Bleeding disorders

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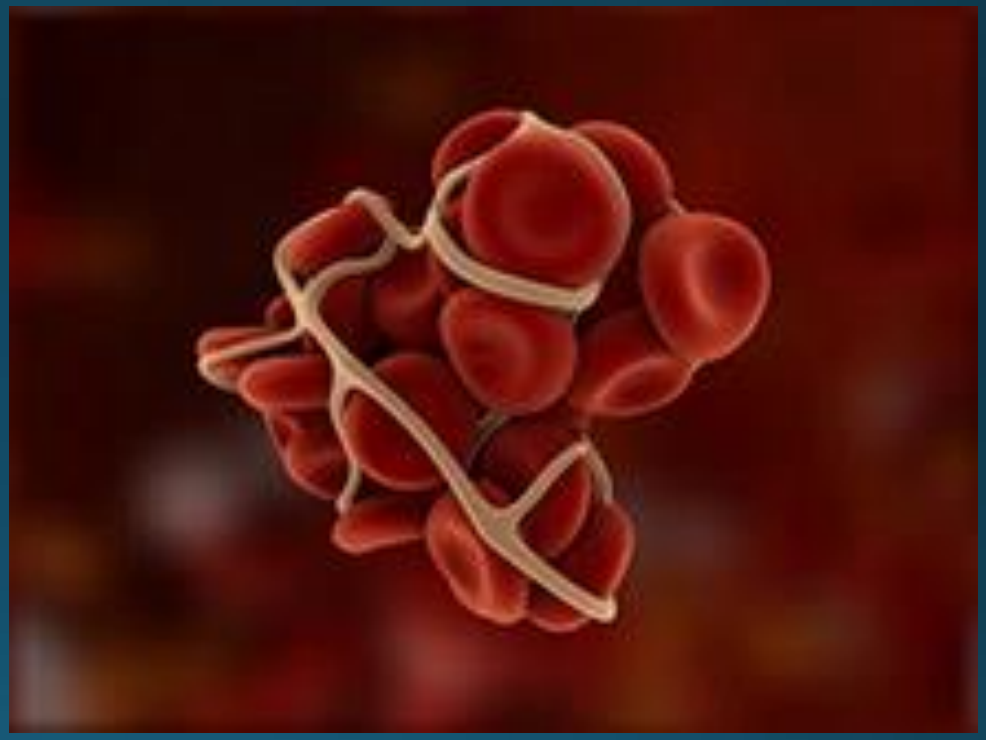
Haemostasis

- Vessel wall
- Platelets
- **Clotting factors**
- Fibrinolysis



Objectives

At the end of this lecture student should be able to:

- List congenital and acquired bleeding disorders
- Describe the clinical features ,laboratory abnormalities & management of vWD
- Describe the clinical features , lab investigations of other acquired bleeding disorders-DIC/Vit K deficiency

Coagulation disorders

Clotting factor defects

Acquired

Congenital

Coagulation disorders

Acquired

- Deficiency of Vit K dependent factors
- Liver disease
- **DIC**
- Inhibitors of coagulation factors
- Others

Congenital

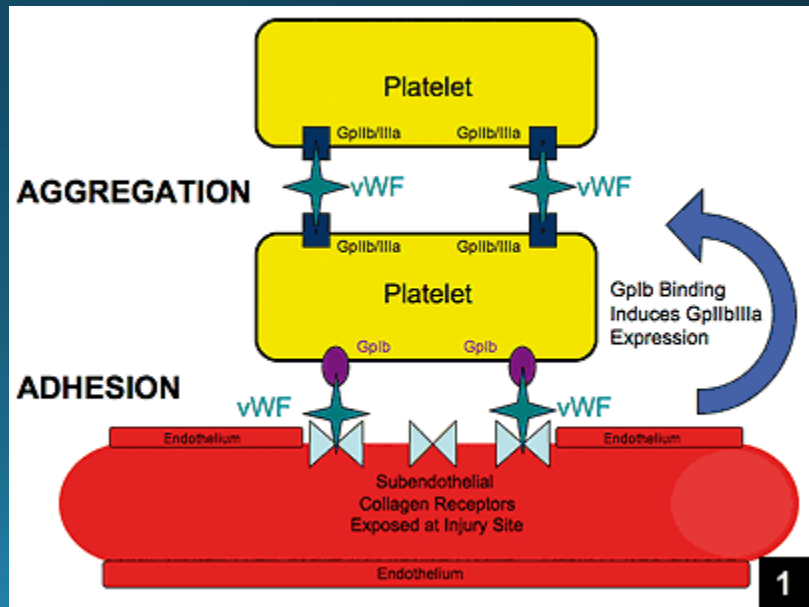
- **F VIII def-Haemophilia A**
- **F IX def-Haemophilia B**
- Other factor def
- VWD

