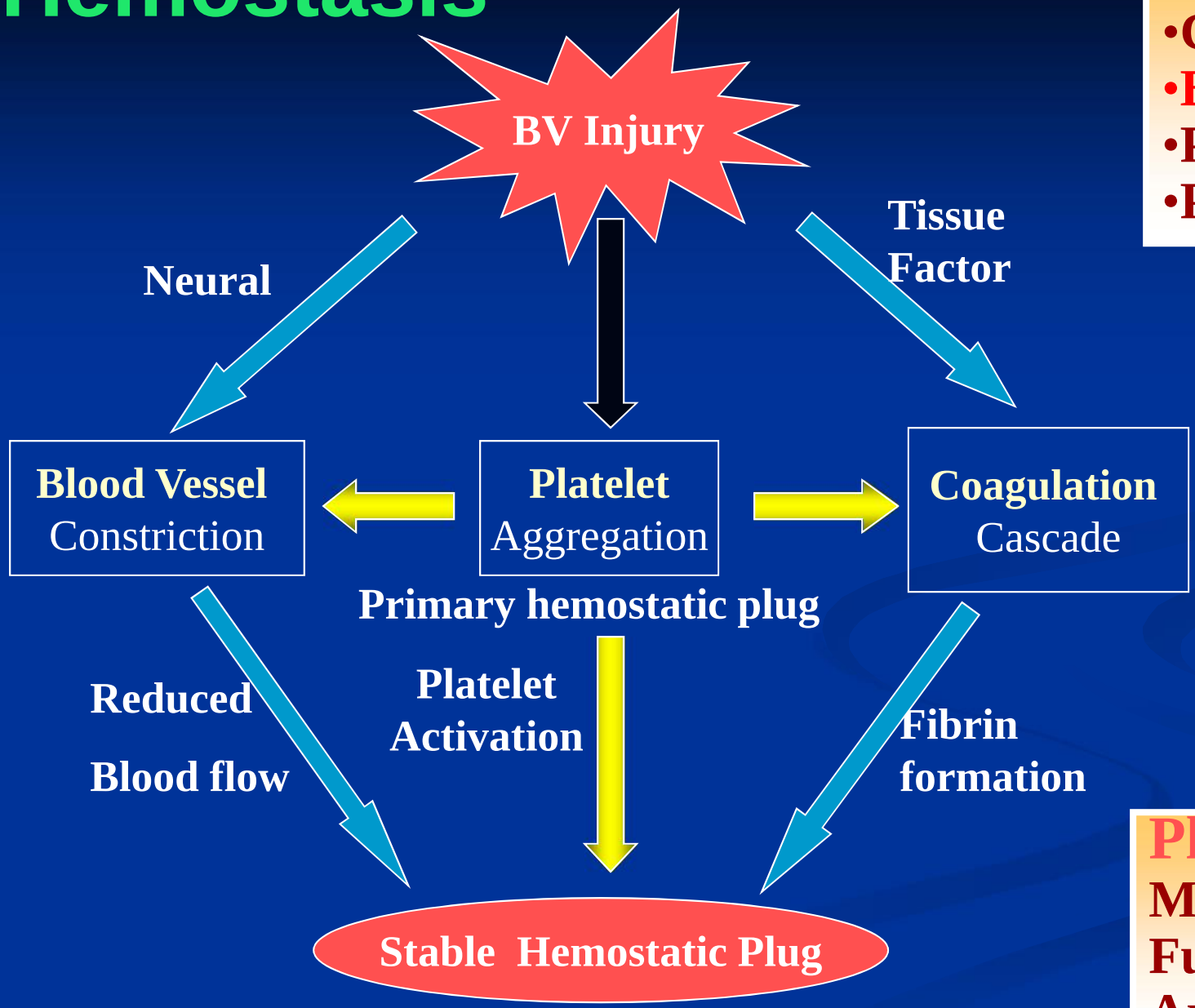
Coagulation Disorders

Dr. Muhammad Shamim
Assistant Professor, BMU

Introduction

- Local Vs. General
  - Hematoma & Joint bleed → Coagulation
  - Skin/Mucosal Petechiae & Purpura → PLT
- wound / surgical bleeding
  - Immediate → PLT
  - Delayed → Coagulation

