

# Coagulation Disorders

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Praha

# Etiology

- **Vascular defects**
- **Platelets**
- **Coagulation factors**
  
- **Inherited**
- **Acquired**

# The approach to bleeding patient

- **Personal History**
  - spontaneous?
  - bleeding after surgery, trauma, during pregnancy, delivery, menstruation, etc.?
- **Family History**
  - Any relatives with similar symptoms?
- **Physical examination**
  - Signs of bleeding?

# Physical Examination - Skin

- Petechiae



# Physical Examination - Skin

**Henoch-Schönleinova purpura**



**Senile purpura**



# Physical Examination – any other signs?

- Mouth, tongue, nose
- Hematuria
- GIT bleeding
- Gynaecological bleeding

Epistaxis



subkonjunktival hemmorhage

# Coagulation factor disorders

Hemartros in hemophilia A



**Ecchymoses**



# Brain hemorrhage

- Neurological symptoms



-warfarin overdose



INITIATION

DAMAGED SURFACE



TRAUMA



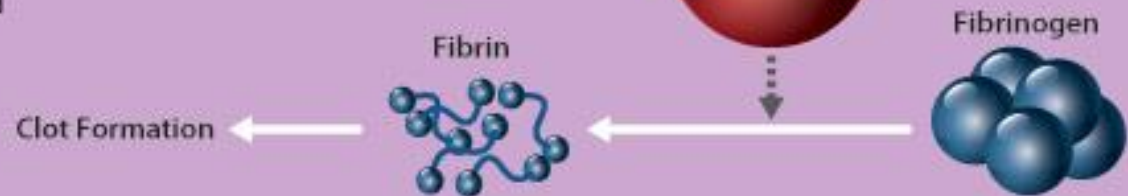
PROPAGATION



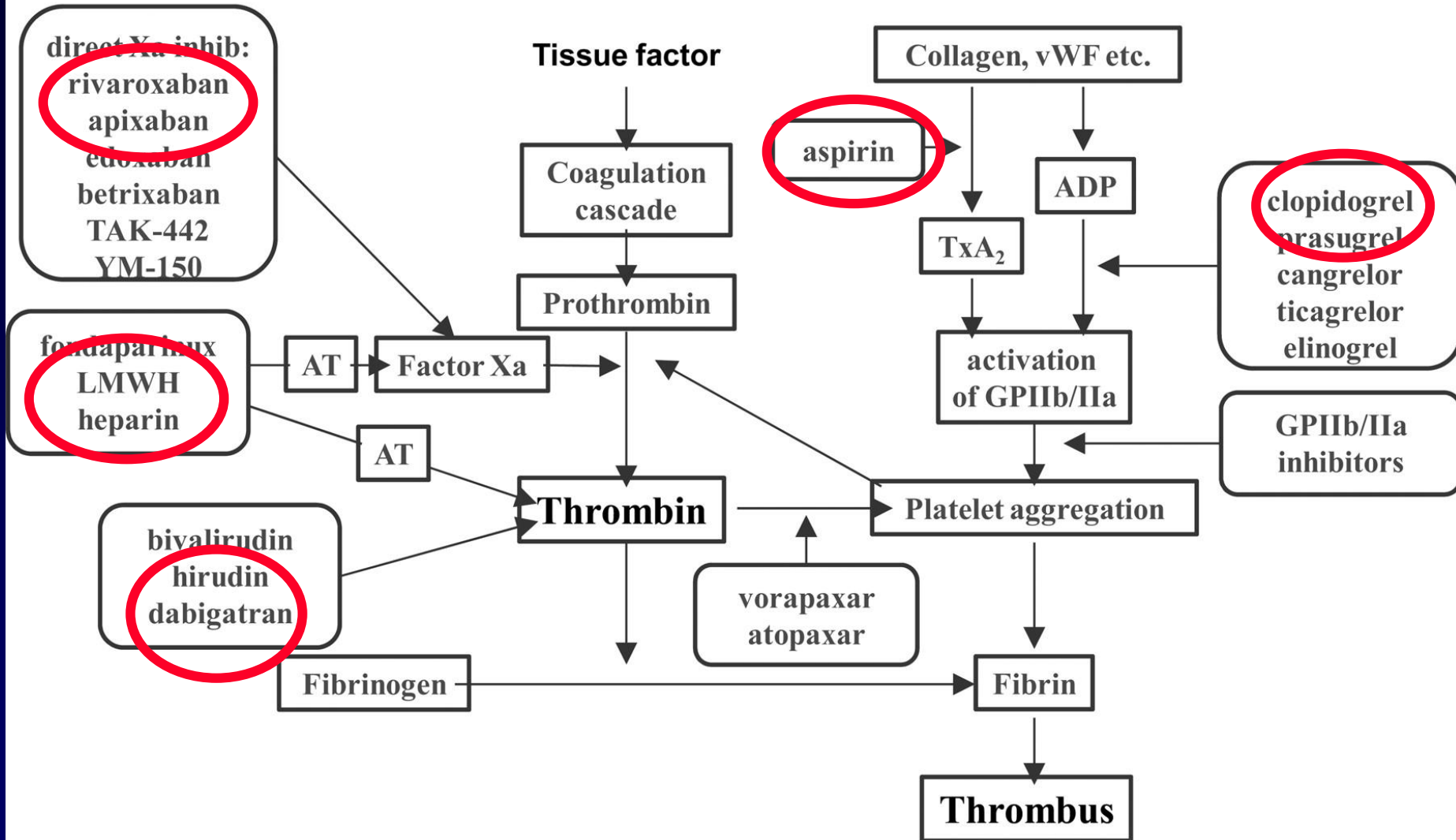
Vitamin K antagonist:  
warfarin

Direct thrombin  
inhibitor: dabigatran

FIBRIN FORMATION

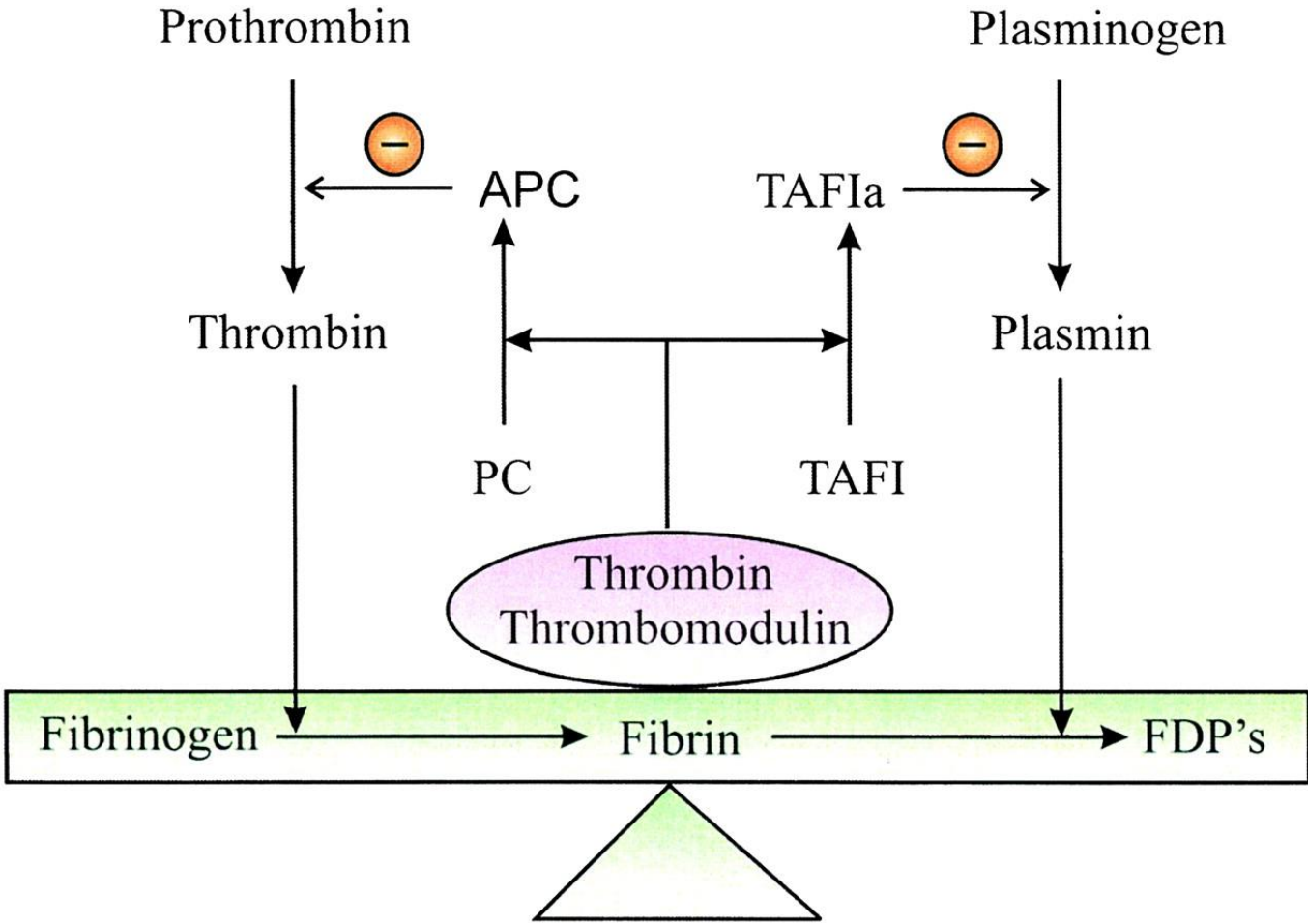


# Targets of Antithrombotic Agents



# Coagulation Cascade

# Fibrinolytic Cascade



# Laboratory Evaluation of the Coagulation Pathways

Partial thromboplastin time  