F XII/Contact factor def do not cause bleeding disorders

Von Willebrand Disease

- Von Willebrand factor(VWF)
  - Synthesis in endothelium and megakaryocytes
  - Large protein/Multimer
  - Carrier of factor VIII
  - Anchors platelets to subendothelium
  - Bridge between platelets
- VWD

  Reduced level/abnormal function of VWF



Von Willebrand Disease

- VWD is the most common inherited bleeding disorder
- *Males and females are affected equally(*Inheritance –AD)

Deficiency of VWF results in defective platelet adhesion and causes a secondary deficiency in factor VIII

- Bleeding that appears similar to that caused by platelet dysfunction or hemophilia
- Mucocutaneous bleeding is common
- Haemarthroses/muscle haematomas -rare

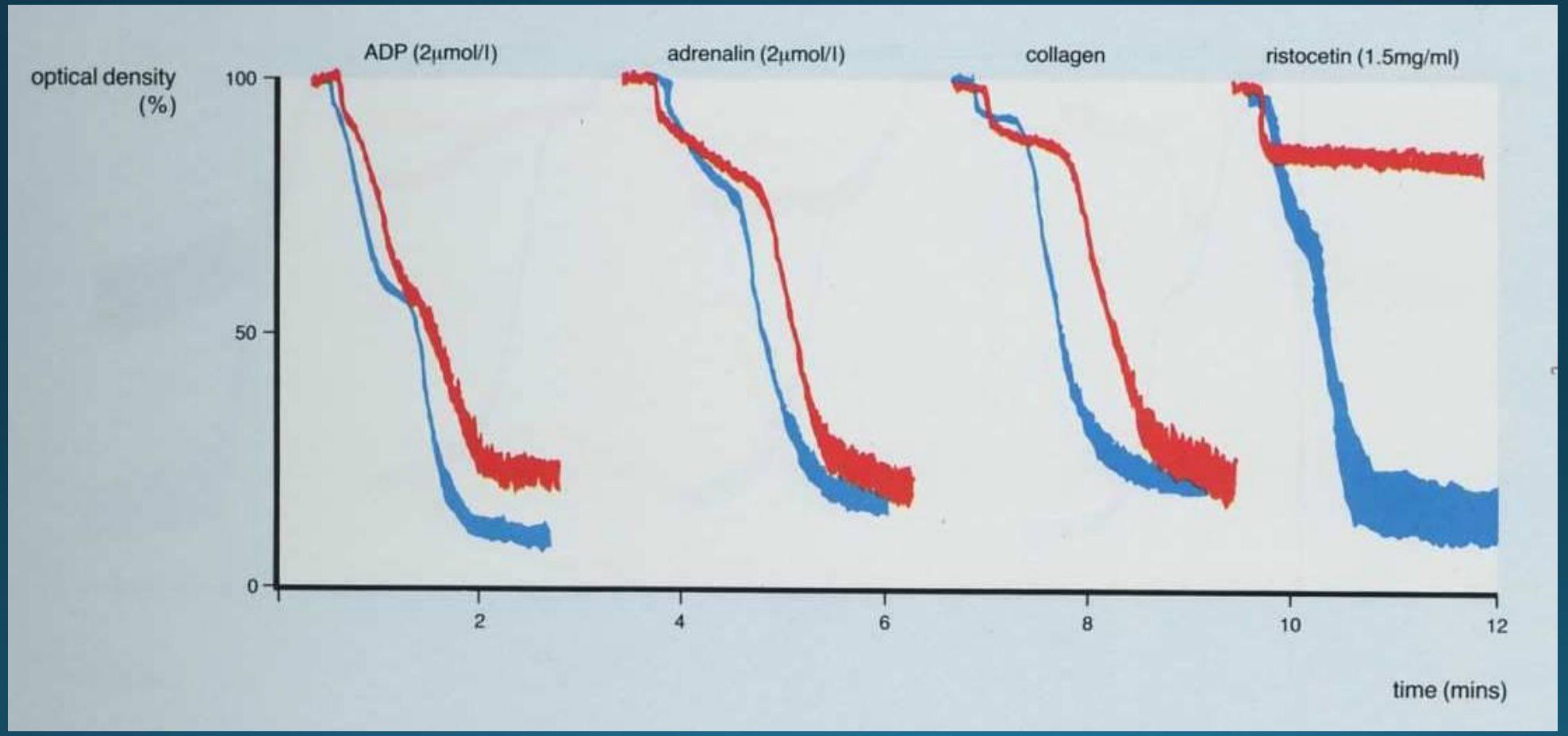
Von Willebrand Disease

- **Type I(70-80%) :**a mild-to-moderate quantitative deficiency in VWF.
- **Type II(10-15%) :** is due to qualitative abnormalities of VWF.
- Type III : a severe quantitative deficiency

