



# Hemorrhagic diathesis

Ústav patologické fyziologie 1.LFUK

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# Bleeding - classification

## **etiology:**

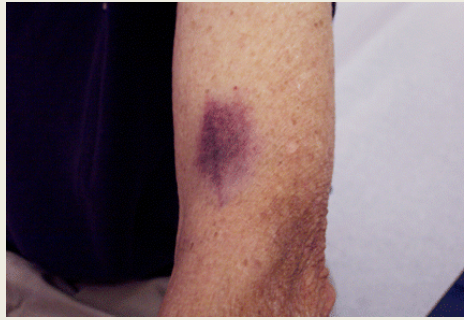
- acquired (more frequent, PT history, esp. medications) or inherited (family history).
- surgical, posttraumatic, coagulopathy, thrombocytic, vascular.

## **presentation:**

- isolated or part of a syndrome,
- mucosal or skin
- spontaneous or induced, new or repeated,
- at expected locations (menstrual)

# Clinical approach

- Signs of systemic disease? (sepsis, anemia, lymphadenopathy, hepatosplenomegaly, non-hematol. sites ?)
- **Bleeding sites:** mucosa (oral cavity), skin (petechia, <1cm purpura, >1cm ecchymoses), vagina, urethra, anus, urine, stool.



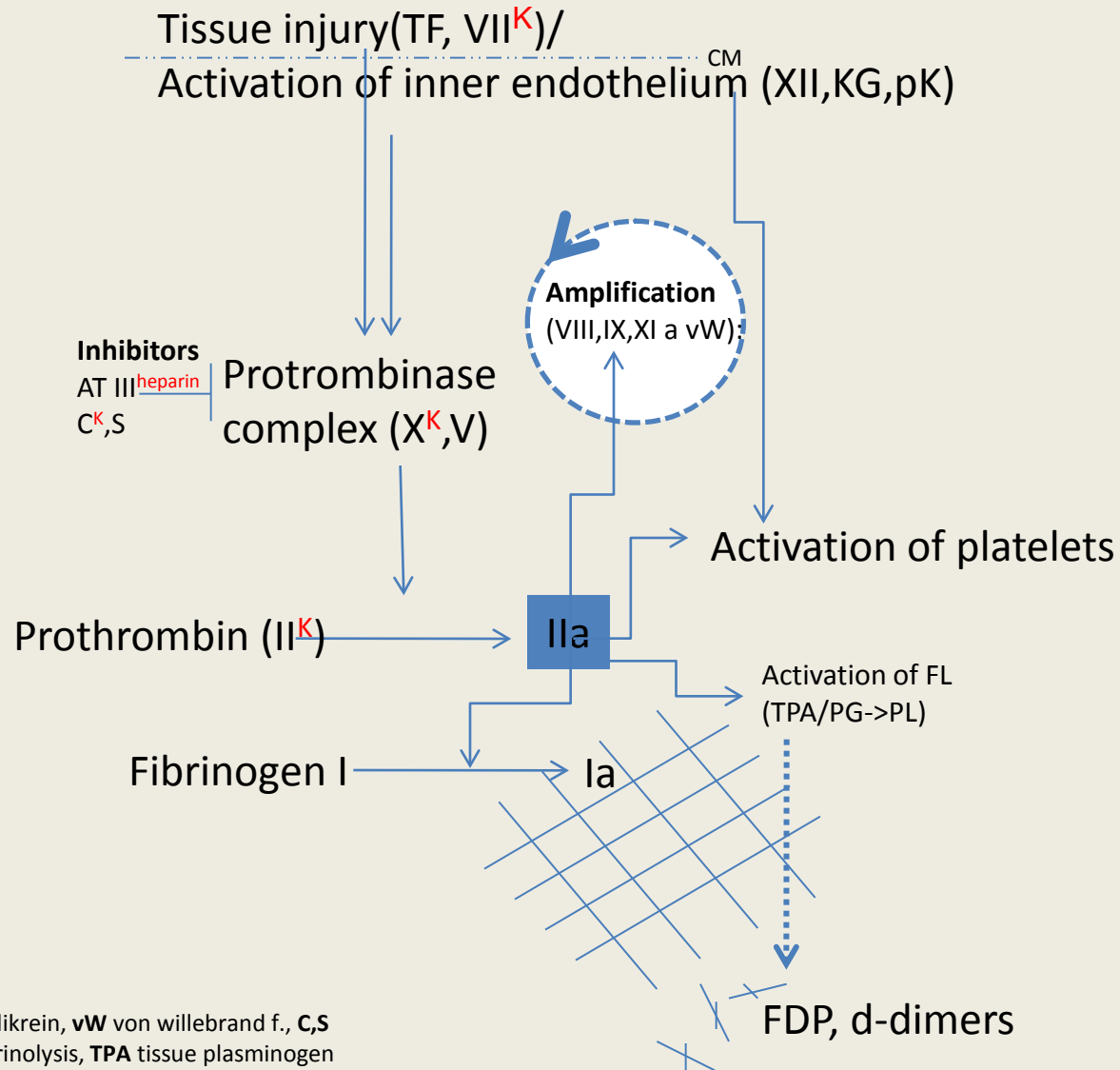
Zdroj: ASH Image bank

- **Laboratory tests:** blood cell count (Hgb: anemia, platelets: TCpenia), coagulation (APTT/INR). Other tests.

# Laboratory approach

- **Platelets** (primary hemostasis= aggregation/adhesion)
- **Blood coagulation factors** (secondary hemostasis=fibrin clot)
- **Inhibitors of coagulation cascade**  
(ATIII, C, S)
- **Fibrinolytic factors** (tertiary hemostasis)  
(TPA, PG, PL)

# Laboratory approach

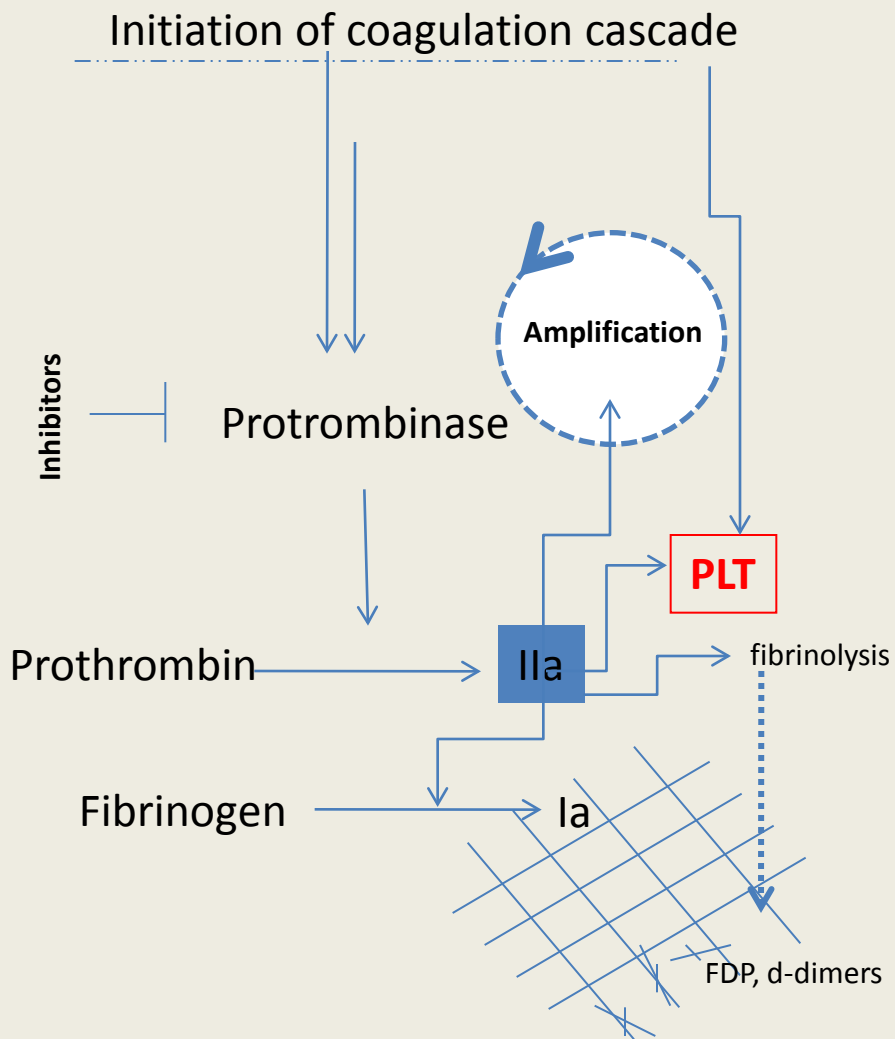


TF tissue factor, KG kininogen, pK prekalikrein, vW von willebrand f., C,S protein C,S, ATIII antithrombin III, FL fibrinolysis, TPA tissue plasminogen activator, PG plasminogen, PL plasmin, CM cytoplasmic membrane