Hemostasis



Lab Tests

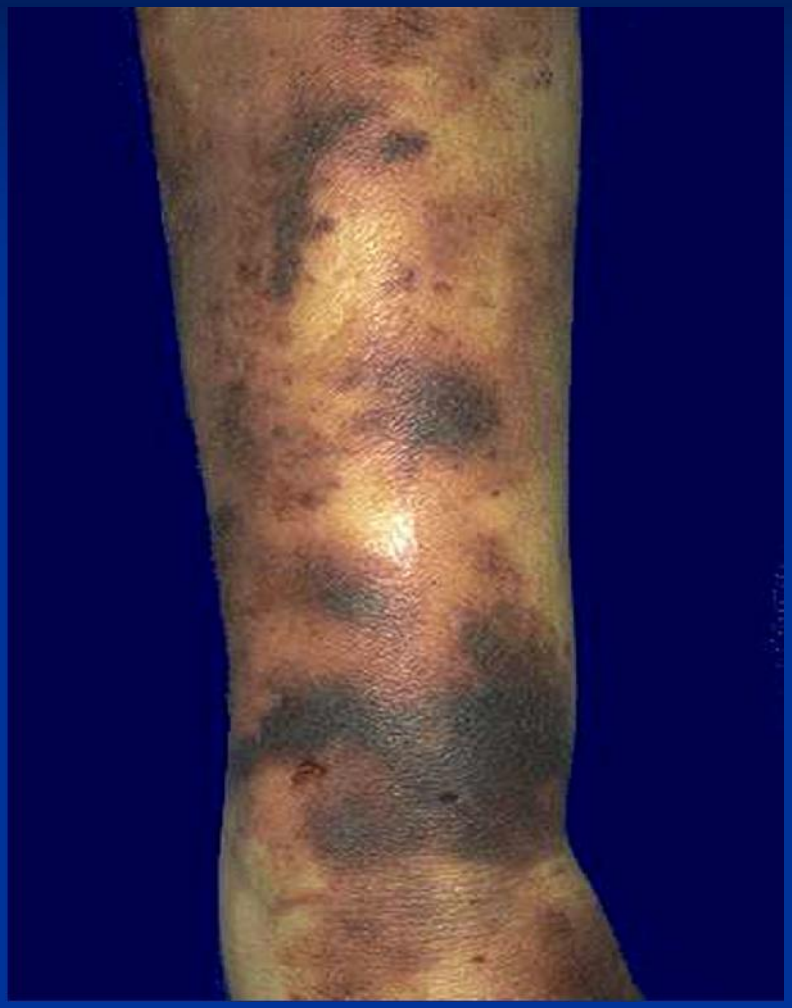
- CBC-Plt
- BT,(CT)
- PT
- PTT

Plt Study

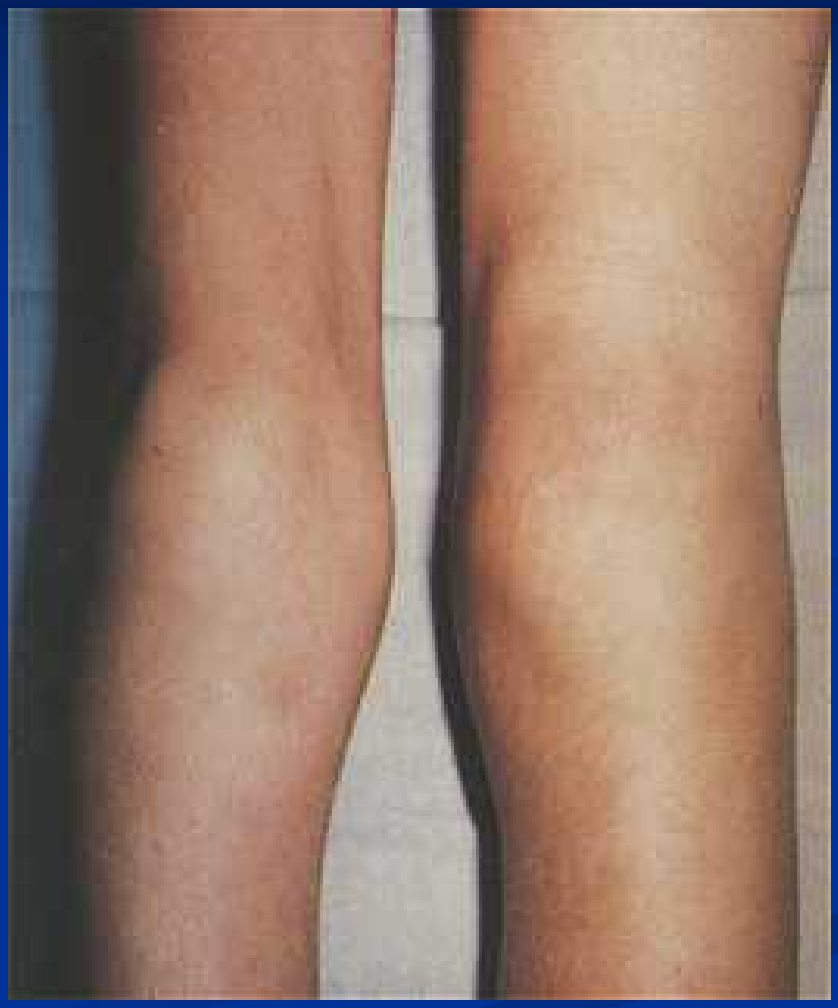
- Morphology
- Function
- Antibody

Platelet

Coagulation



Petechiae, Purpura



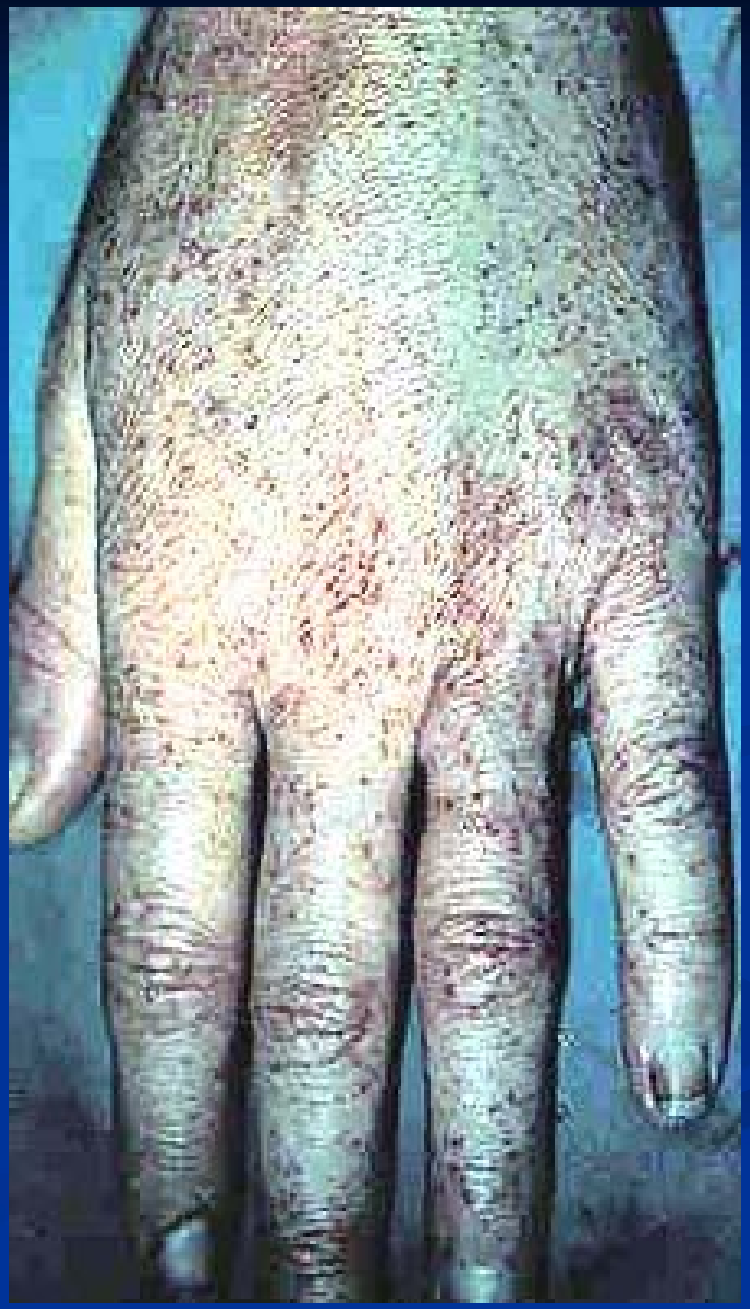
Hematoma, Joint bl.