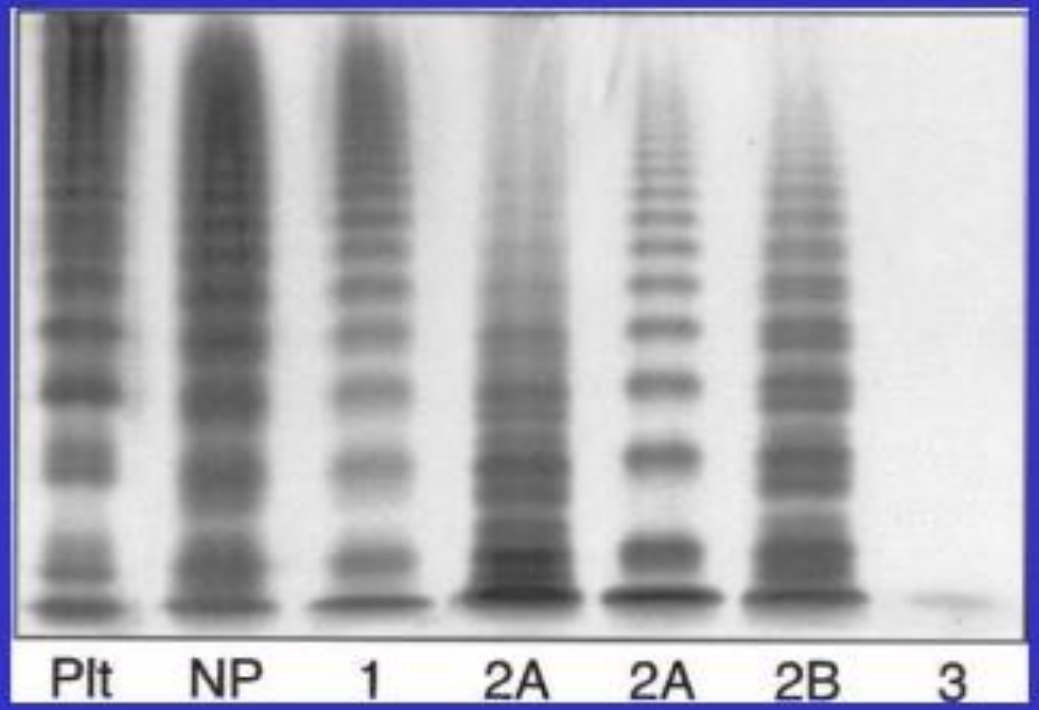
Investigations

- FBC+BP-Normal platelet count *(except type 2B)*
- BT-increased (PFA 100 test-abnormal)
- Clotting tests-APTT-may be prolonged
- VWF level-Low
- F VIII-may be low
- Platelet function tests- Decreased aggregation with restocetin
- VWF multimer analysis- for sub typing