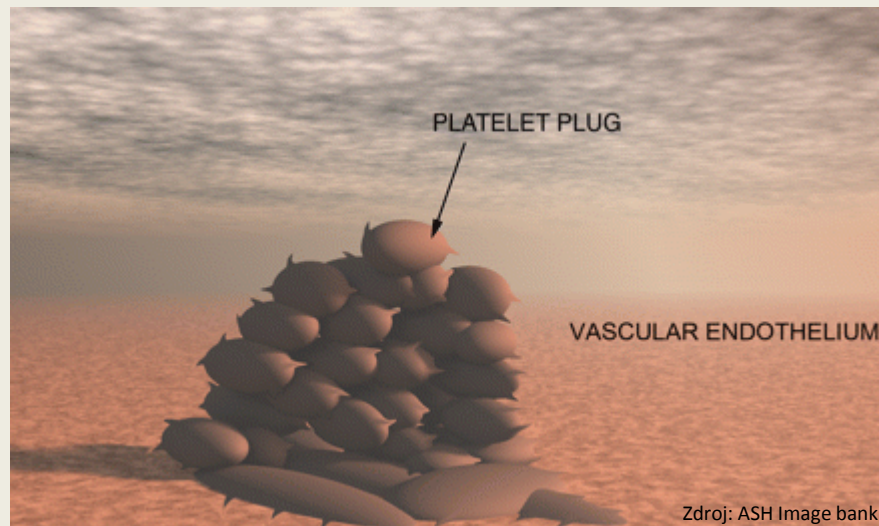
# Bleeding Disorders

- Trombocytopenia/pathia
- Coagulopathy
- Vasculopathy

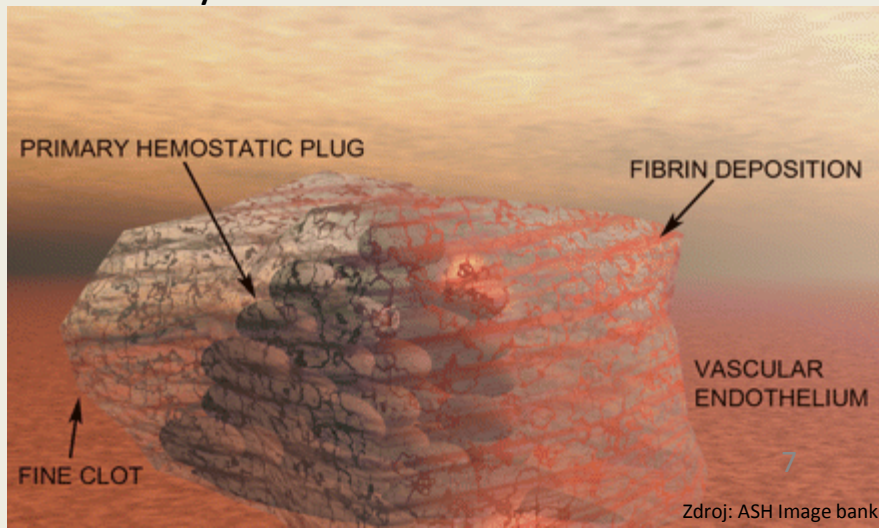
# Role of platelets and endothelium



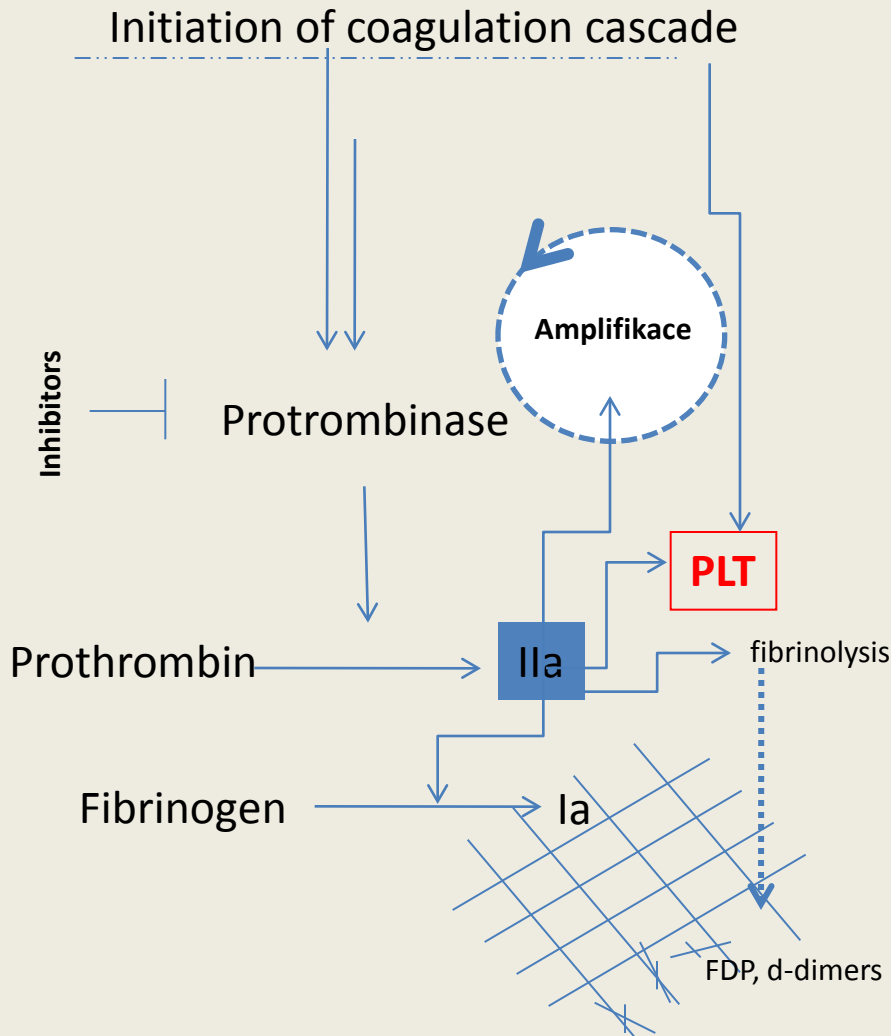
Primary hemostasis



Secondary hemostasis



# Trombocytopenia/pathia



**Number:** 150-450.000/uL, CAVE ~ under 20

**Morphology:** MPV (~ 6 fL)

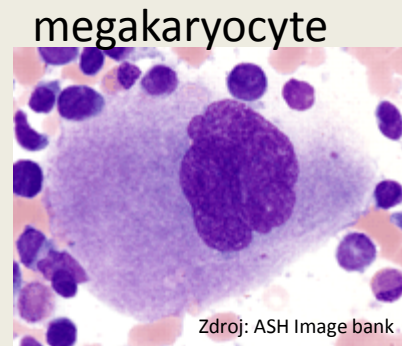
**Function tests:** adhesion/aggregation (ADP, ristocetin)

**Tests for granules:** ELISA/RIA

**Classification:**

Quantitative : TC penia (! pseudoTCpenia)

Qualitative: TC pathia





# Trombocytopenia

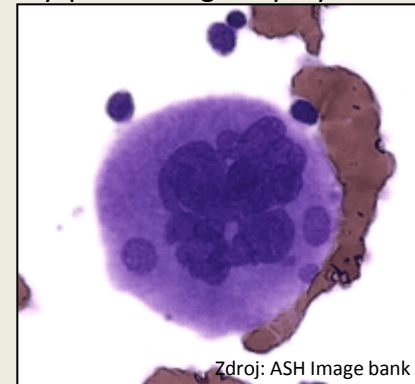
- PG:

1) **decreased production of PLT in BM** (aplasia, dysplasia, tumor infiltration, pharmacologic, ethylic, nutrition megaloblastic anemia, HIV a parvoviral, inherited).

2) **increased destruction of PLT:**

autoimmune (ITP, secondary to SLE, CLL, lymphomas), angiopathic (DIC, TTP/HUS), hypersplenism, relative(blood transfusion).

