; ADP, Collagen, Ristocetin, Arachidonic Acid, Adrenaline)
III.Von Willebrand Factor ( Antigen & Activity )
IV.Factor XIII assay (F XIII Deficiency >> normal PT & PTT)
V.Human Plasminogen Activator Inhibitor (PAI-1)
VI.Alpha 2 AntiPlasmin Inhibitor (α2 AP)

### Take Home Message

Although screening tests are used widely to identify hemostatic abnormalities associated with bleeding, they are NOT perfect → The Clinical suspicion for a bleeding disorder is Critical to determine extent of the laboratory investigations

**Not important slide but, we have to cover the management (mentioned in the objectives)**




Management in preoperative stage:

**Anti-platelets**

**Aspirin:** Discontinue approximately 7 days prior to non cardiovascular surgery

**P2Y12 receptor blockers(clopidogrel, prasugrel, ticlopidine, ticagrelor):** Should be discontinued 7 to 10 days, Clopidogrel and Ticlopidine should be stop at least 5 days

**Anticoagulant**

**Oral direct thrombin inhibitors and factor Xa inhibitors**

Interval between last dose and procedure for (Low bleeding risk)

- Dapigatran
- Rivaroxban
- Apixaban
- edoxaban

give last dose two days before procedure

# MCQ's

**Q1**: A 25-year-old woman presents with increasing weakness. She reports that she has had history of menorrhagia and easy bruising. She has no other prior medical history. She has no family history of bleeding disorders and denies a history of substance abuse. On physical examination she is tachycardic and pale, with multiple bruises on her body. Laboratory studies show a low iron level and decreased mean corpuscular volume. Coagulation studies are notable for a normal prothrombin time (PT), a prolonged partial thromboplastin time (PTT), a normal platelet count, and a prolonged bleeding time. Which of the following is the most likely diagnosis?
(A) Aspirin ingestion
(B) Factor VII deficiency
(C) Factor IX deficiency
(D) Hemophilia A
(E) Von Willebrand disease (vWD)
**Q2**: A previously healthy 20-year-old woman presents to the emergency department with fever, jaundice, and confusion. Her examination is notable for a temperature of 102 F, scleral icterus, scattered petechiae on her palate and extremities, and disorientation on mental status examination. Laboratory studies reveal a platelet count of 20,000/mm a hemoglobin of 8 g/dL, an elevated indirect bilirubin level, and a creatinine of 5 mg,dL. Her prothrombin time (PT)- and partial thromboplastin time (PTT) are both normal. Her peripheral blood smear reveals decreased platelets and schistocytes. Which, of the following is the most likely- diagnosis in this patient?
(A) Autoimmune hemolytic anemia
(B) Disseminated intravascular coagulation (DIC)
(C) Idiopathic thrombocytopenic purpura (ITP)
(D) Thrombotic thrombocytopenic purpura (TTP)
(E) Von Willebrand disease
**Q3**:A 15-year-old white boy presents with a hemarthrosis of the right knee joint and a recent history of protracted bleeding from cuts or scrapes. He has no family history of bleeding disorders. The-patient also notes, a long history of chronic abdominal discomfort and diarrhea, which has been worse for the past 6 months, occasionally accompanied by fever. Physical examination reveals a patient at the 5th percentile for both height and weight; an actively bleeding rectal fissure is
also noted. Both prothrombin time (PT) and the partial thromboplastin time (PTT) are prolonged. Laboratory evaluation, of the blood is likely to reveal low levels of which of the following?
(A) Factor VIII
(B) Factor IX
(c) Factors II,VII,IX,and X
(D) Factors II,VII,IX,and X
(E) von Willebrand factor
**Q4**:A 12-year-old patient complains of easy bruising and nosebleeds, small ecchymoses can be seen on the patient's skin. The patient reports feeling ill in the last week with mild fever and a sore throat. The nosebleeds are not prolonged and stop soon after pressure is applied. A blood test shows a mild thrombocytopenia. The most likely diagnosis is:
A. Immune thrombocytopenic purpura
B. Aplastic anaemia
C. Bernard Soulier syndrome
D. Glanzmann's thrombasthenia
E. Thrombotic thrombocytopenic purpura

**Answers:1.E, 2.D,3.C,4.A**

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**Thank you**

**If you have any question please contact with us at:**
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