No aggregation with ristocetin



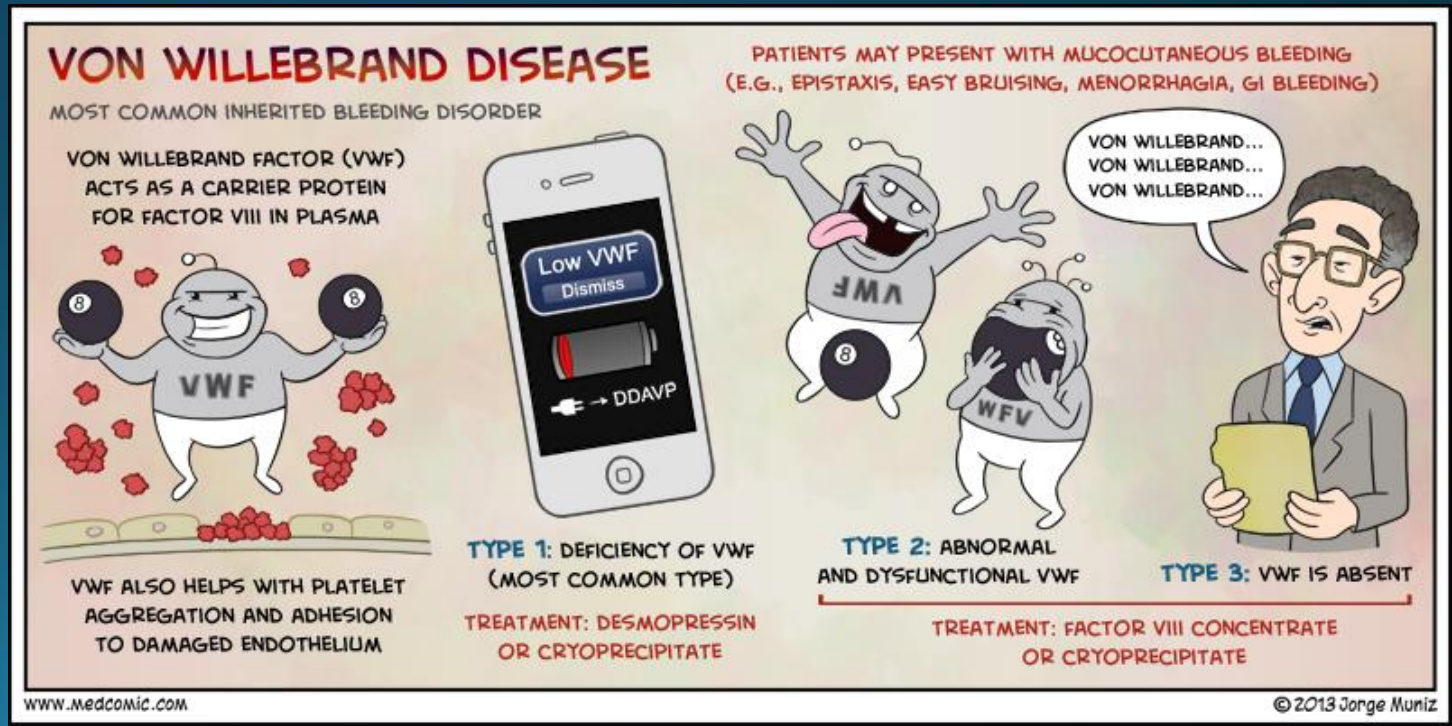
Multimer Structure of vWF



- Type 1; Decease in all multimer sizes
- Type 2; Decrease in large multimers
- Type 3; Absence of VWF

Treatment

- Local measures
- Antifibrinolytics- Tranexamic acid
- Drugs-DDAVP
- Blood products-Cryoprecippitate
- Factor concentrate- plasma derived FVIII/VWF conc.



Other inherited factor deficiencies

- V,VII,combined V&VIII,X,XI,XIII-Rare
- XI def-Ashkenazi Jews
- XIII def-severe bleeding, umbilical stump bleeding-Clotting screening tests are normal

bleeding disorders

aren't just  for boys.

[girls bleed too]

Acquired Bleeding disorders

Acquired Bleeding disorders

- Deficiency of Vit K dependent factors
- Liver disease
- **DIC**
- Inhibitors of coagulation
- Others

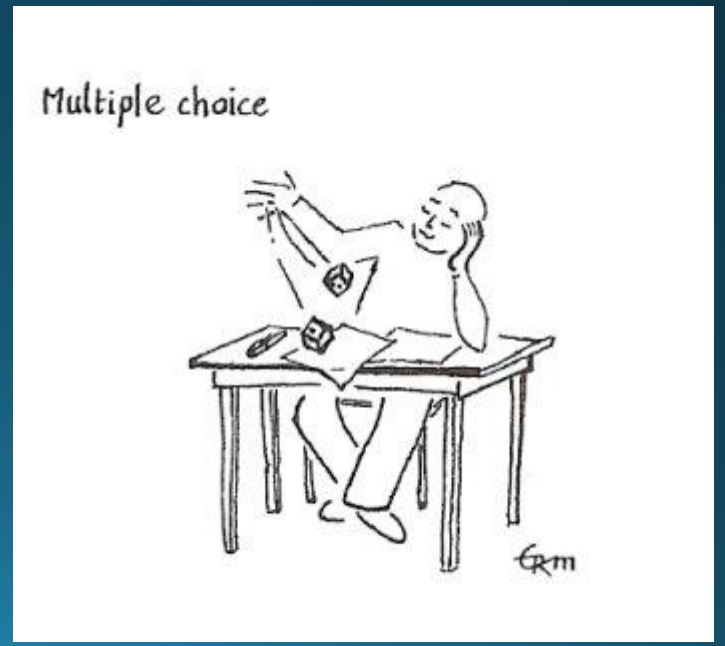
Disseminated Intravascular Coagulation (DIC)