Primary Hemostatic Disorders

Defect of platelet plug formation

1. platelets
2. small vessels or capillaries
3. plasma proteins
   - required for adhesion to subendothelium

Petechiae

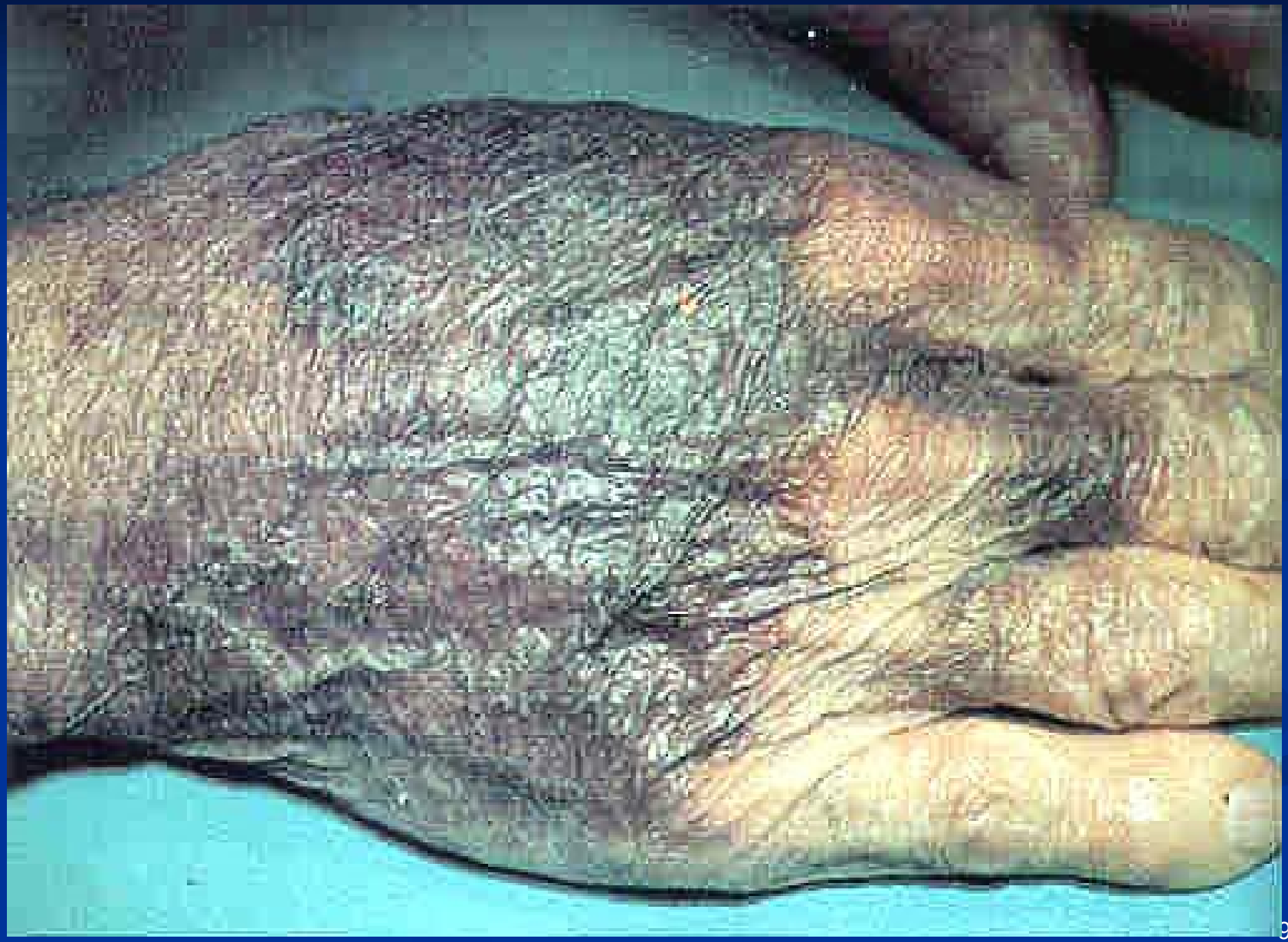


Vascular defect - ë fragility

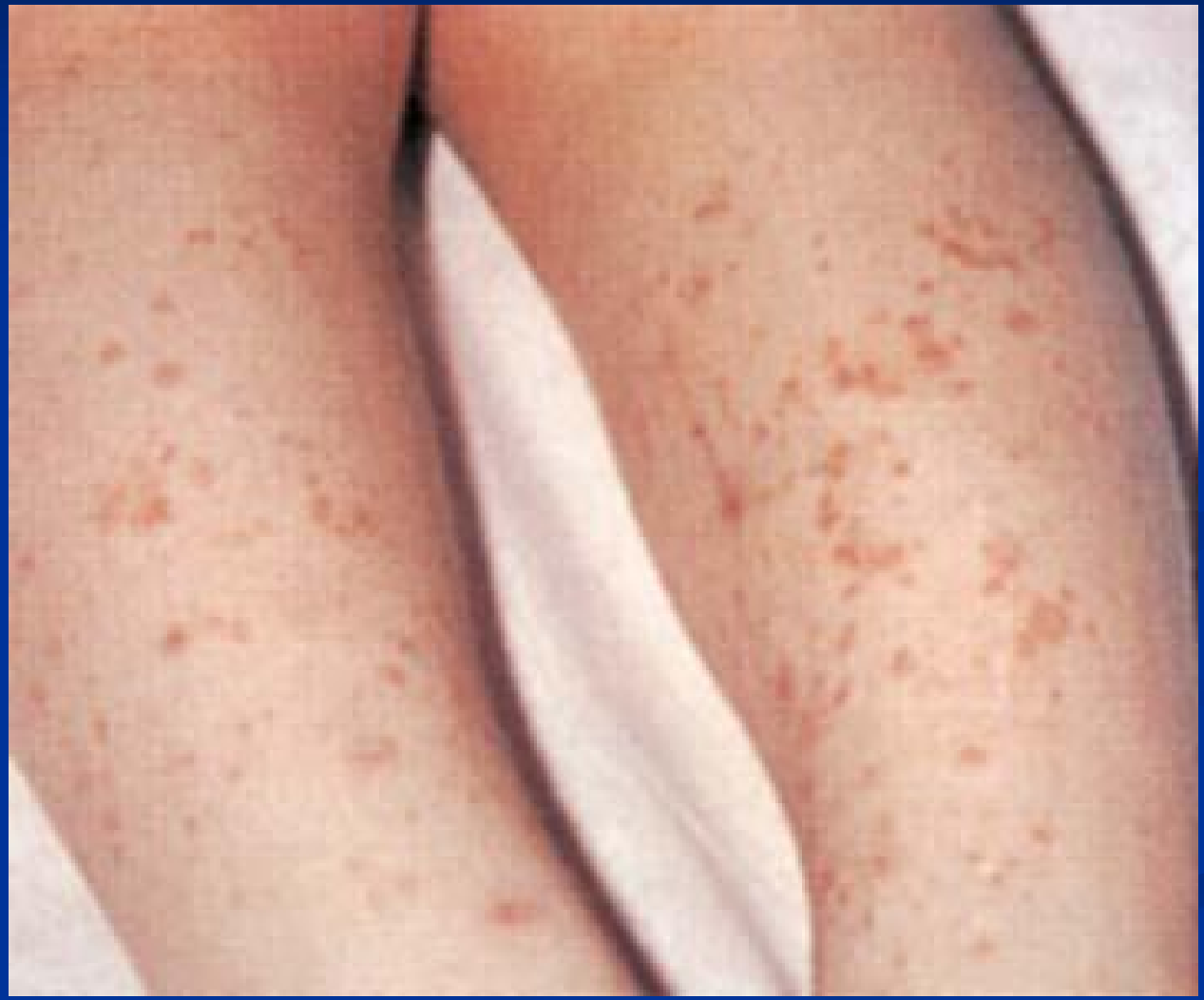
Petechiae, purpura, ecchymoses

- **senile purpura**
- **vitamin C deficiency (scurvy)**
- **connective tissue disorders**
- **Infectious and hypersensitivity vasculitides**
  - **Rickettsial & meningococcal infections**
  - **Henoch-Schonlein purpura (immune)**

Senile Purpura



Henoch-Schonlein purpura