Dysplastic megakaryocyte



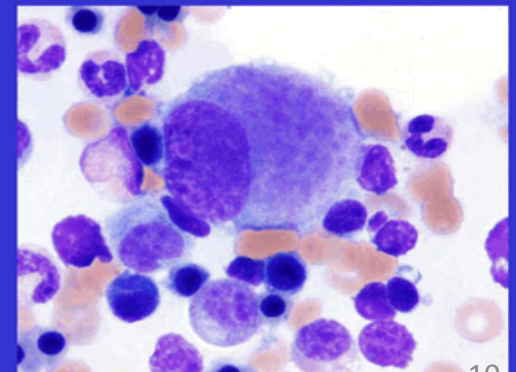
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# Immune Trombocytopenic Purpura

- **PG:** IgG/IgM against GP IIb/IIIa, TC destruction
- **CL:** bleeding, chronic often relapsing, primary/secondary.....Compl.: intracranial!
- **DG:** exclusion of other possible causes (BM and PB analyses)
- **TH:** steroids, IVIg, Splenectomy, TPO other immunosuppression

Figure 6.

Zdroj: ASH Image bank



Bone marrow showing an immature megakaryocyte with cytoplasmic budding. Young megakaryocytes are seen in increased numbers in ITP.

# Trombocytopenia

- PG: 1) **Inherited thrombocytopenia**: defect of membrane glycoprotein, loss of granules
- 2) **Acquired thrombocytopenia**:  
medications (aspirin, NSAID, ATB, Heparin)  
organ failure (Liver, Kidney, DIC)  
paraneoplastic (MM, NHL, MDS, MPS)
  
- CL: mucosal bleeding
- DG: BT, abnormal PLT function tests
- TH: PLT transfusion (if bleeding, before surgery)