- Widespread inappropriate intravascular deposition of fibrin
- Due to-

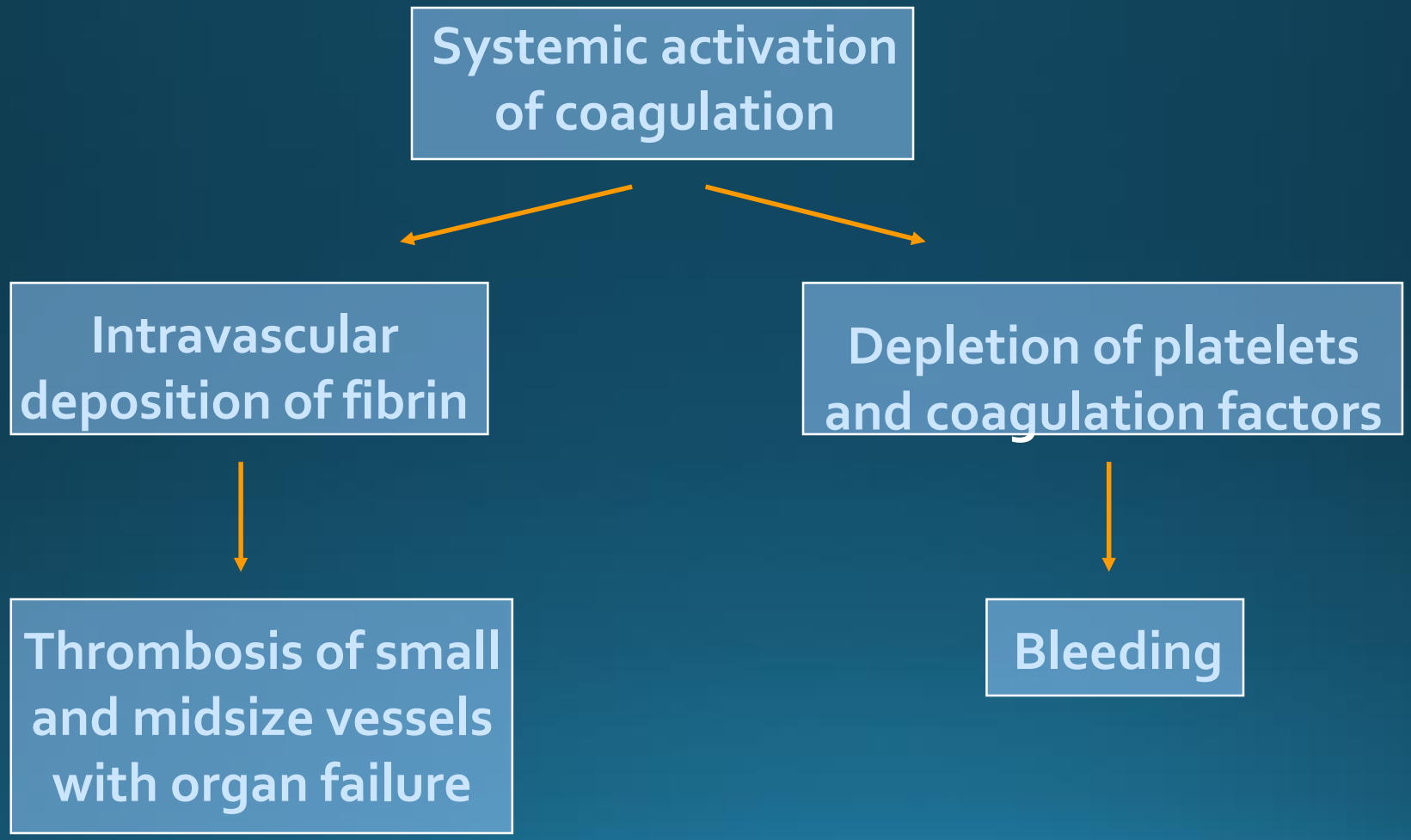
1. Procoagulant that are introduced/produced
2. Widespread endothelial damage

DIC -Causes

- Infections
- Obstetric complications- **amniotic fluid embolism/septic abortions/eclampsia/placental abruption**
- Malignancy-haematological/Non haematological
- Widespread tissue damage-trauma/burns
- Incompatible blood transfusions
- Surgery/trauma/burns
- Snake venom
- Misc:Pancreatitis/massive blood loss



Disseminated Intravascular Coagulation (DIC) Mechanism



Intrinsic pathway
(Endothelial injury)

Trauma
Burns
Gram-negative sepsis
Hypoxia
Acidosis
Shock
Vasculitis

Extrinsic pathway
(Tissue injury)