(PTT)

Surface activating agent  
(Ellagic acid, kaolin)  
Phospholipid  
Calcium

Prothrombin time  
(PT)

Thromboplastin  
Tissue factor  
Phospholipid  
Calcium

*Intrinsic pathway*

*Extrinsic pathway*

Thrombin time

Thrombin

*Common pathway*

*Fibrin clot*

# Lab tests

**Time to bleed** 3-5 min

**Platelets** 150-350 x 10<sup>9</sup>/l

**APTT** 28-40 sec

**PT (INR)** 10-15 sec, 0.8-1.2

**TT** <18 sec

**Fbg** 2-4g/l

**FDP** negative

**D-dimers** 0-180

**ATIII** 70-140%

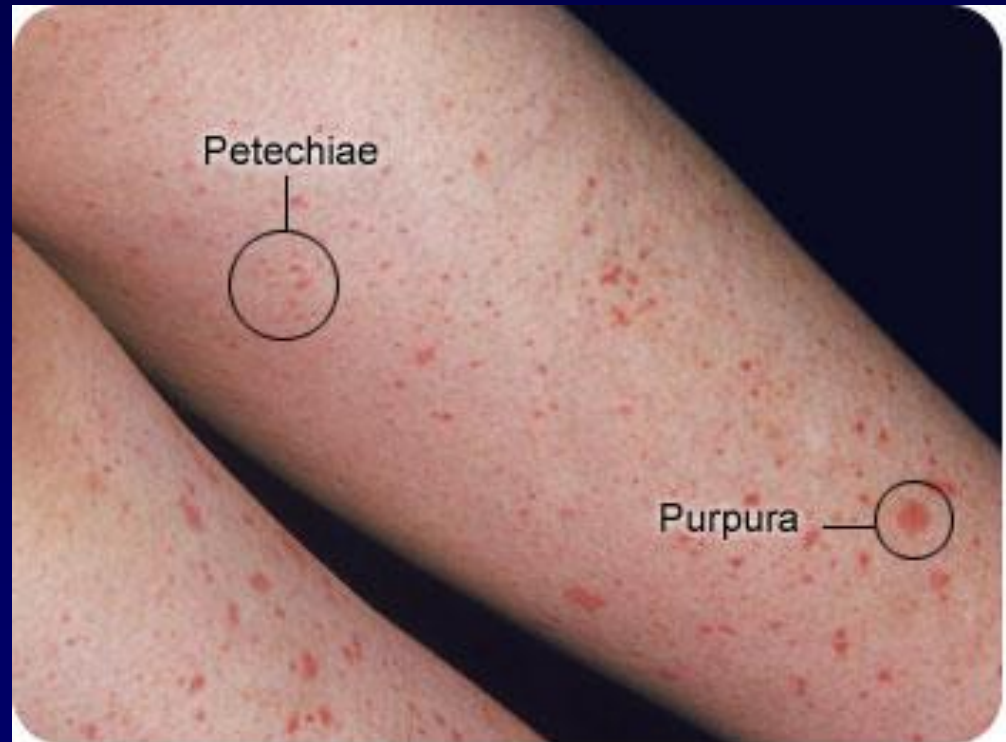
# Kazuistika I - charakteristika pacienta