Platelet disorders

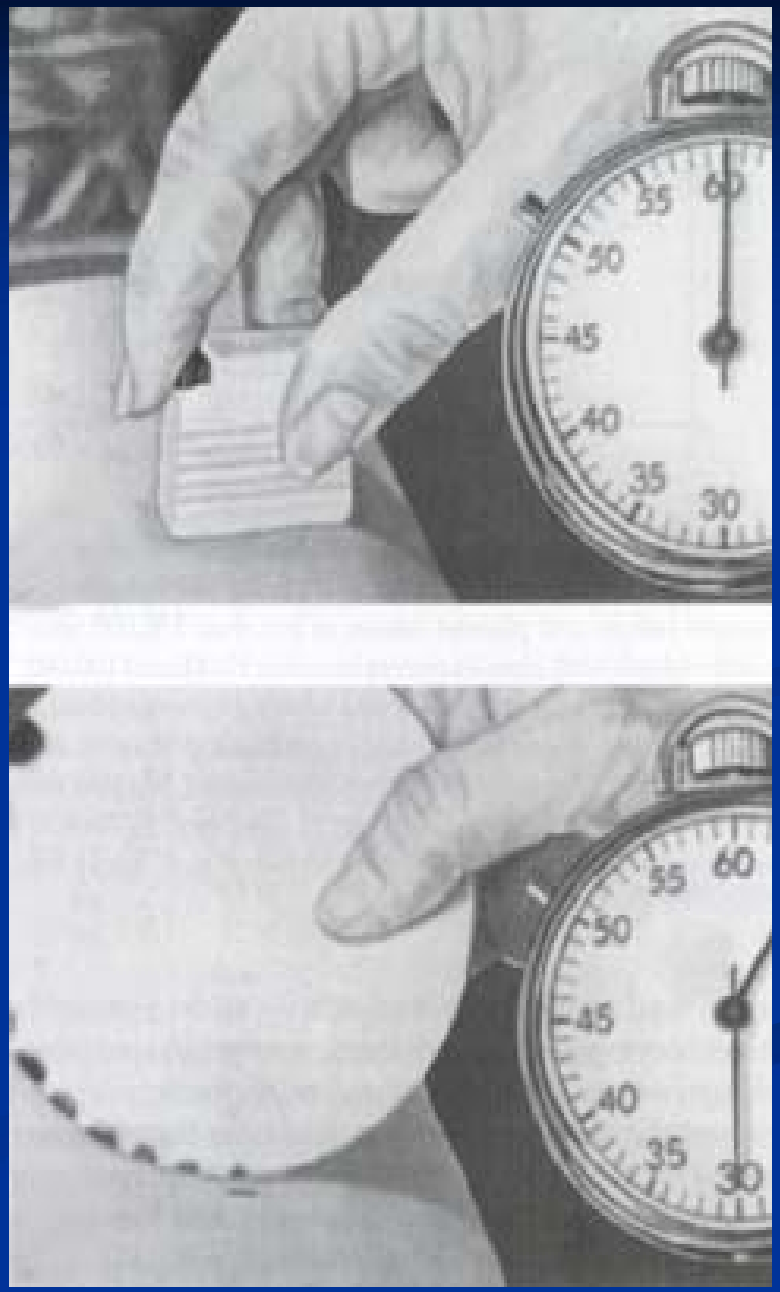
- í platelets (thrombocytopenia)
  - petechiae
  - spontaneous bleeding after trauma
  - CNS bleeding (severe í plt)
- Platelet dysfunction
  - mucocutaneous bleeding

Prolonged bleeding time (BT)

Bleeding time test

Timer is started upon incision

Bleeding time = time to complete cessation of free blood flow from incision



Thrombocytopenia - Causes

- **Marrow injury/failure**
  - aplastic anemia
  - drugs, infections
  - megaloblastic anemia
- **Decreased survival**
  - immune (ITP, drugs, infections)
  - nonimmune (DIC, TTP)
- **Splenic sequestration**