Trauma
Obstetric complications
Complications of cancer

Thrombin generation

Intravascular fibrin deposition

Plasminogen activation

Platelet consumption

Thrombocytopenia

Plasmin generation

Thrombosis

Fibrinolysis

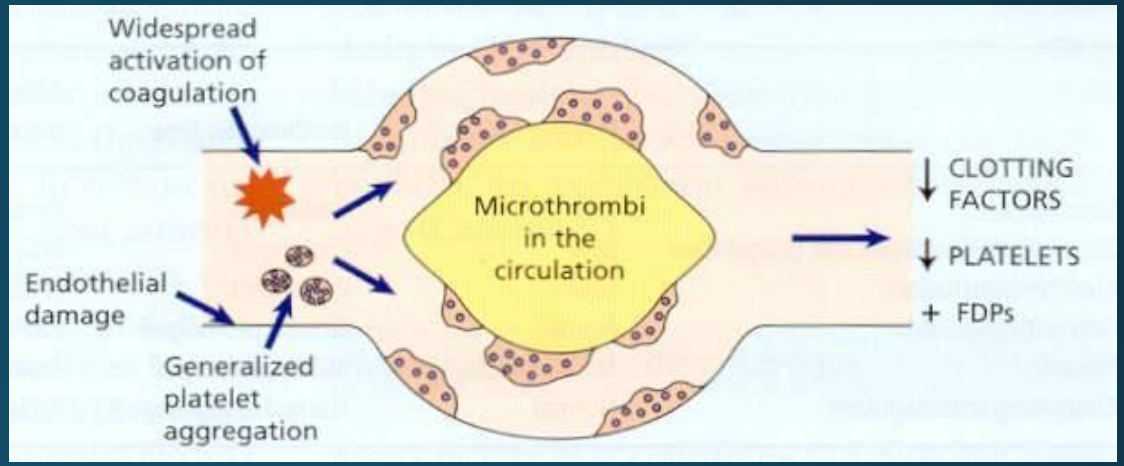
Clotting factor degradation

Hemolytic anemia

Tissue ischemia

Fibrin degradation products (inhibit Fibrin polymerization and platelet aggregation)

Bleeding



Investigations

- Consumption of clotting factors

↑ APTT

↑ PT

↑ TT

↓ Fibrinogen

- Presence of fibrinogen

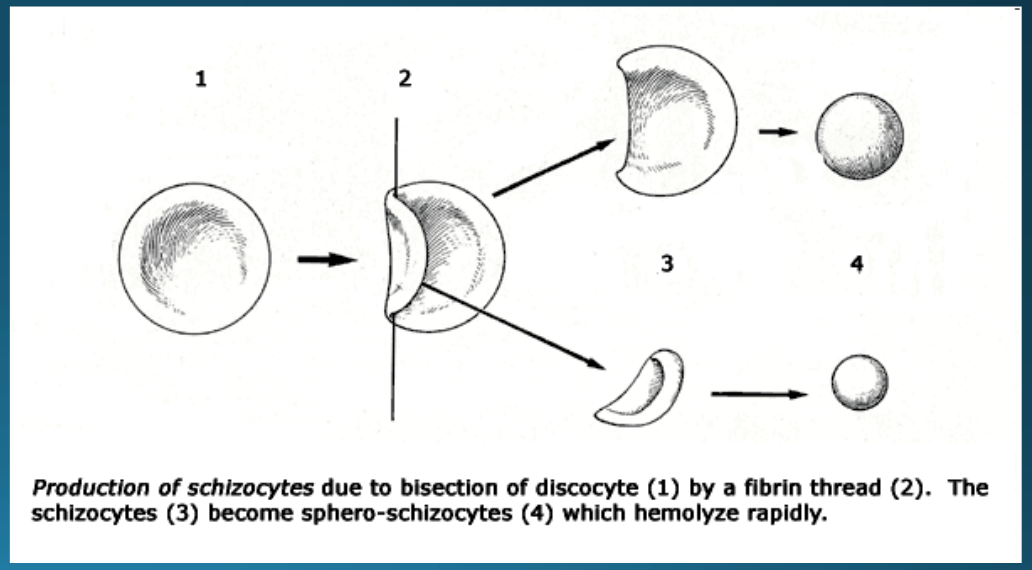
↑ FDP

- Intravascular clot

↓ Platelet

RBC fragmentation

DIC-Microangiopathic haemolysis



Production of schizocytes **due to bisection of discocyte (1) by a fibrin thread (2). The schizocytes (3) become sphero-schizocytes (4) which hemolyze rapidly.**

