Coagulation Disorders

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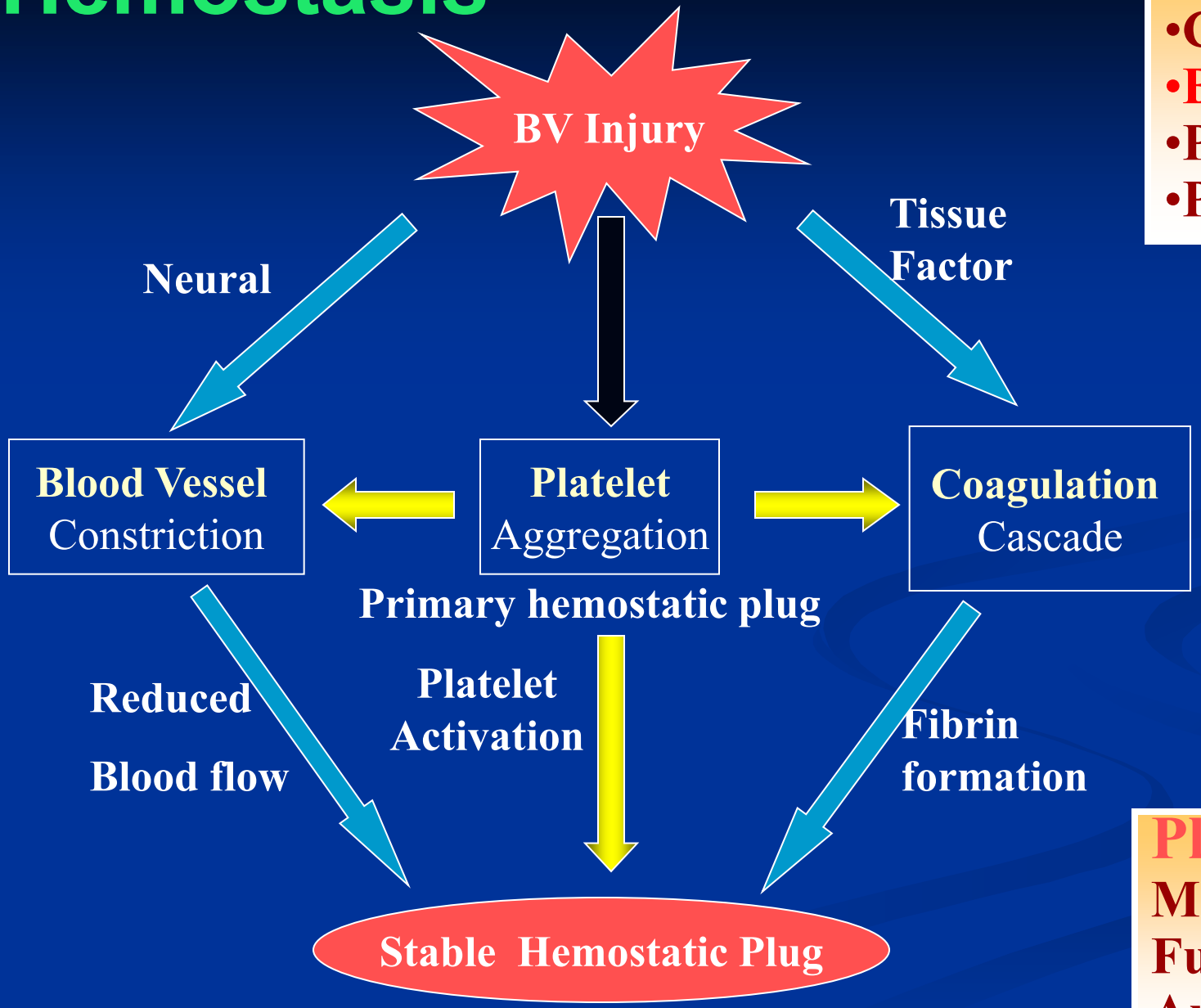
Introduction