Idiopathic Thrombocytopenic Purpura

- **Acute - children (post infection)**
- **Chronic - adults (ë females, 20-40 yrs)**
  - **autoimmune disorder**
  - **antiplatelet antibodies (IgG against platelet glycoproteins)**
  - **IgG coated platelets removed by spleen (í platelet survival)**
- **Usually ë megakaryocytes in BM**

Thrombotic Thrombocytopenic Purpura (TTP)

- Endothelial injury and activation of intravascular thrombosis
- Microvascular occlusion by thrombi (fibrin surrounding platelet aggregates)
- Ischemic dysfunction of multiple organs
- Hemolytic uremic syndrome (HUS)
  - toxin released by E coli 0157:H7

Pentad features

1. Thrombocytopenia (fibrin surrounds plt aggretates ì thrombi)
2. Neurologic deficits (CNS ischemia)
3. Renal failure (renal ischemia)
4. Microangiopathic hemolytic anemia (vessel narrowing)
5. Fever

Platelet dysfunction

Inherited - autosomal recessive

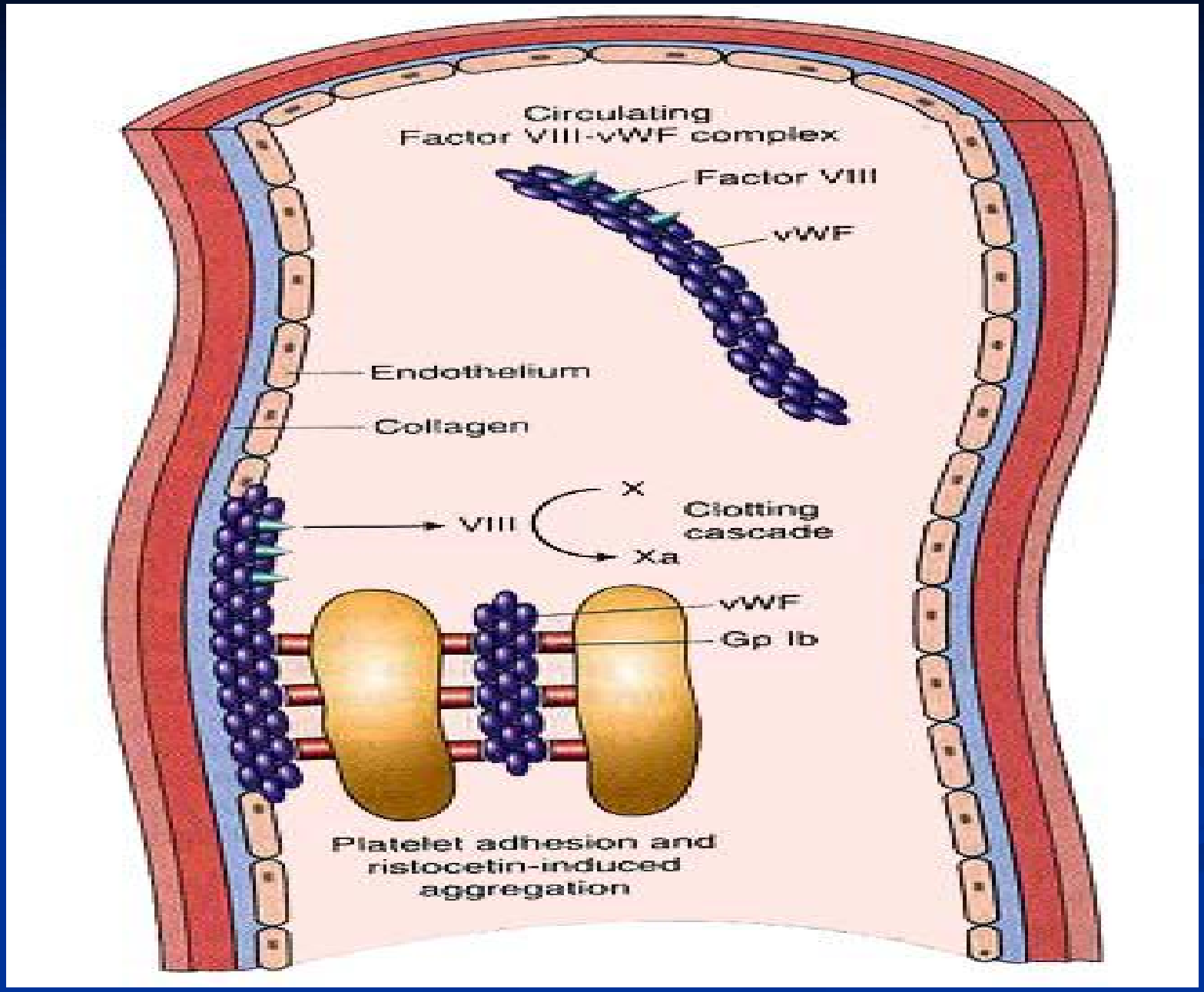
- Bernard-Soulier disease
  - large platelets
  - lack of glycoproteins (1b-IX complex)
  - failure of platelet adhesion
- Glanzmann's thrombasthenia
  - normal platelet morphology
  - lack of glycoproteins (IIb-IIIa complex)
  - defect of platelet aggregation