DIC-Bleeding

DIC-Bleeding

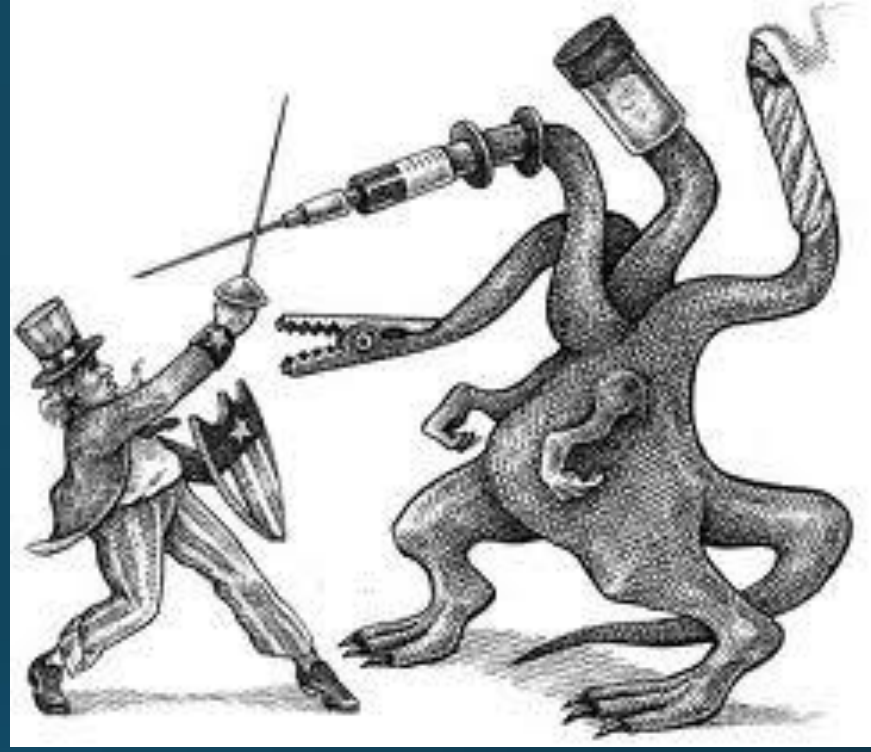
DIC-Thrombosis

Small fibrin thrombi can form in small arteries of brain, heart, **lungs**, kidneys, and other organs to produce ischemic tissue damage.

DIC-Management

- **Treatment of underlying disorder**

- Supportive treatment- Platelet transfusion
  cryoprecipitate
  FFP
  RBC



- Anticoagulation with heparin-for thrombosis

Deficiency of Vit K dependent factors

- Haemorrhagic disease of the new born
- Dietary
- Biliary obstruction
- Malabsorption
- Vit k antagonists-Warfarin

Haemorrhagic disease of the new born

- Low vit K dependent factors at birth
- Contributory factors-breast feeding
  liver cell immaturity
  ↓ gut bac .synthesis
- Bleeding-2nd-4th day
- Deficiency of Vit K dependent factors-II/VII/IX/X