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

Hemostasis



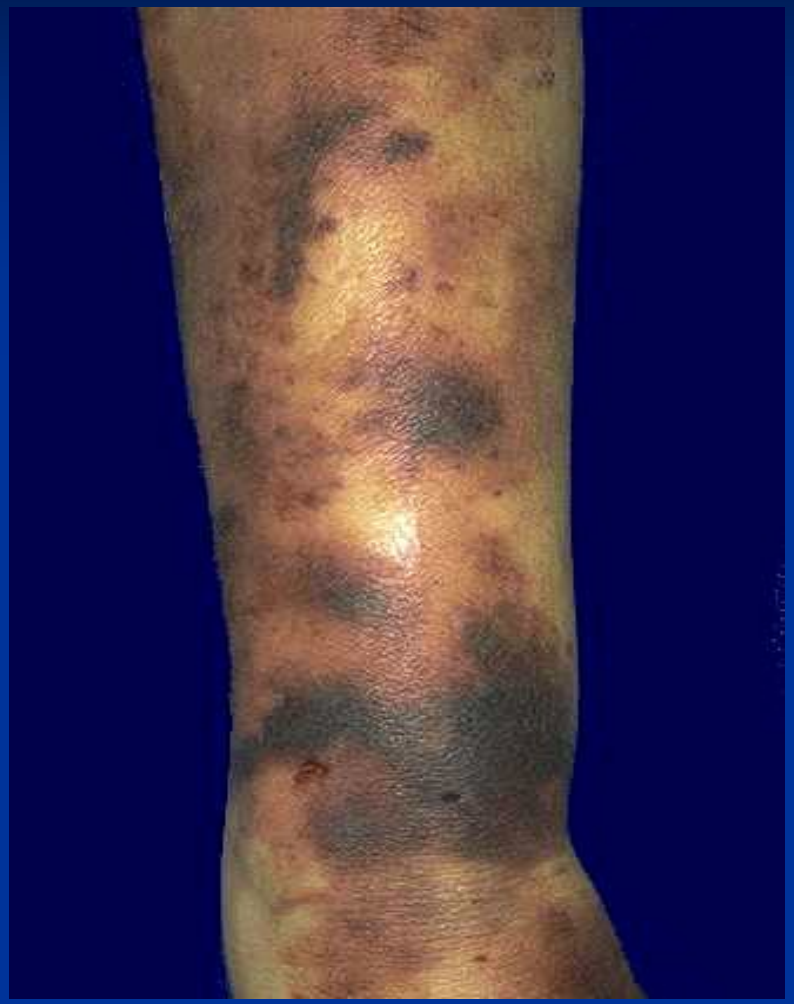
Lab Tests

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

Plt Study

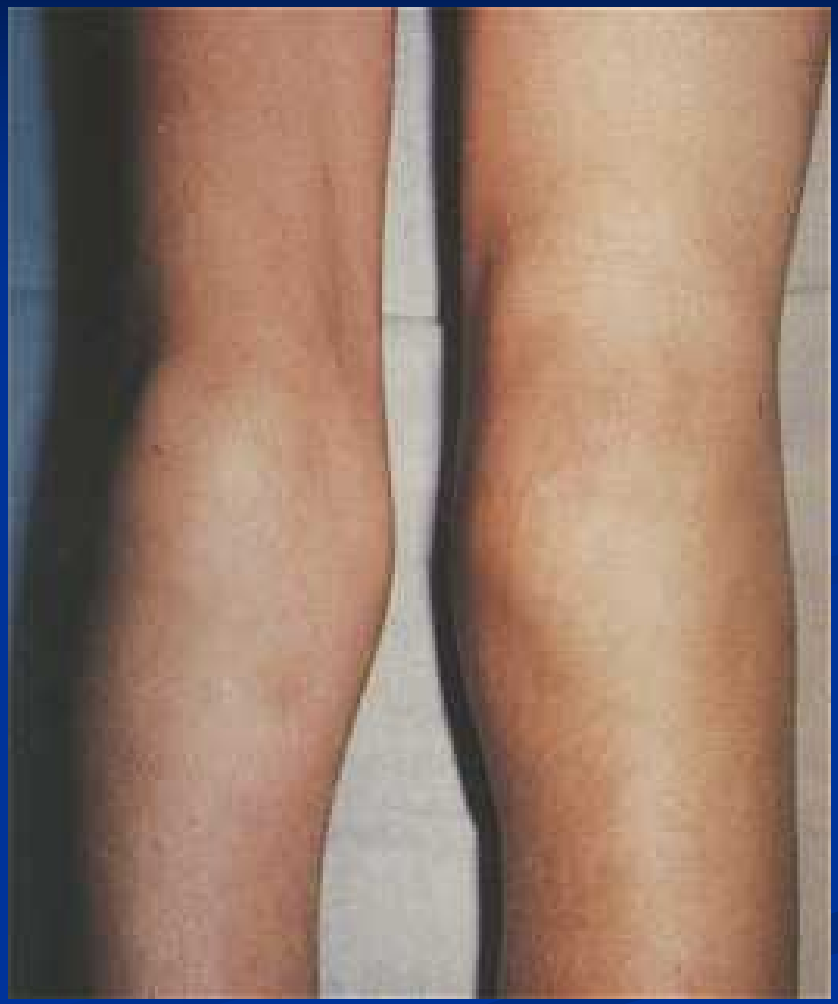
Morphology
Function
Antibody

Platelet



Petechiae, Purpura

Coagulation



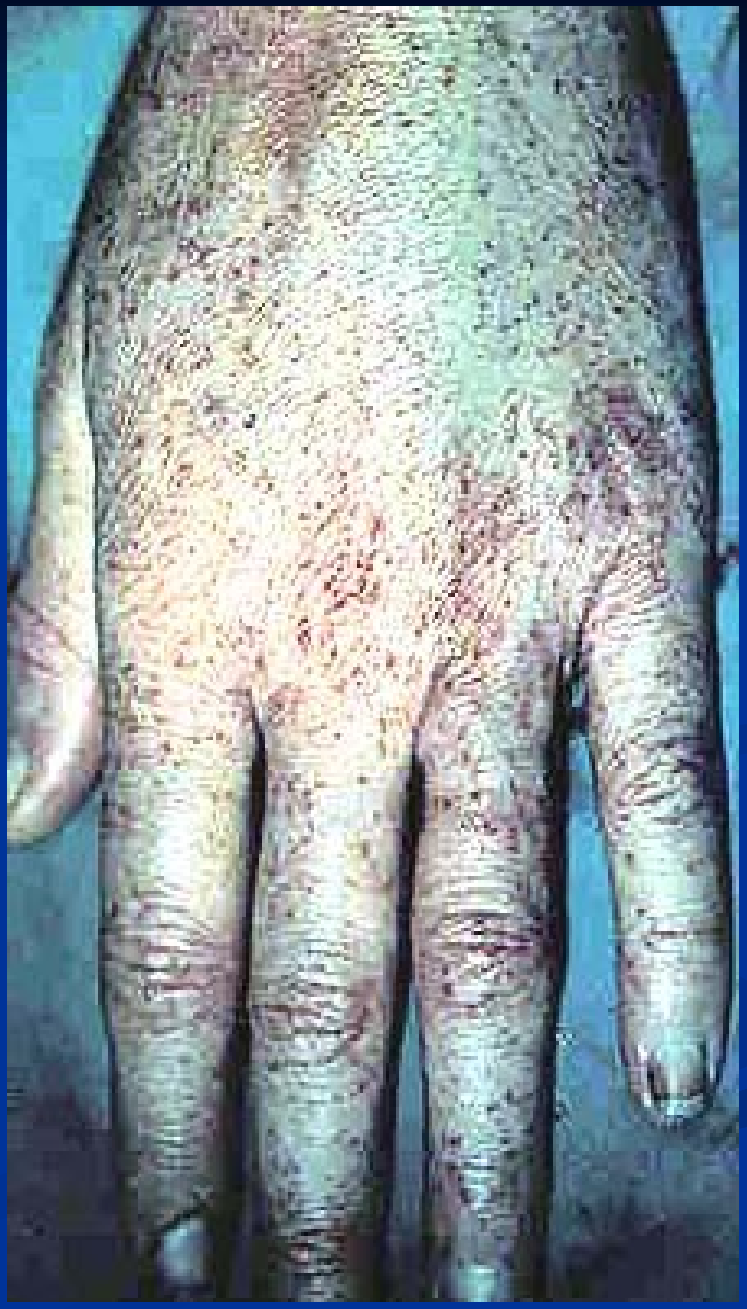
Hematoma, Joint bl.