Acquired - common

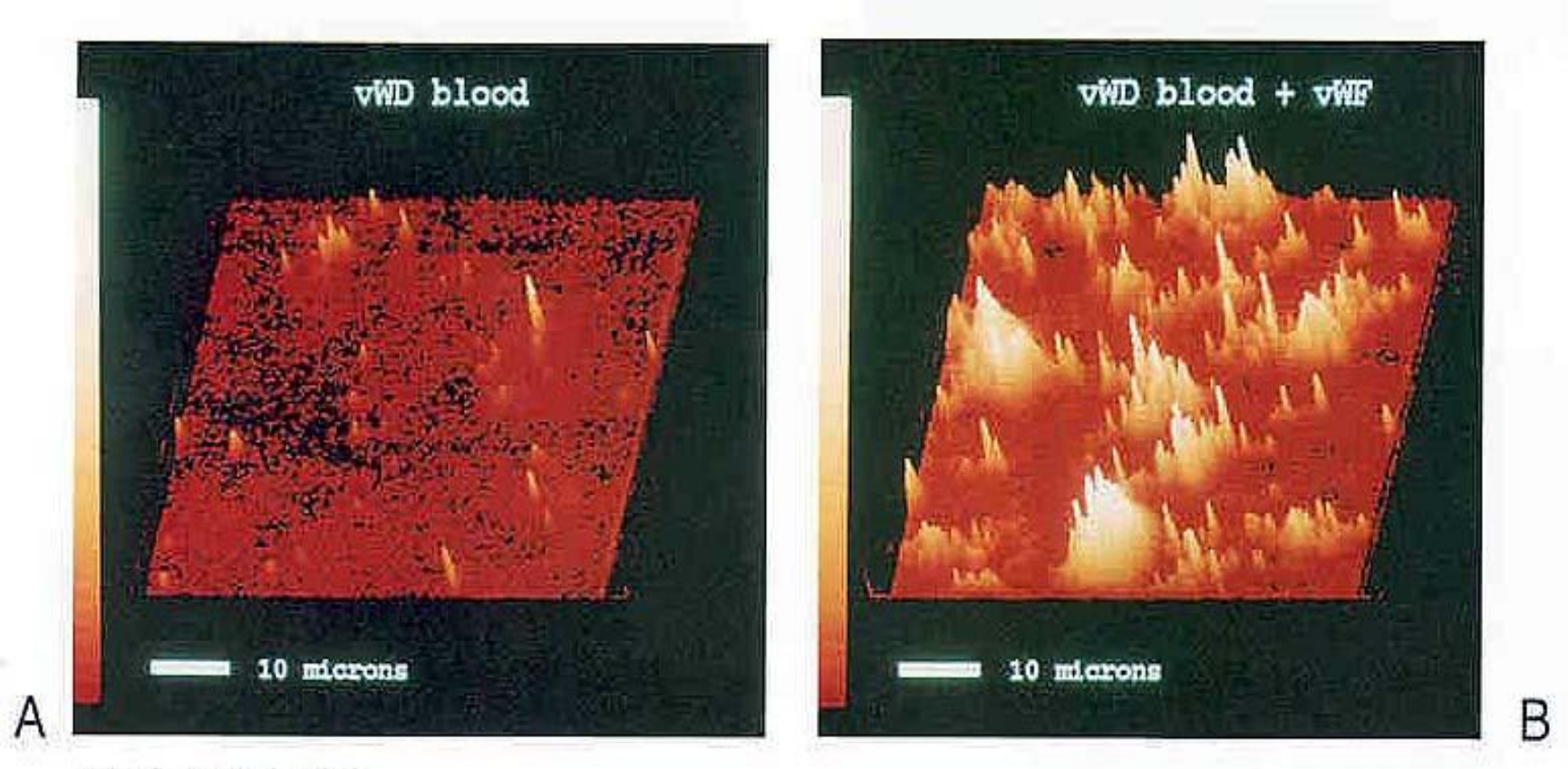
- Aspirin and NSAID
  - cyclo-oxygenase inhibitors
  - lack of thromboxane A_2 and PGE
  - failure of platelet aggregation
- Systemic disorders - i.e. uremia

Plasma proteins defect (for adhesion to subendothelium)

- **von Willebrand disease**
  - **quantitative or qualitative deficiency of vWF molecule**
  - **binds to exposed subendothelial collagen**
  - **mediates initial platelet adhesion**


Circulating
Factor VIII-vWF complex
Factor VIII
vWF
Endothelium
Collagen
X
VIII
Clotting
cascade
Xa
vWF
Gp Ib
Platelet adhesion and
ristocetin-induced
aggregation

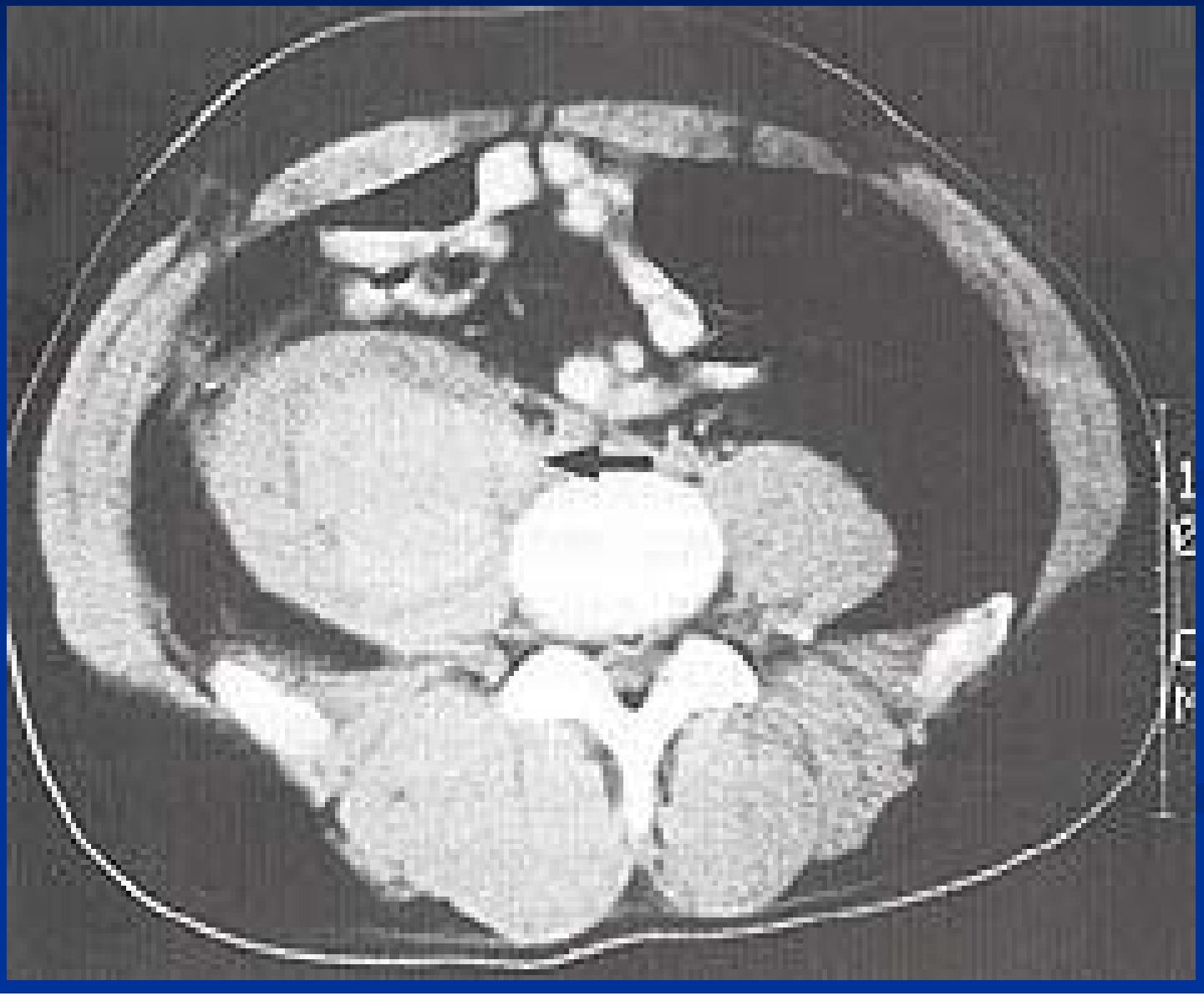
Exposure of blood to collagen membrane
Left - vWF deficient; Right - addition of vWF