# Coagulopathy

- **Inherited:**

Hemophilia and other inherited coagulopathy

Von Willebrands disease

- **Acquired:**

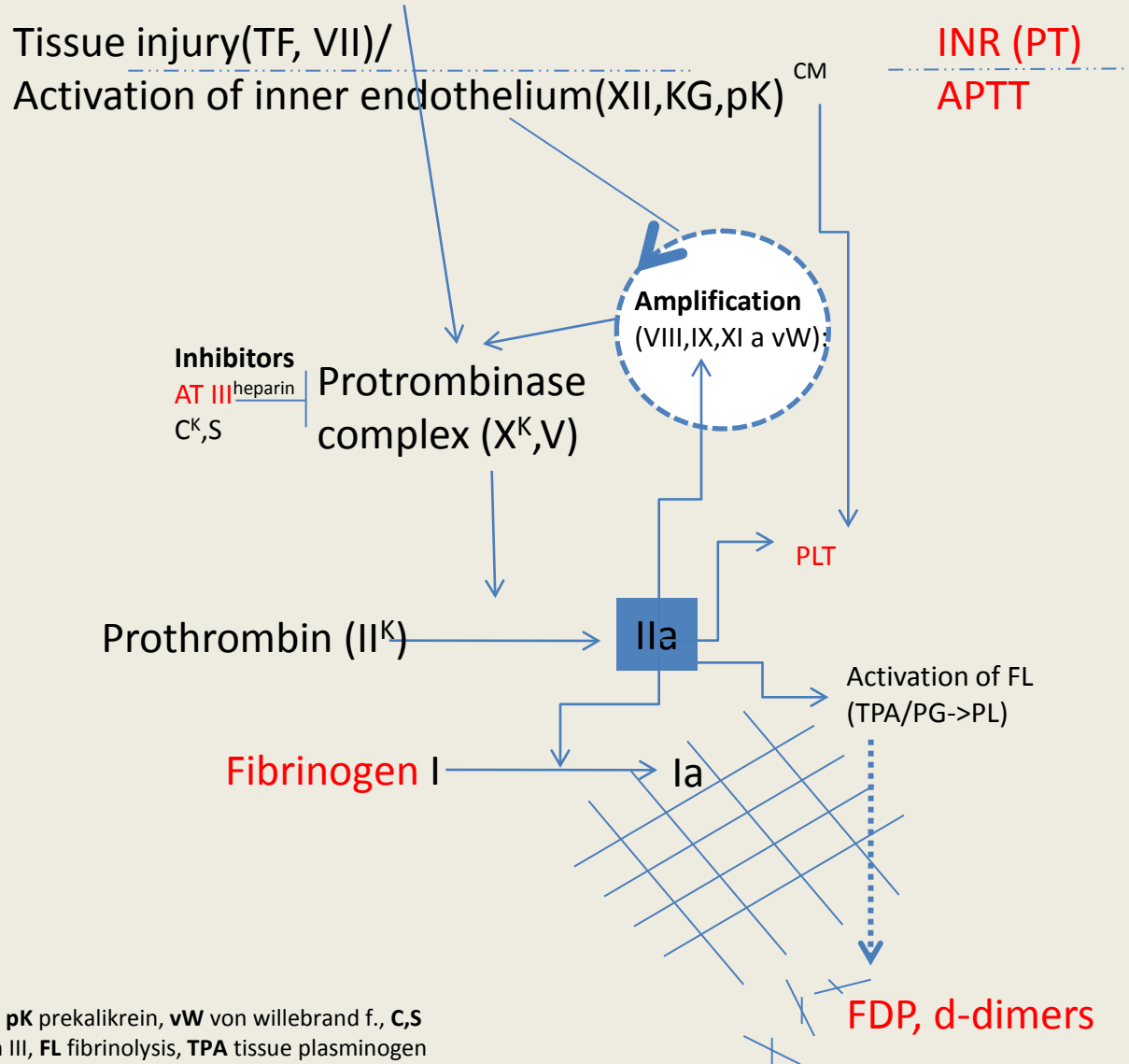
Deficiency of vit. K

Liver disease

Overdose of anticoagulants (Heparin, Warfarin)

DIC, acquired anticoagulants, massive transfusion

# Laboratory approach



TF tissue factor, KG kininogen, pK prekalikrein, vW von willebrand f., C,S protein C,S, ATIII antithrombin III, FL fibrinolysis, TPA tissue plasminogen activator, PG plasminogen, PL plasmin, CM cytoplasmic membrane

# Hemophilias

- **Pg:** inherited deficiency of VIII, IX, XI (<2% severe, >5% mild), 1:10.000
- **CL:** Hemarthros and other spontaneous hematomas
- **DG:** APTT prolonged, DNA Mutation, X chromosome-linked, recessive
- **C:** autoimmune (inhibitors VIII, IX), infection
- **TH:** substitution with a deficient factor
- **PR:** diagnosis at fetal age, cryoprecipitate

# Other inherited coagulopathies

- Deficiencies: I, II, V, VII, IX, X, XII, XIII, 1:100.000
- **CL**: no spontaneous hematomas, infreq.  
Hypercoagulation states (XII)
- **K**: post-surgery bleeding
- **DG**: prolongation of APTT, INR, APTT/INR
- **TH**: fresh frozen plasma
  
- Specific defects: dysfibrinogenemia (AD), afibrinogenemia (lethal-abortions)

# Von Willebrands disease

- Deficiency of vW (partial AD/total AR), 1:5.000
- **PG**: vW multimers on endothelium and PLT bind and protect VIII, facilitate aggregation/adhesion of PLT.
- **CL**: mucosal bleeding, thrombocytopenia
- **DG**: TC analyses (agregometry-ristocetin, Imuno-, DNA-seq), prolongation of APTT, BT, decrease of VIII
- **C**: menorrhagia, bleeding following NSAID
- **TH**: administration of VIII (as in hemophilia)



# Acquired koagulopathy – vit. K def.

- **PG:** dietary, hepatopathy, malabsorption, warfarin overdose, ...
- Vit K:cofactor ( $\gamma$  carboxylation II, VII, IX, X, C, S)
- **DG:** prolongation PT>APTT
- **C:** 1) neonatal hemorrhagic disease
- 2) esophageal variceal bleeding (liver cirrhosis)
- **TH:** vit. K administration(10mg i.v.), FFP