Primary Hemostatic Disorders

Defect of platelet plug formation

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

Petechiae

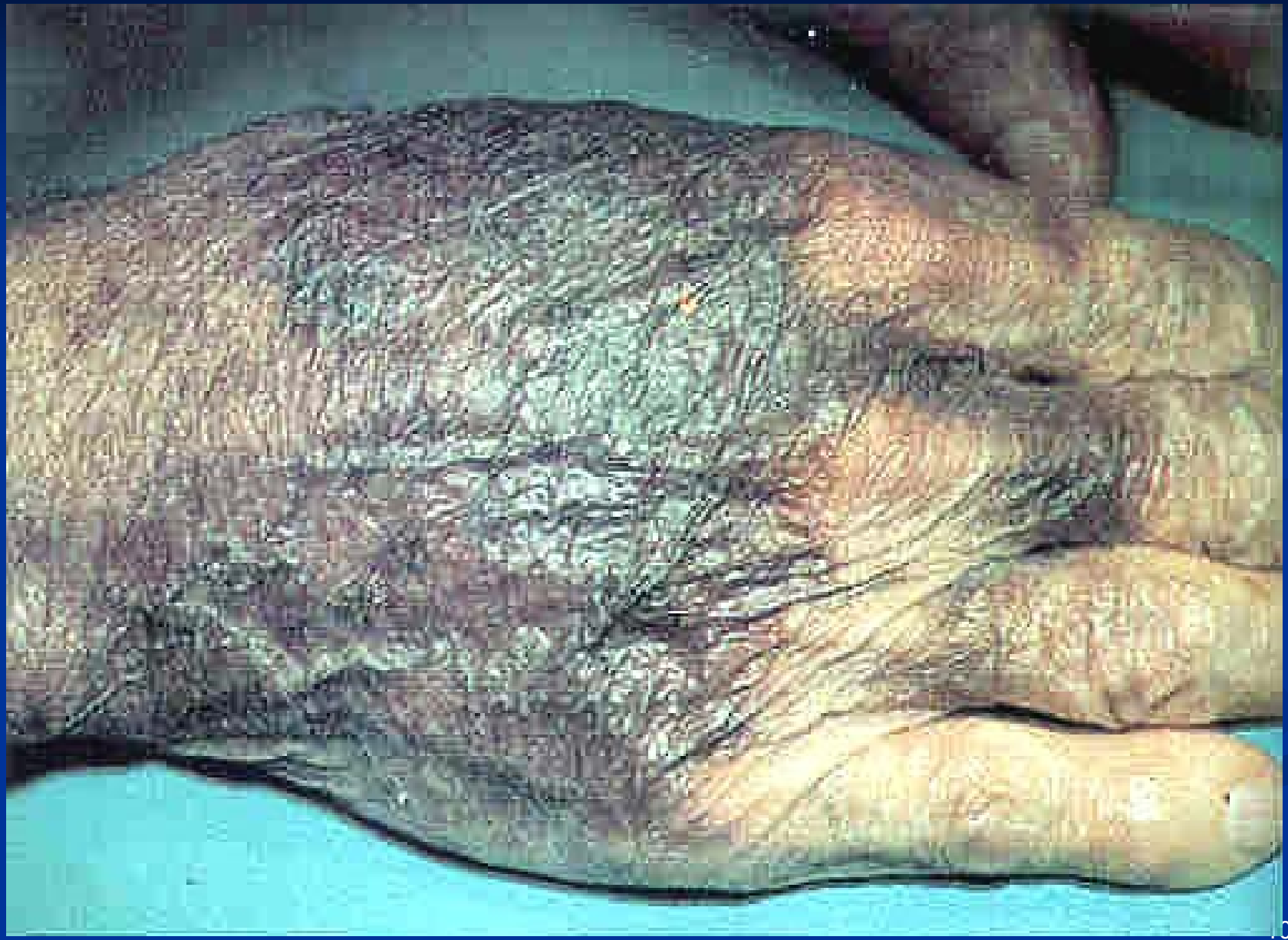


Vascular defect - ↑ fragility

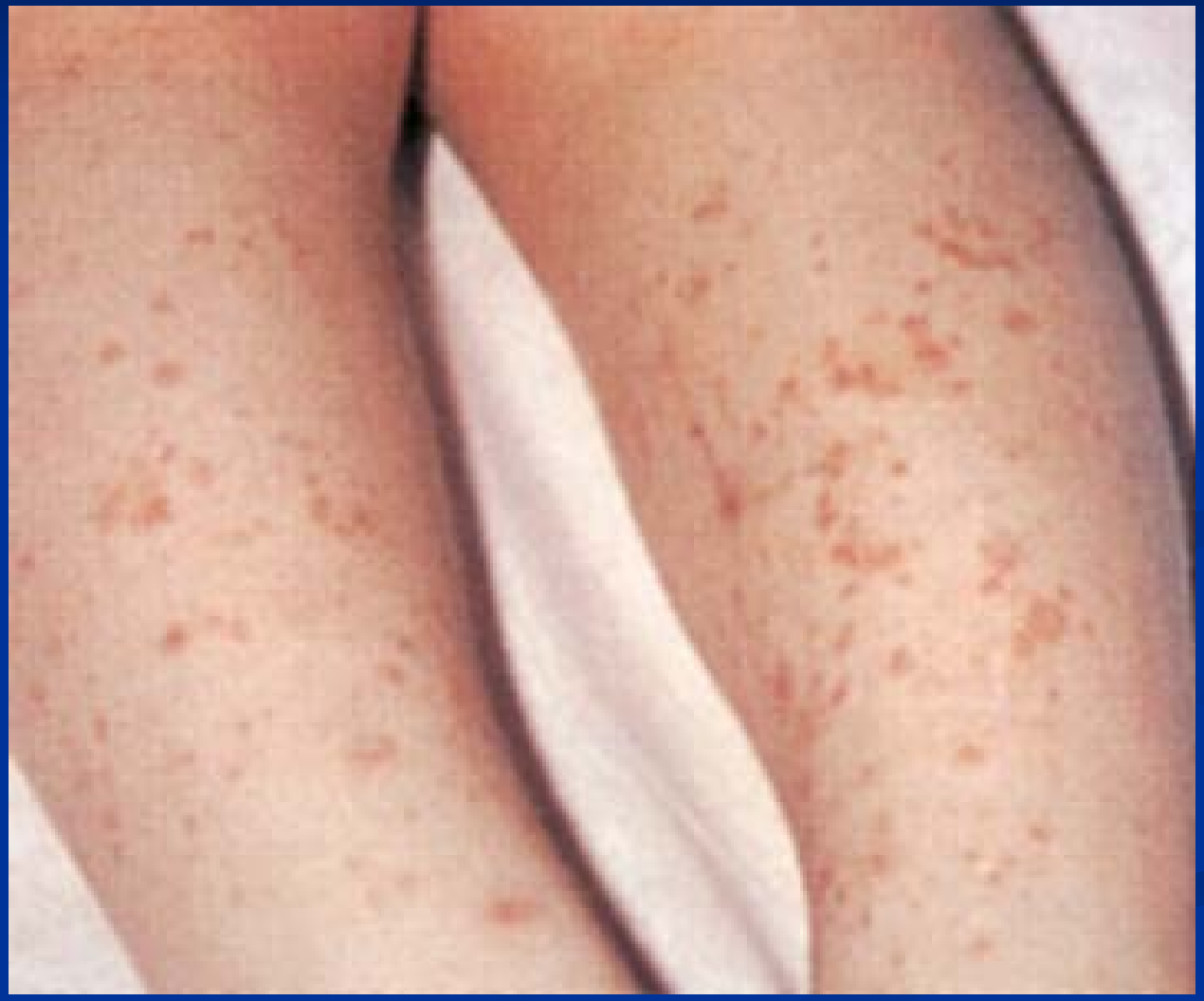
Petechiae, purpura, ecchymoses