Diagnosis

- PT & APTT-Prolonged
- Platelet-NL
- Fibrinogen-NL
- FDP-absent

Treatment

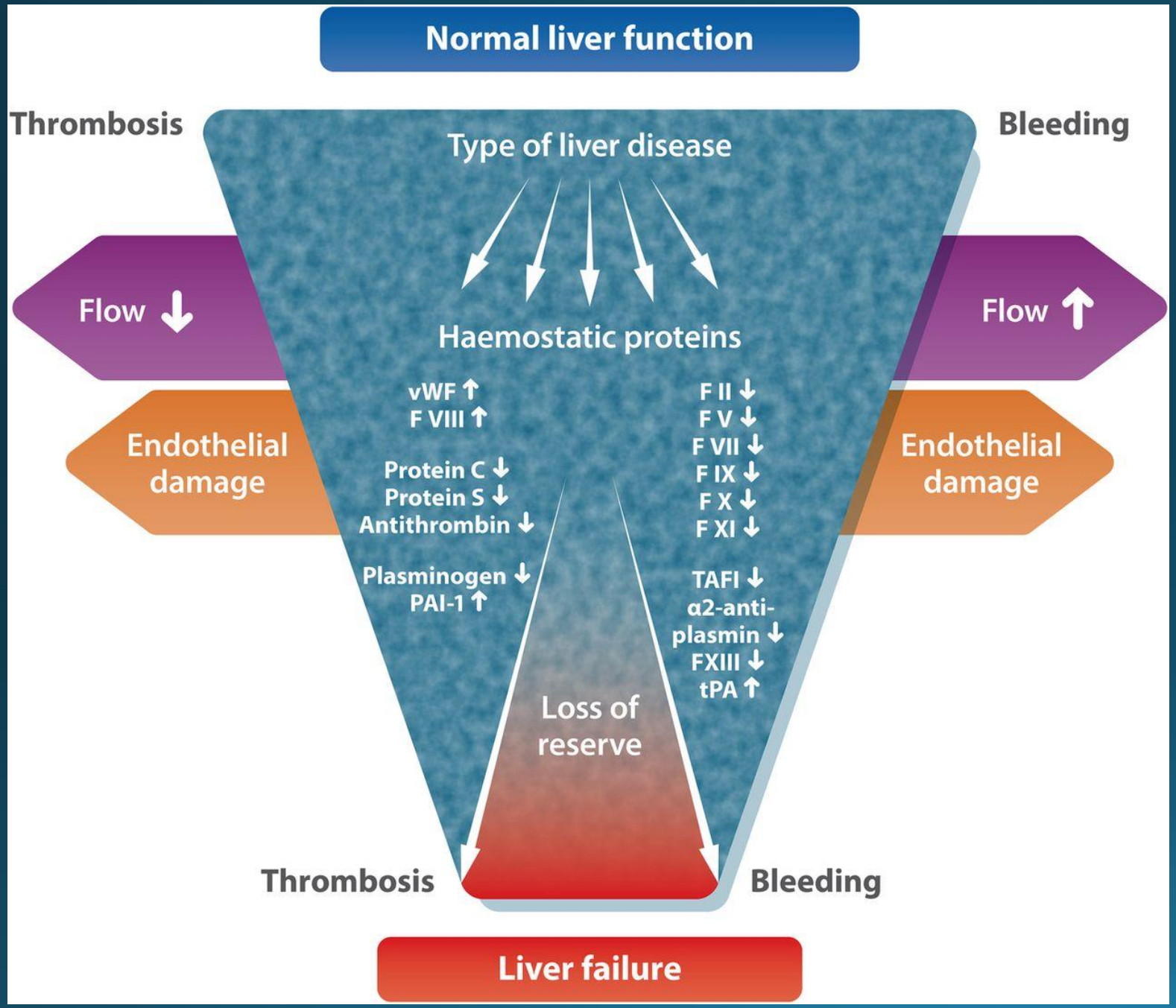
- Prophylaxis: IM 1 mg Vit K
- Bleeding neonates-IV Vit K, Prothrombin complex concentrate(PCC)

Liver Disease and Hemostasis

1. Decreased synthesis of II, VII, IX, X
2. Decreased Fcator V and fibrinogen
3. Dysfibrinogenemia
4. Enhanced fibrinolysis-increased plasminogen activator
5. DIC (release of thromboplastin from damged liver cells/ decreased pro c,ATIII/ decreased alpha-2-antiplasmin)

decreased clearance of activated coagulation factors & fibrinolytic system.

5.Thrombocytoepnia due to hypersplenism & reduced thrombopoietin


Normal liver function
Thrombosis
Bleeding
Type of liver disease
Flow
Flow
Haemostatic proteins
vWF ↑
F VIII ↑
F II ↓
F V ↓
F VII ↓
F IX ↓
F X ↓
F XI ↓
Endothelial damage
Endothelial damage
Protein C ↓
Protein S ↓
Antithrombin ↓
Plasminogen ↓
PAI-1 ↑
TAFI ↓
α2-anti-plasmin ↓
FXIII ↓
tPA ↑
Loss of reserve
Thrombosis
Bleeding
Liver failure

Inhibitors to clotting factors

- Antibodies against clotting factors
- FVIII-Acquired haemophilia

Causes: Post partum

Autoimmune diseases

Old age

Cancer

- Severe bleeding

Inhibitors to clotting factors

- Prolonged clotting tests cannot be corrected by adding normal plasma

Summary

- Acquired or inherited defects in vessel/platelet/clotting factors/fibrinolysis
- Acquired conditions common
- VWD is the commonest inherited bleeding disorder

What are the vascular disorders associated with bleeding?


Thank
you

Table 177–5 • VASCULAR DISORDERS ASSOCIATED WITH BLEEDING

CONGENITAL
Hereditary hemorrhagic telangiectasia
Cavernous hemangioma
Connective tissue disorders
- Ehlers-Danlos syndrome
- Osteogenesis imperfecta
- Pseudoxanthoma elasticum

ACQUIRED DISORDERS AFFECTING VASCULAR HEMOSTATIC FUNCTION
Scurvy
Immunoglobulin disorders
- Cryoglobulinemia
- Benign hyperglobulinemia
- Waldenström's macroglobulinemia
- Multiple myeloma
- Henoch-Schönlein purpura

Glucocorticoid excess
- Cushing's syndrome
- Glucocorticoid therapy