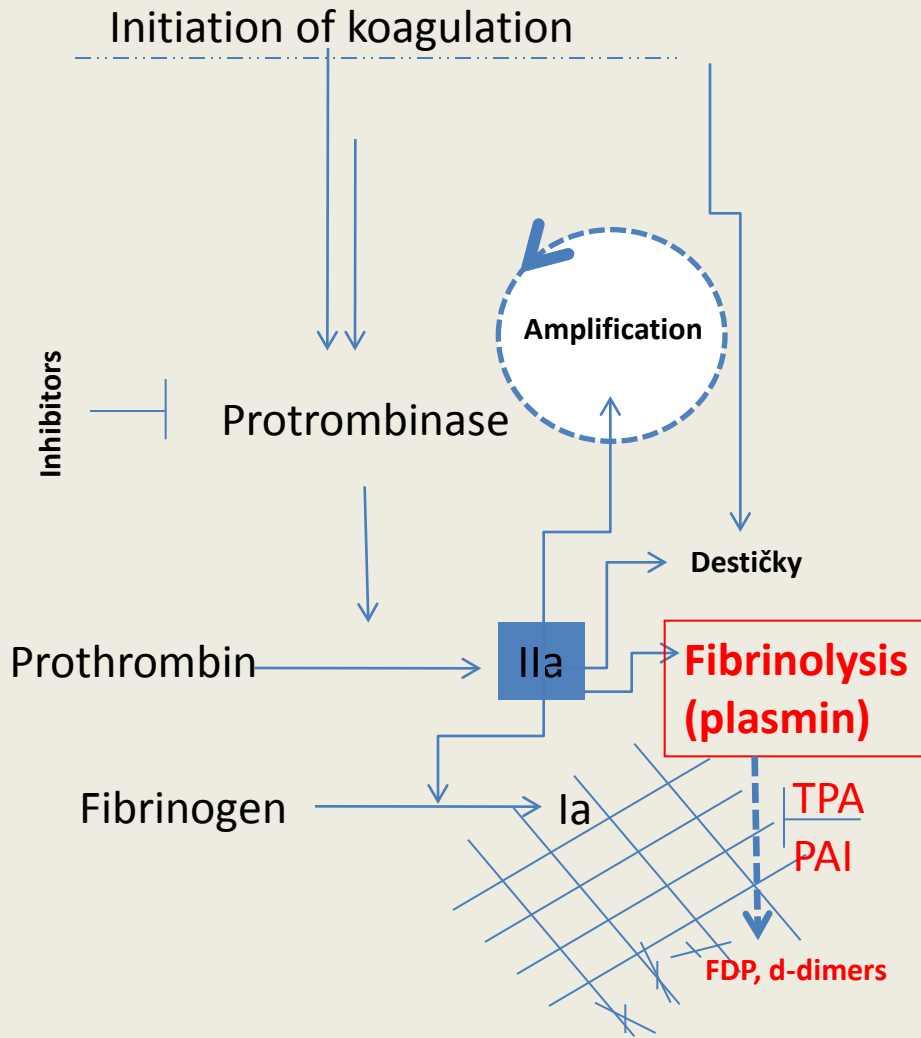
# Acquired koagulopathy - inhibitors

- **PG:** VIIIi, IXi, vWi (neutralization antibodies)
- **DG:** prolongation of APTT, dilution test with healthy plasma
- **CL:** prolonged postsurgical and posttraumatic bleeding, paraneoplasia, ...
- **TH:** steroids, substitution upon bleeding

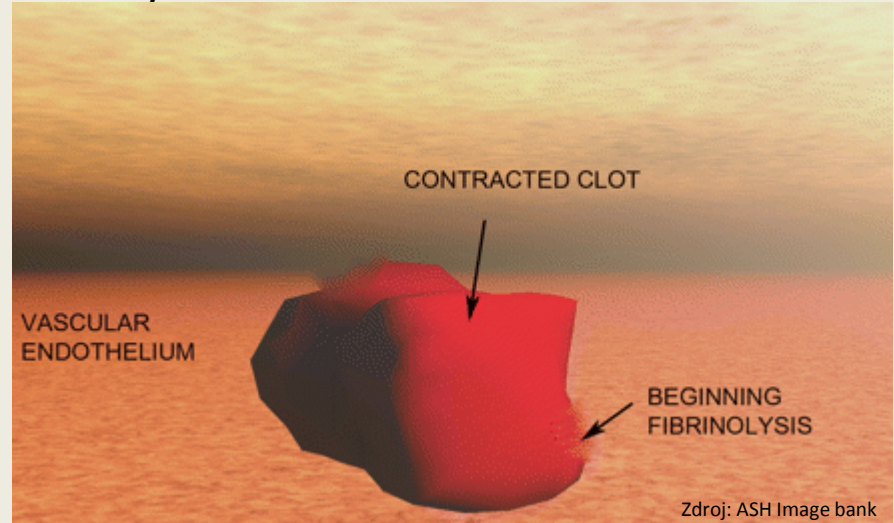
# Vasculopathy

- PG: **Osler-Weber-Rendu sy** (AD, starts in adults) : abnormal structure of vessels leading to teleangiectasia.
- CL: epistaxis, Iron deficiency, menorhagia
- TH: local
  