- 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

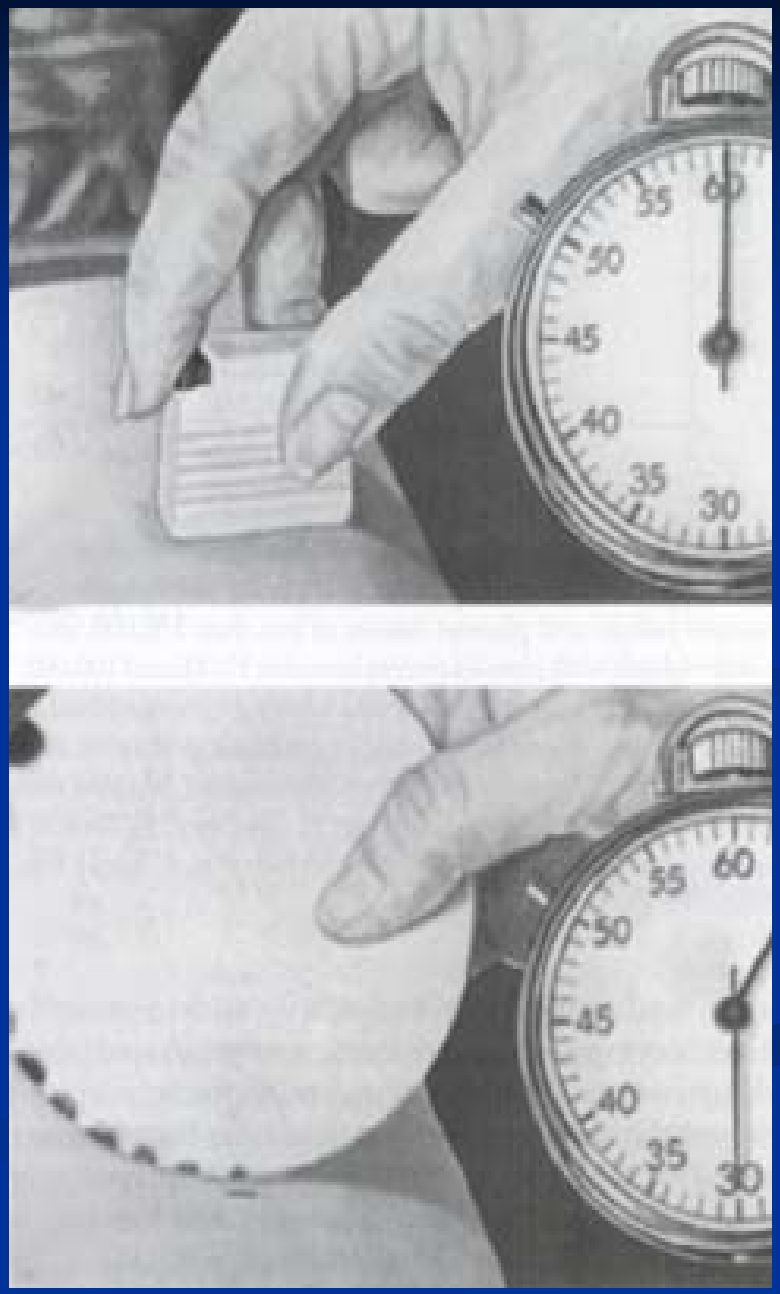
- ↓ platelets (thrombocytopenia)
  - petechiae
  - spontaneous bleeding after trauma
  - CNS bleeding (severe ↓ plt)
- Platelet dysfunction
  - mucocutaneous bleeding

