Blood pathology 2

BLEEDING DISORDERS

A) Hereditary bleeding disorders

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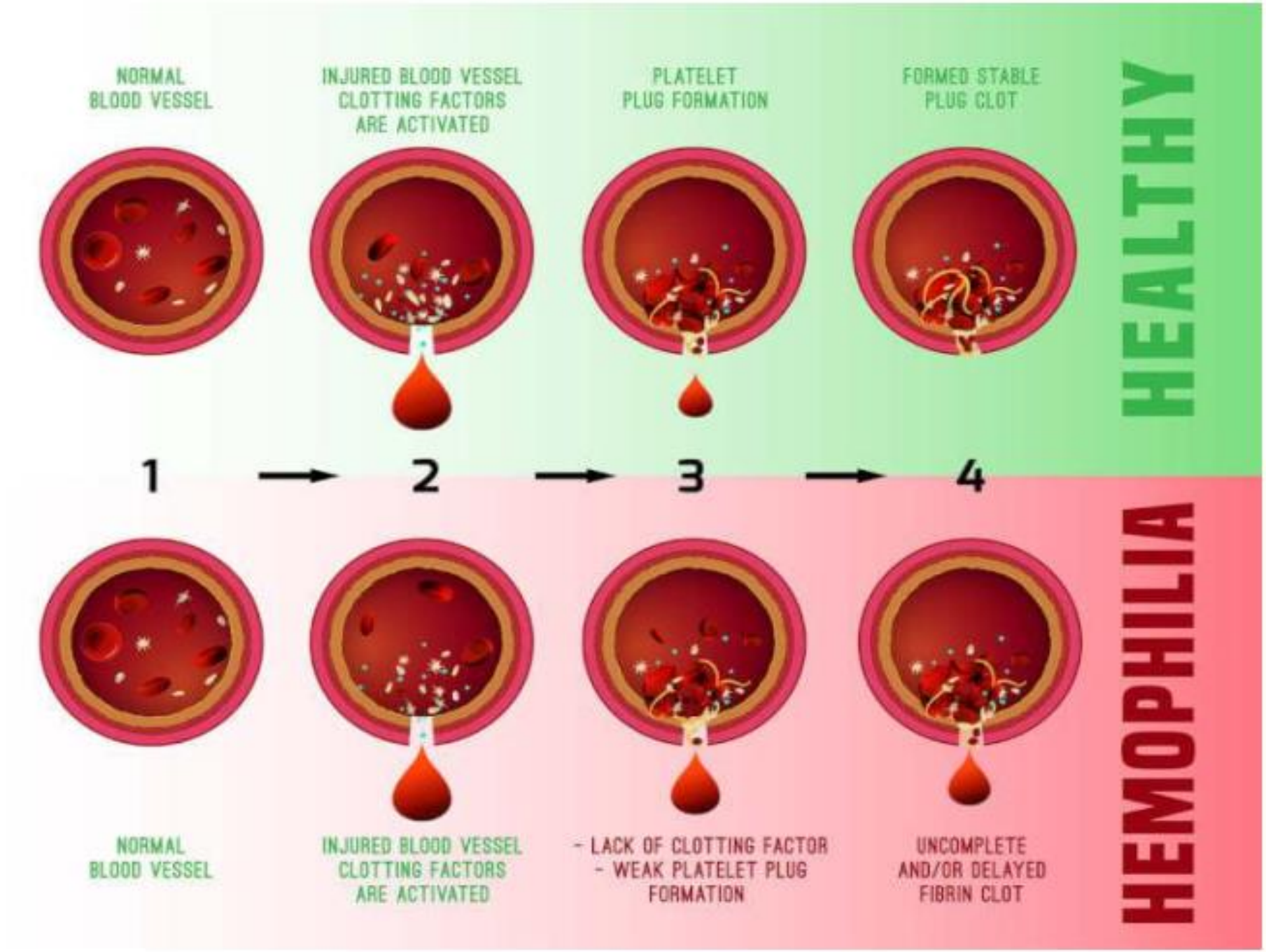
- **A) Hereditary bleeding disorders**

- **Hereditary deficiencies** of each of the coagulation factors have been described. **Haemophilia A** (factor VIII deficiency) , **hemophilia B** (Christmas disease ,factor IX deficiency) and von **Willebrand disease** (vWD) are the most common ; the others are rare.