- PG: **Henoch Schonlein purpura** (autoimmune)
- CL: purpura lower extremities, mesenterial vasculitis, arthritis, nephritis
- TH: immunosuppression
  
- **Other: scurvy**

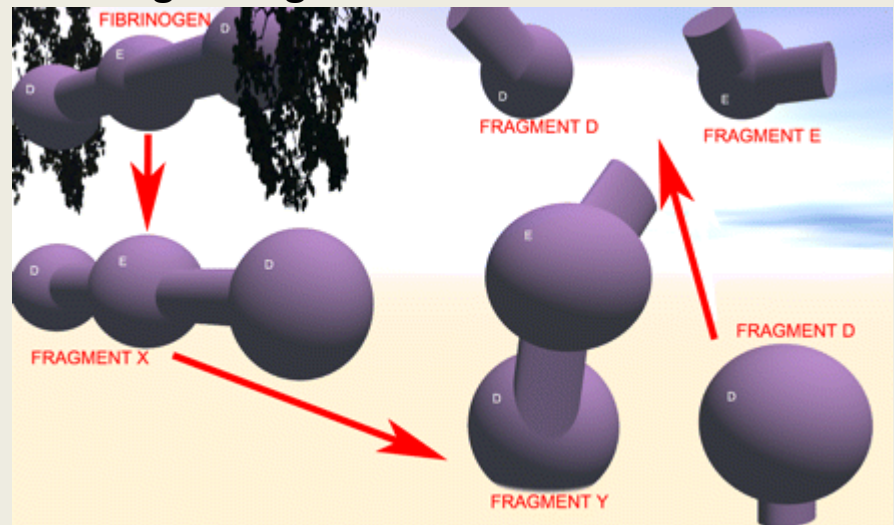
# Role of fibrinolysis



## Tertiary hemostasis



## Fibrinogen degradation

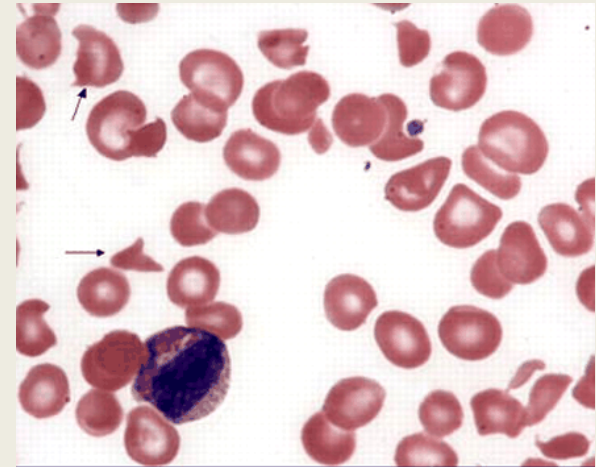


# Failure of hemostasis : DIC

- **PG**: secondary: trauma, surgery, tumors (TF), organ failure, sepsis, shock (hyperactivation of endothelium)
- **CL**: 1. faze: activation of coagulation cascade (procoagulation state = thrombosis and organ microthrombosis), *latent period*  
2. faze: consumption coagulopathy = fibrinolytic bleeding, *life-threatening state*.

# Failure of hemostasis : DIC

- **DG:** 1. faze: shortened APTT/PT, elevated d-d, decreased PLT and ATIII.
- 2. faze: prolonged APTT/PT, TT, low FBG. Schistocytes:



- **TH:** 1. faze: anticoagulation, administration of ATIII, FFP. 2. faze: FFP, PLT, FBG, ERY.

# Hemorrhagic diathesis - review

- Mechanisms of blood clotting system: prim./sec./terc. hemostasis
- Disorders: Thrombocytopenia/pathy, Vasculopathy, Coagulopathy
- DIC – failure of hemostatic mechanisms