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 (↑ females, 20-40 yrs)
  - autoimmune disorder
  - antiplatelet antibodies (IgG against platelet glycoproteins)
  - IgG coated platelets removed by spleen (↓ platelet survival)
- Usually ↑ 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 → thrombi)
2. Neurologic deficits (CNS ischemia)
3. Renal failure (renal ischemia)
4. Microangiopathic hemolytic anemia (vessel narrowing)
5. Fever

Platelet dysfunction

Inherited - autosomal recessive

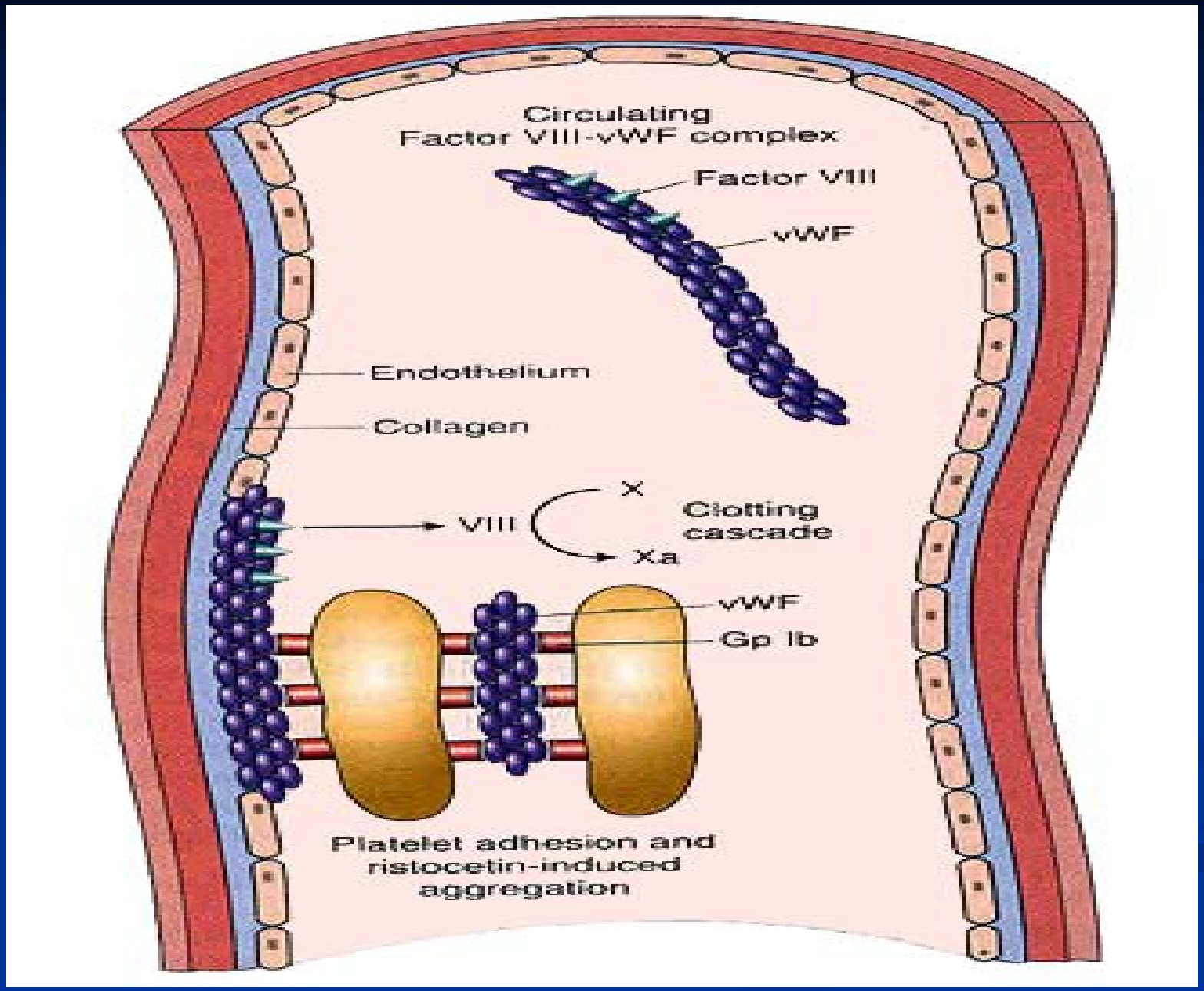
- Bernard-Soulier disease
  - large platelets
  - lack of glycoproteins (1b-IX complex)
  - failure of platelet adhesion
- Glanzmann's thrombasthenia
  - normal platelet morphology
  - lack of glycoproteins (IIb-IIIa complex)
  - defect of platelet aggregation