- **HEMOPHILIA A (FACTOR VIII DEFICIENCY)**

- **Hemophilia A** is the most common of the hereditary clotting factor deficiencies. The prevalence is of the order of 30-100 per million population. The inheritance is sex-linked, but up to 33% of patients have no family history and result from spontaneous mutation. This mutation leads to a severe clinical form of hemophilia A. The defect is an absence or low level of **VIII factor** in plasma.
- **Factor VIII** is a protein that is synthesized in the liver and spleen. The **factor VIII gene** is located near the tip of the long arm of the **X chromosome**.


NORMAL
BLOOD VESSEL
INJURED BLOOD VESSEL
CLOTTING FACTORS
ARE ACTIVATED
PLATELET
PLUG FORMATION
FORMED STABLE
PLUG CLOT
HEALTHY
1
2
3
4
NORMAL
BLOOD VESSEL
INJURED BLOOD VESSEL
CLOTTING FACTORS
ARE ACTIVATED
- LACK OF CLOTTING FACTOR
- WEAK PLATELET PLUG
FORMATION
UNCOMPLETE
AND/OR DELAYED
FIBRIN CLOT
HEMOPHILIA

- **Clinical features**

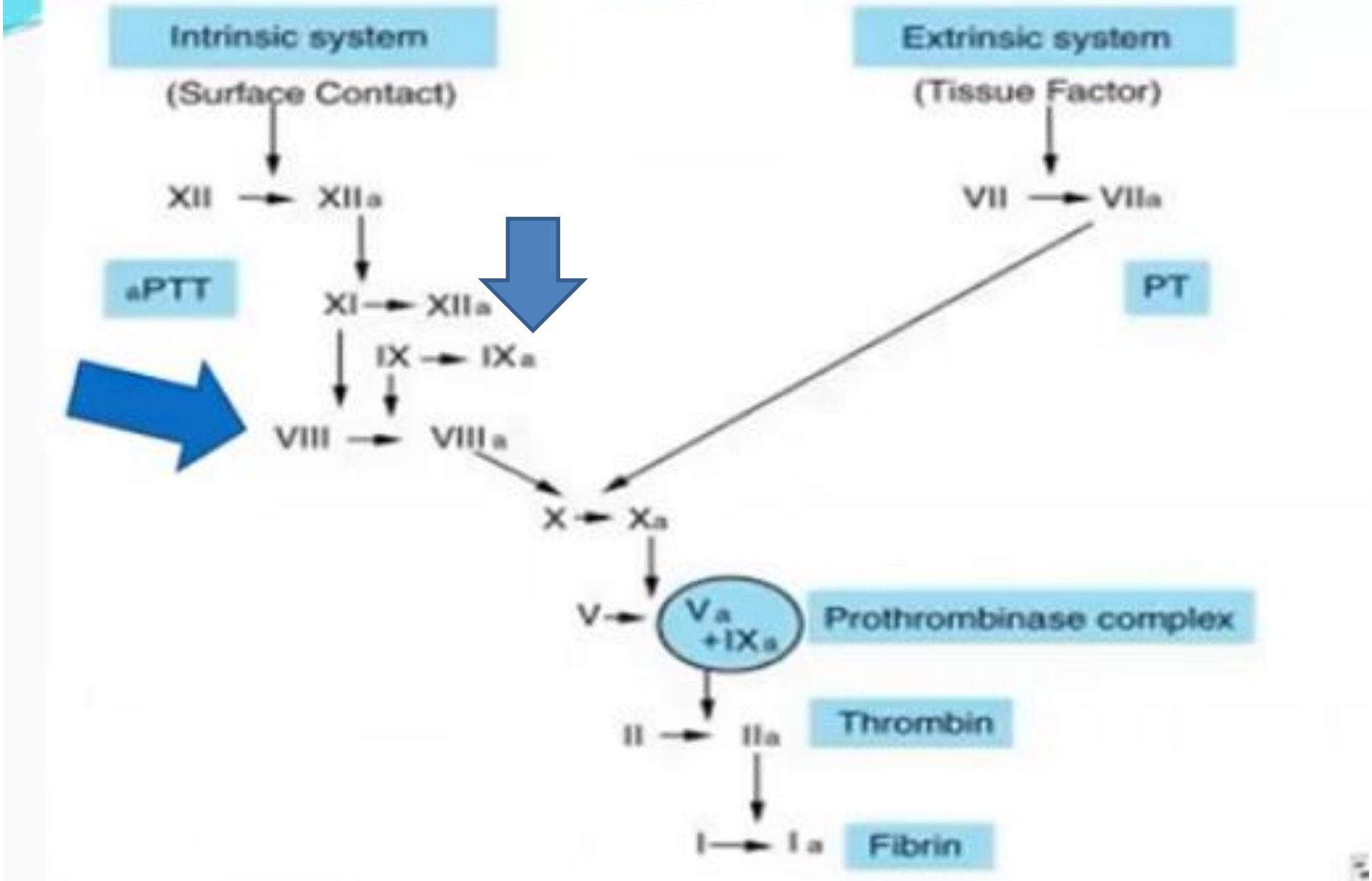
- Infants may suffer from post-circumcision hemorrhage or develop joint and soft tissue bleeds.