Secondary Hemostasis

- Consolidates initial platelet plug into stable clot
- Disorders ì deficiencies of plasma clotting factors
- Clinical ì bleeding from large vessels into joints (hemarthroses), muscles, deep soft tissues (hematomas, large ecchymoses)
- Onset ì delayed after trauma

CT scan showing large hematoma of right psoas muscle

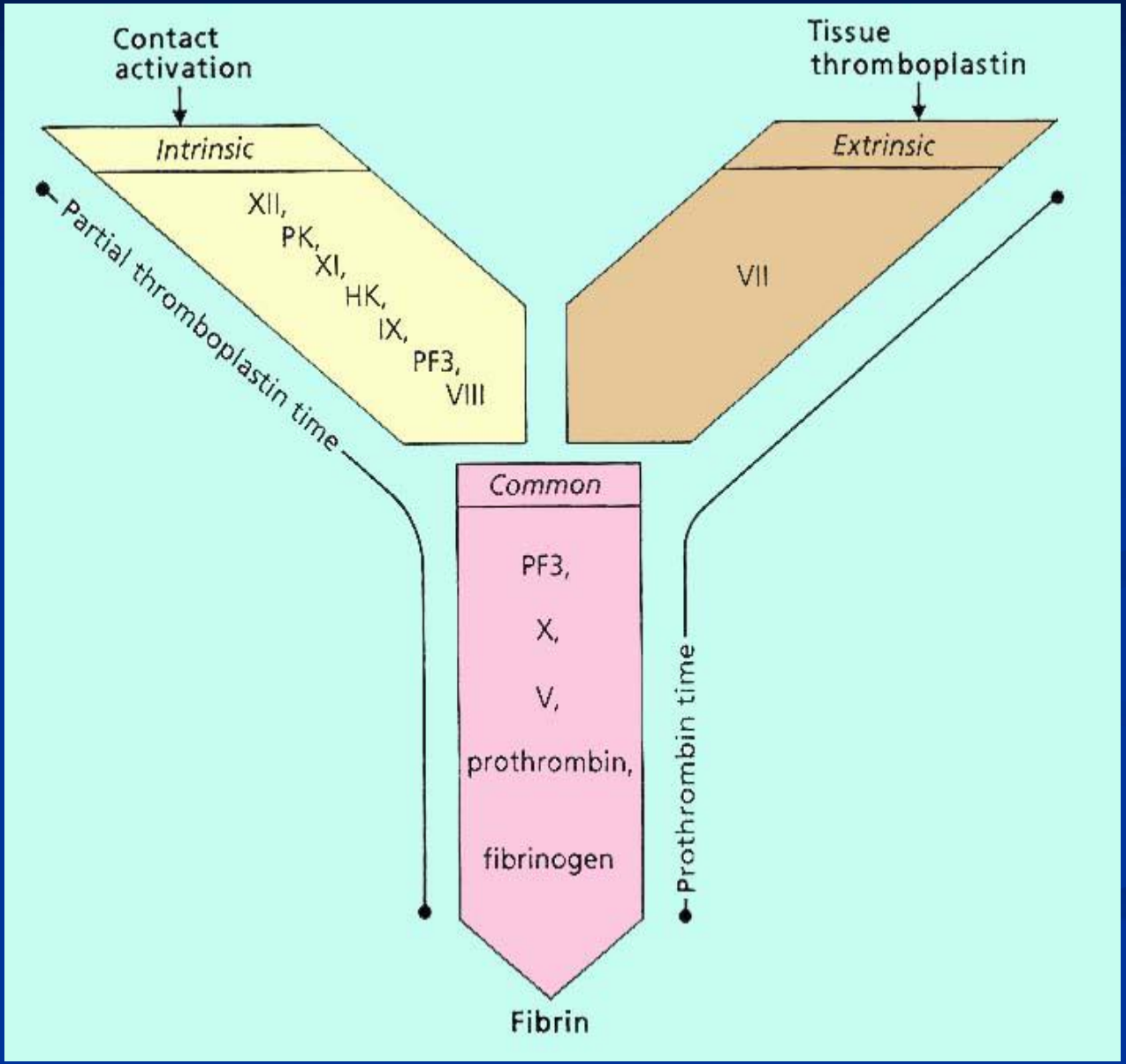


Secondary Hemostastic Disorders

Laboratory findings

- Normal bleeding time, platelet count
- Prolonged prothrombin time (PT)
  - deficiencies of II, V, VII, X
- Prolonged activated partial thromboplastin time (aPTT)
  - all factors except VII, XIII

Screening Tests of Blood Coagulation



Classic hemophilia (hemophilia A)

Factor VIII Deficiency

- X-linked disorder (affects males)
- Most common hereditary disease with severe bleeding
- 30% new mutations (non-hereditary)
- Spontaneous hemorrhages