Acquired - common

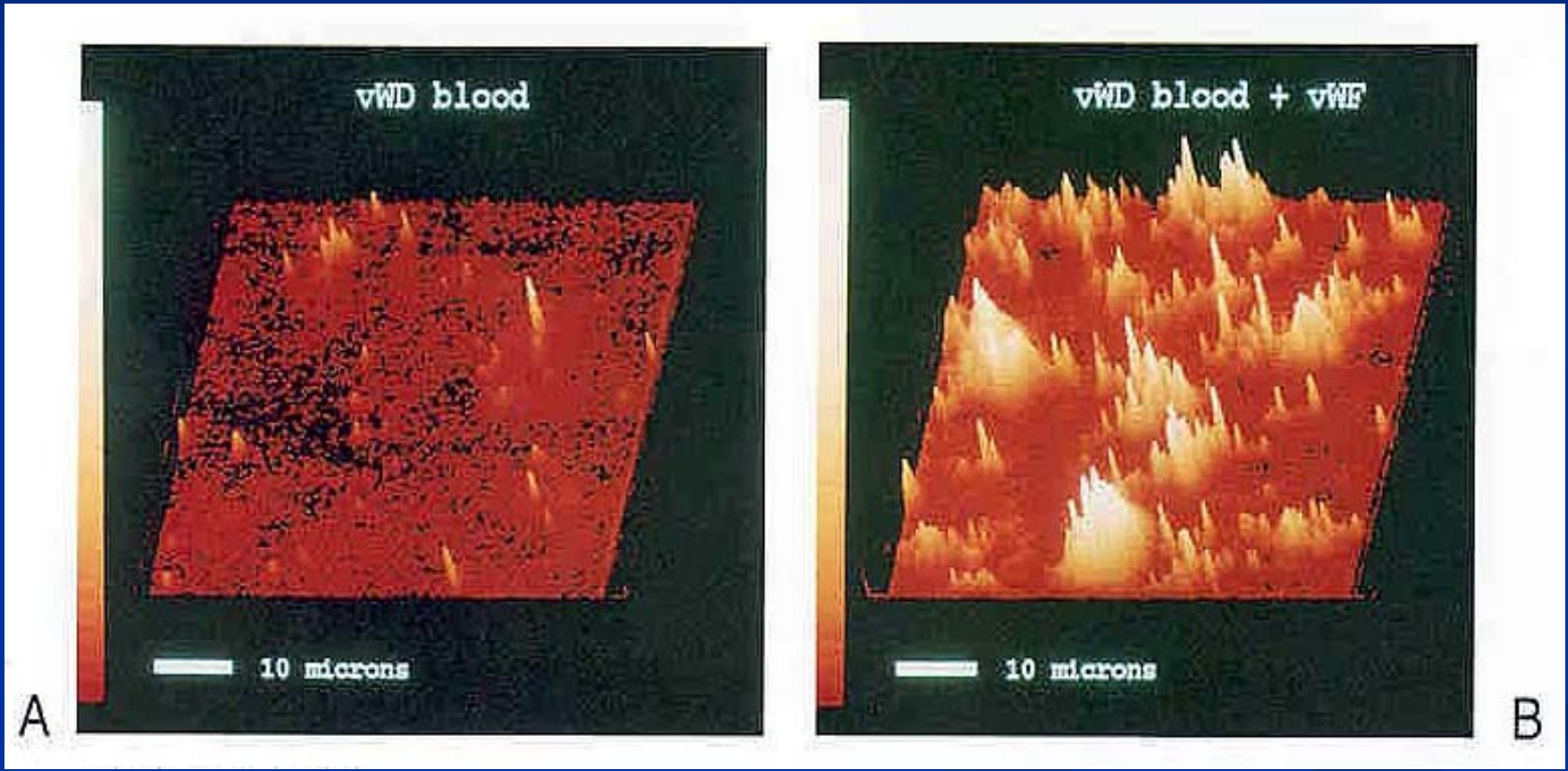
- Aspirin and NSAID
  - cyclo-oxygenase inhibitors
  - lack of thromboxane A_2 and PGE
  - failure of platelet aggregation
- Systemic disorders - i.e. uremia