- excessive bruising when they start to be active.

- Prolonged bleeding occurs after dental extraction.

- Spontaneous haematuria and gastrointestinal haemorrhage.

- Operative hemorrhages


Intrinsic system
(Surface Contact)
Extrinsic system
(Tissue Factor)
XII
XIIa
VII
VIIa
aPTT
PT
XI
XIIa
IX
IXa
VIII
VIIIa
X
Xa
V
Va
+IXa
Prothrombinase complex
II
IIa
Thrombin
I
Ia
Fibrin

- **Laboratory Diagnosis:-**

1- Prolongation of the partial thromboplastin time (PTT).

2- Bleeding time normal .

3- Platelets count normal .

4- Prothrombin time (PT) normal .

5- Factor VIII : low .

6- Factor IX normal .

- Carriers are now better detected with DNA probes.

  Chorionic biopsies at 8-10 weeks from pregnancy provide sufficient fetal DNA for analysis.

- **Treatment**

- Bleeding case are treated with factor VIII therapy.

- Spontaneous bleeding is usually controlled if the patient's **factor VIII level** is raised to 30-50% of normal.

- Recombinant factor VIII preparations are now available for clinical use.

- **HAEMOPHILIA B (FACTOR IX DEFICIENCY)**

- The inheritance and clinical features of factor IX deficiency (Christmas disease) are identical to those of hemophilia A. factor IX is coded by a gene close to the gene for factor VIII near the tip of the long arm of the X chromosome. **Factor IX synthesis**, like that of prothrombin, factor VII , factor X , and protein C is vitamin K-dependant. Bleeding case are treated with high-purity factor IX .

- **Laboratory diagnosis:-**

1- APTT prolongs

2- Whole blood clotting time prolong.

3- Low factor IX.

4- Bleeding time normal.

5- prothrombin time (PT) normal.

Hemophilia A *("A"ight)*

- X-linked recessive
- Decreased synthesis of Factor VIII (8)
- Treat with recombinant Factor VIII