- Clinical grading
  - severe = <1% circulating factor VIII
  - Moderate = 1-5%
  - mild = 5-75%
- Abnormal aPTT
- Diagnosis ì factor assays
- Treatment ì factor VIII concentrate
  - cryoprecipitate (less desirable)

Christmas disease (hemophilia B)

- X-linked recessive disorder
- Similar to classic hemophilia
- Requires evaluation of factor VIII and IX activity levels to diagnose
- Treatment ì
  - factor IX concentrate
  - cryoprecipitate if factor IX unavailable

Acquired coagulation disorder

Vitamin K deficiency

- neonates
- decreased intestinal flora & dietary intake
- oral anticoagulants (coumadin)
- fat malabsorption syndromes

- Required for factors II, VII, IX, X
- Prolonged PT and aPTT

Combined Primary & Secondary Hemostatic Disorders

von Willebrand's Disease

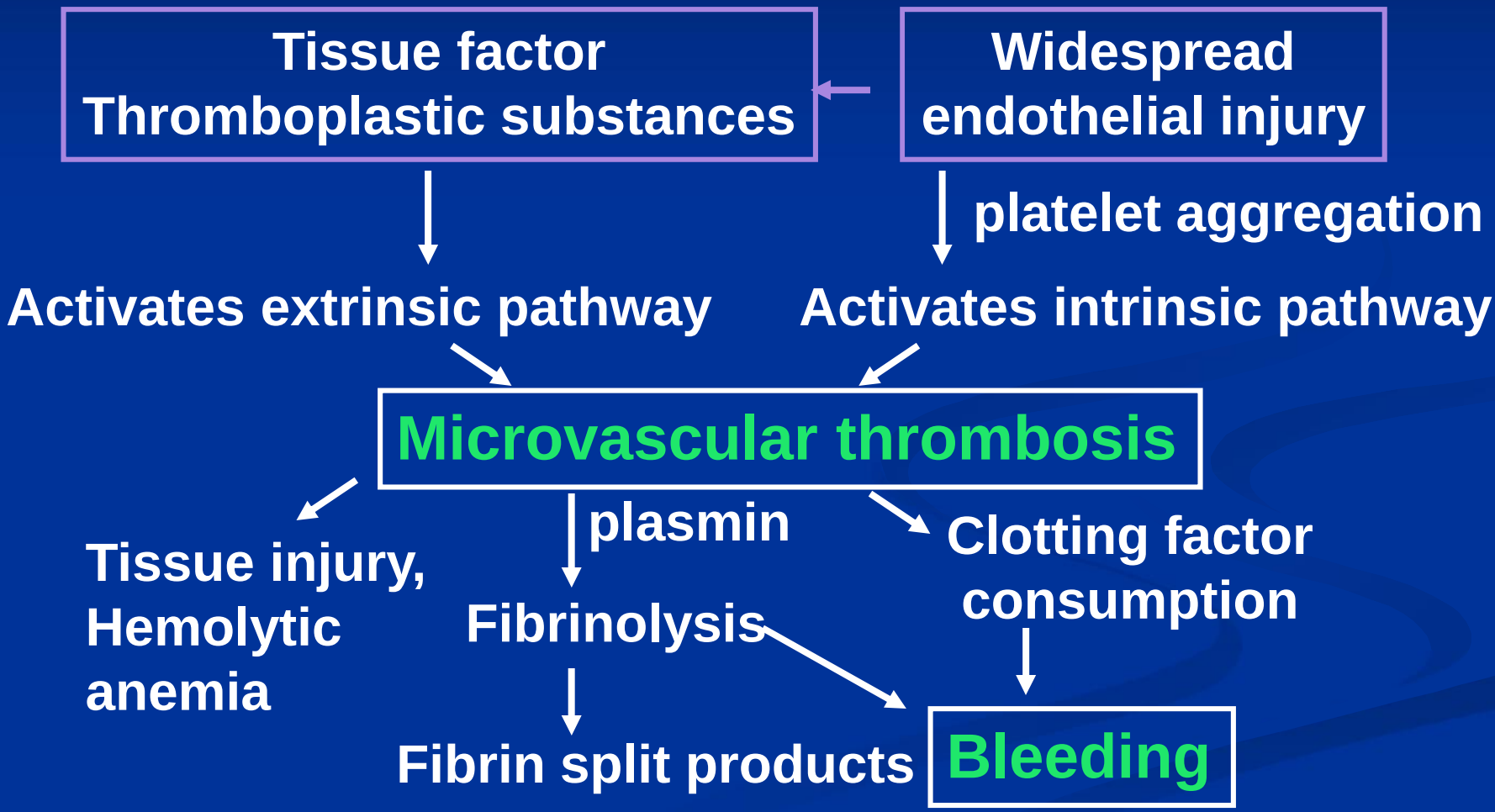
- Autosomal dominant (or recessive)
- Primary defect ì ↓ platelet adhesion
  - prolonged bleeding time
- Secondary defect ì deficiency of factor VIII; normally stabilizes factor VIII in circulation
  - prolonged aPTT

- Clinical ì often mild
  - excessive bleeding from wounds
  - spontaneous bleeding from mucosa
- Different types ì ↓ quantity or loss of selective multimers
- Diagnosis ì ristocetin induced plt aggregation or multimer analysis

Disseminated Intravascular Coagulation

- Primary → platelet consumption
  (↑ bleeding time, ↓ platelets)
- Secondary → factor consumption
  (↑ PT, aPTT)
- Major causes
  - obstetric complications
  - Neoplasms
  - infection (sepsis)
  - major trauma

Multiple initiating factors



- Acute DIC → ↑ bleeding
  - occur in major trauma
  - give fresh frozen plasma
- Chronic DIC → ↑ thrombosis
  - occur in cancer
  - give heparin or anticoagulant
- Treat underlying disease

Severe Liver Disease

- Primary → dysfunctional platelets and/or thrombocytopenia (↑ BT)
- Secondary → decrease in all coagulation factors except vWF (↑ PT, aPTT)
- Vitamin K will promote synthesis of factors II, VII, IX, X

Summary

	BT	Plt	PT	PTT
1º hemostasis	-↑	-↓	-	-
2º Factor VIII/IX deficiency	-	-	-	↑
2º Vitamin K deficiency	-	-	↑	↑
Combined	↑	↓	-↑	↑

Thank you!