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

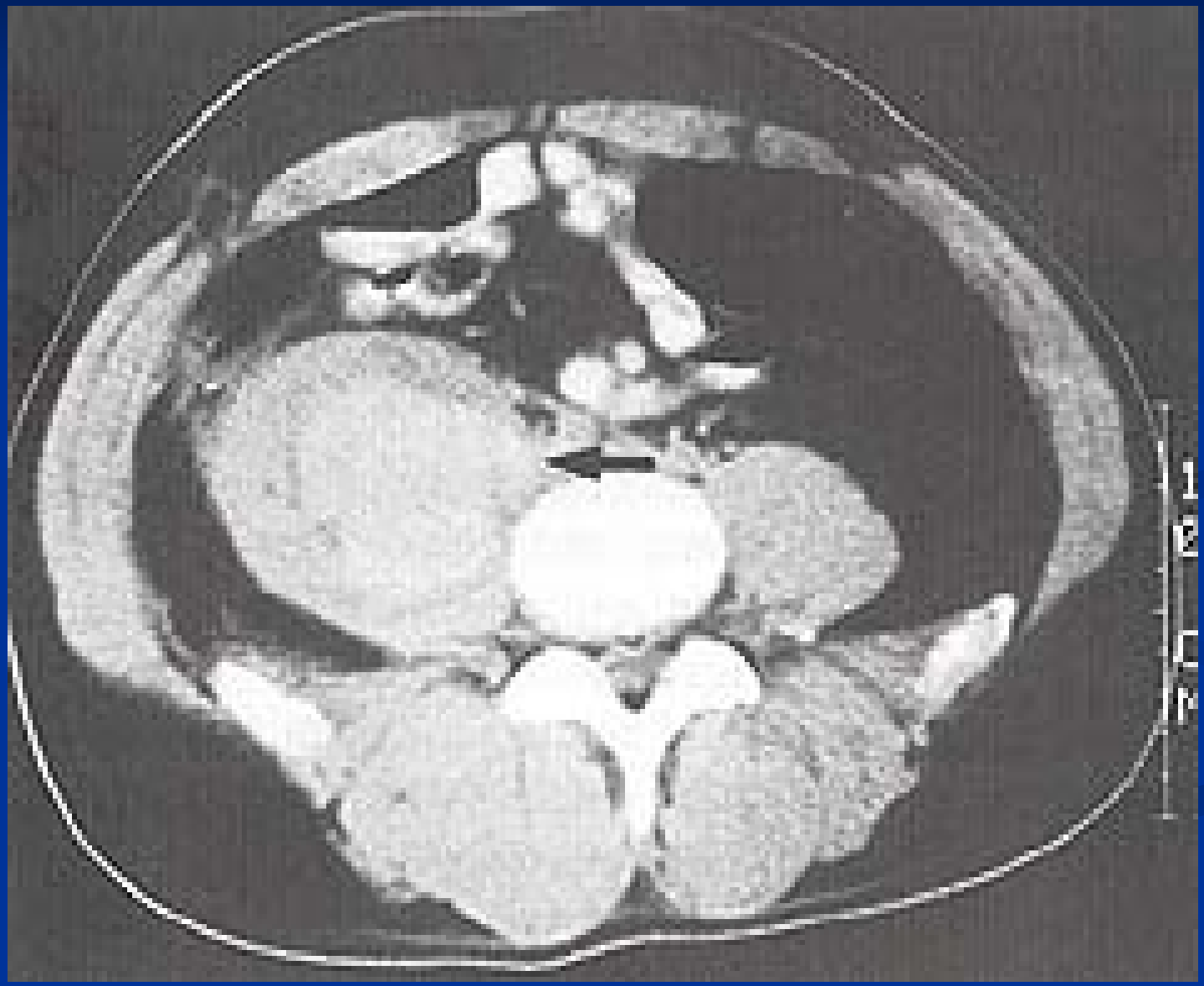
Exposure of blood to collagen membrane
Left - vWF deficient; Right - addition of vWF