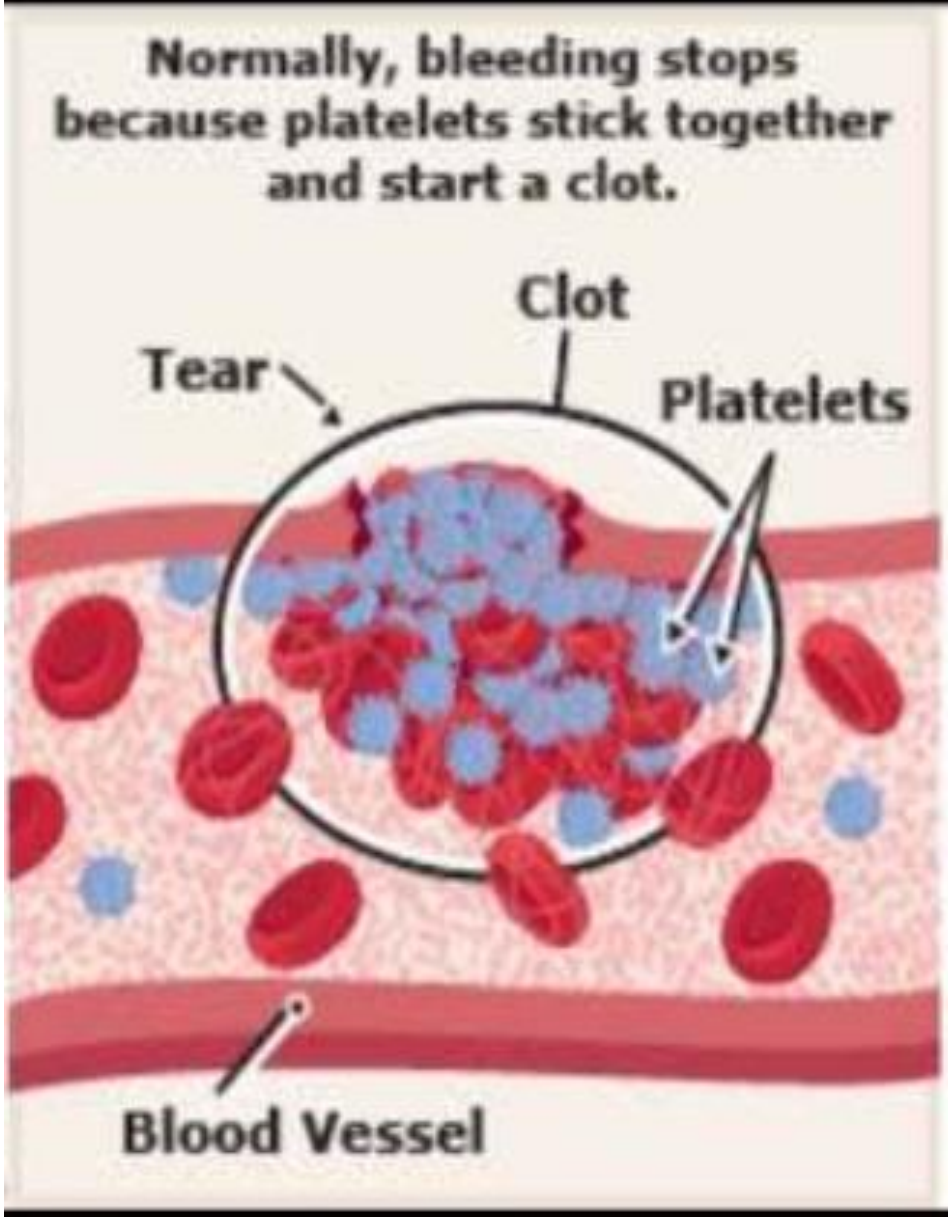
Hemophilia B

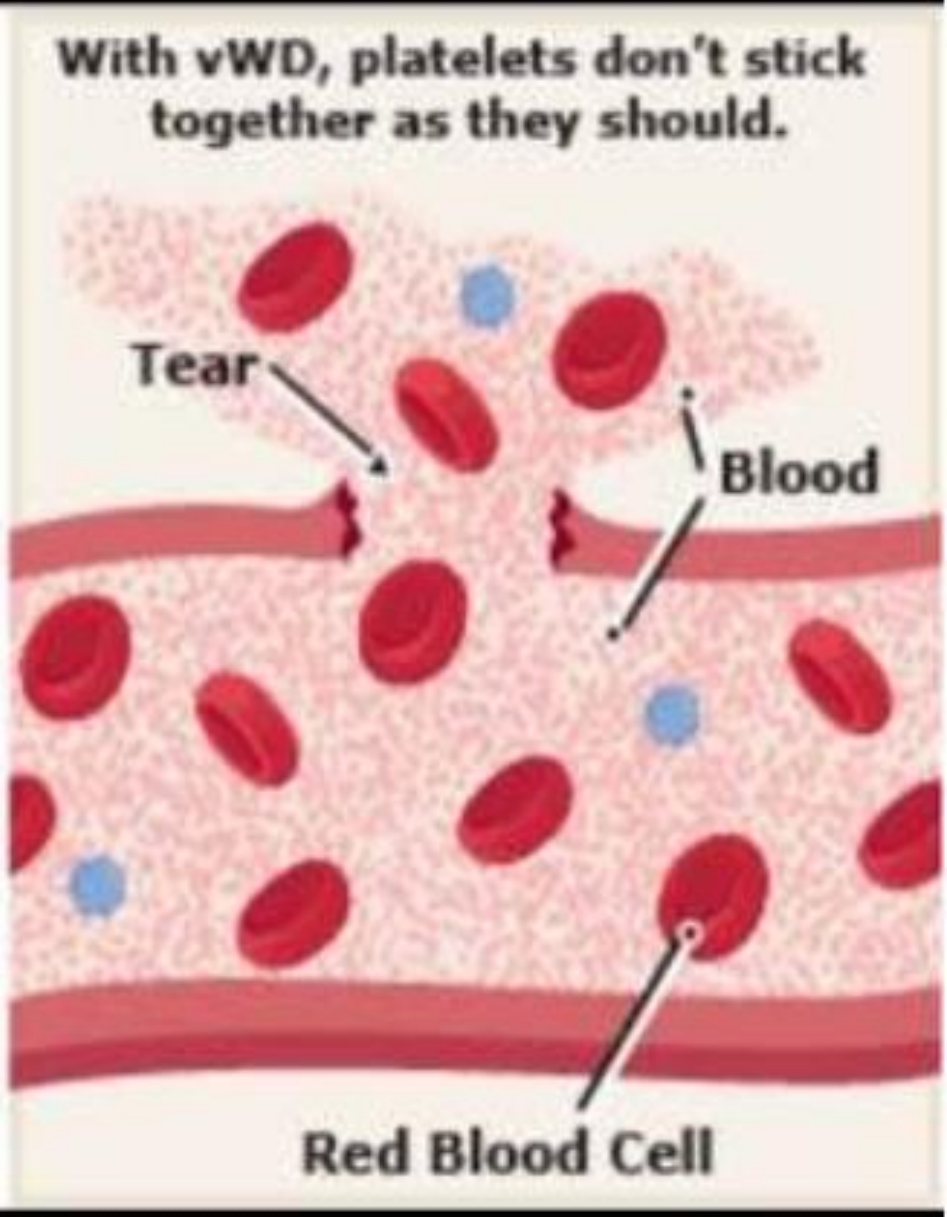
- X-linked recessive
- Decreased synthesis of Factor IX (9)
- Treat with recombinant Factor IX
- Christmas disease

- **VON WILLEBRAND DISEASE (vWD)**

- In this disorder, there is either a **reduced level** or **abnormal function** of **VWF** resulting from a point mutation or major deletion. VWF is produced in endothelial cells and megakaryocytes. It has two roles, it promotes **platelet adhesion** to damaged endothelium and it is the **carrier** for factor VIII , protecting it from premature destruction.

- chronic elevation of VWF is part of the **acute phase response** to injury, inflammation, or pregnancy.
- VWD is the most common inherited bleeding disorder.


Normally, bleeding stops because platelets stick together and start a clot.
Clot
Tear
Platelets
Blood Vessel


With vWD, platelets don't stick together as they should.
Tear
Blood
Red Blood Cell

- **Laboratory findings**

- 1- The bleeding time can be prolonged. This test is usually replaced by platelet function analysis-100(PFA-100 test).

- 2- Factor VIII levels are often low. If low, a factor VIII-VWF binding assay is performed.

- 3- The aPTT may be prolonged.

- 4- VWF levels are usually low

- **Treatment**
- Bleeding case are treated with cryopreciptation.

- Hereditary disorders of other coagulation factors include deficiency of fibrinogen, prothrombin , factors V , VII , combined V & VIII , X , XI , and XIII. These disorders are rare .

Thank You For Listening