Secondary Hemostasis

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

CT scan showing large hematoma of right psoas muscle

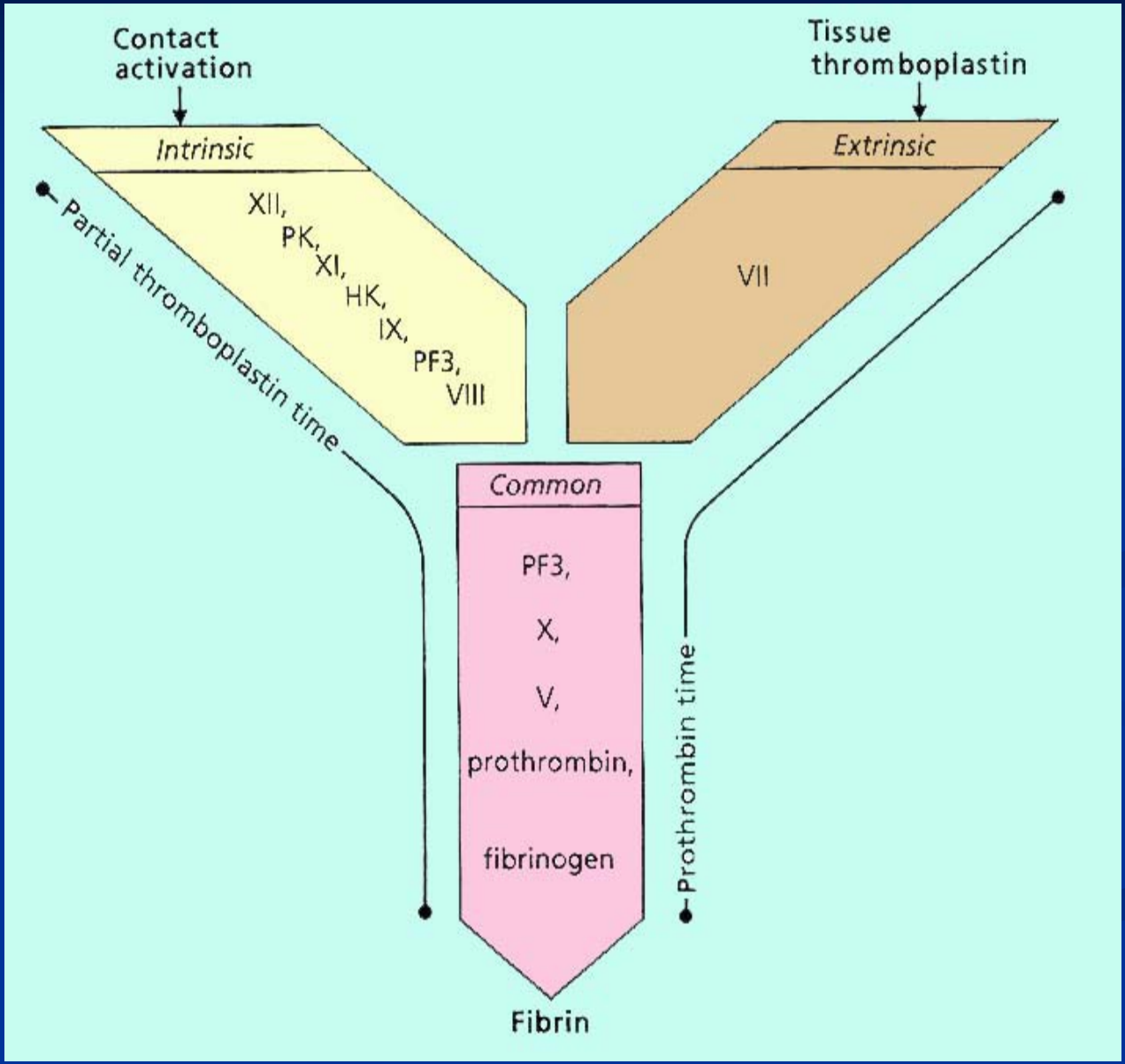


Secondary Hemostastic Disorders

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 → factor assays
- Treatment → 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 →
  - 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

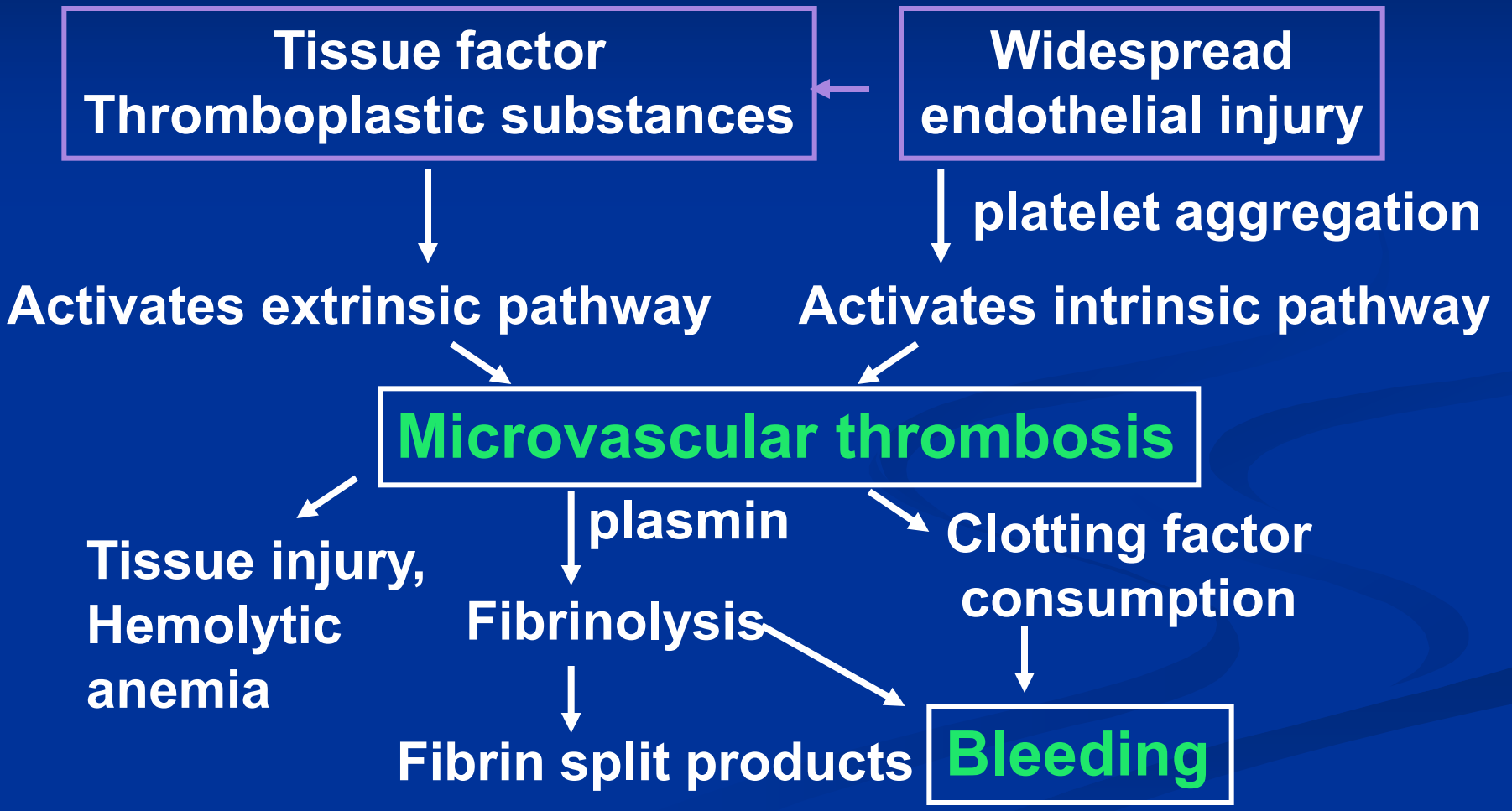
- Autosomal dominant (or recessive)
- Primary defect → ↓ platelet adhesion
  - prolonged bleeding time
- Secondary defect → deficiency of factor VIII; normally stabilizes factor VIII in circulation
  - prolonged aPTT

- Clinical → often mild
  - excessive bleeding from wounds
  - spontaneous bleeding from mucosa
- Different types → ↓ quantity or loss of selective multimers
- Diagnosis → 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!