- Věk v době diagnózy 28 let
- Pylová alergie, jinak anamnéza nevýznamná
- Před dvěma týdny akutní virové onemocnění s horečkami
- Generalizovaná petechiální purpura, krvácení z dásní
- Kromě projevů krvácení fyzikální nález normální



# Case I

- Platelets –  $5 \times 10^3 / \mu\text{l}$
- RBC & WBC normal
- Coagulation parameters normal
- Suggestions?

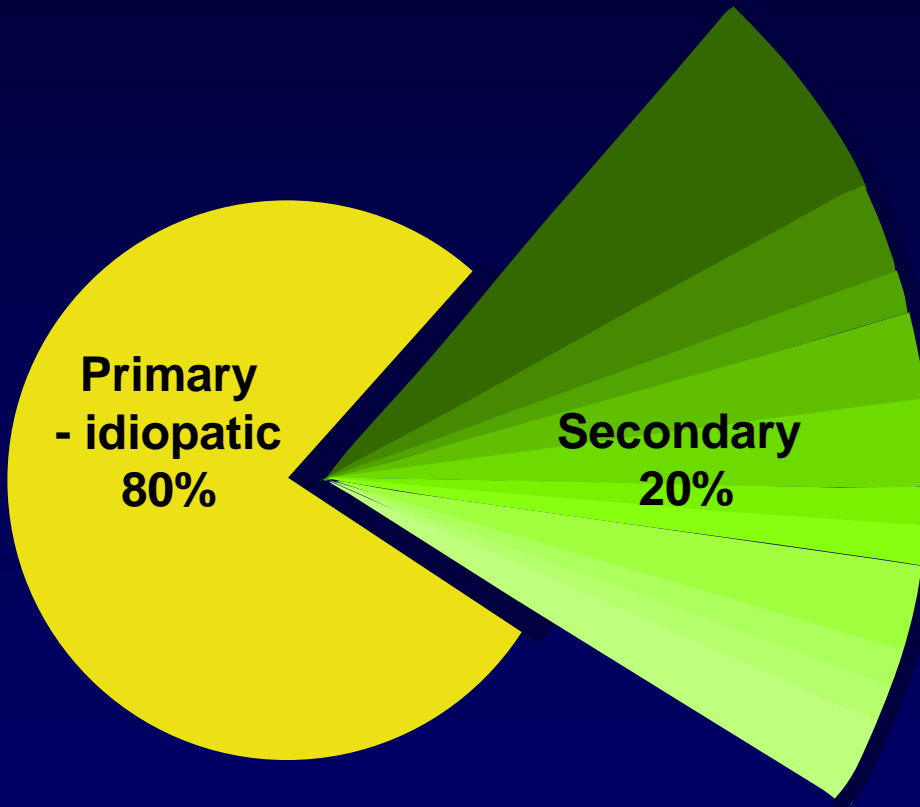


# Thrombocytopenia

- **BM suppression (aplastic anemia, myelodysplastic sy. )**
- **Increased destruction – immune mediated**
  - **posttransfusion, medication, HIT, ITP**
- **Non-immune mediated destruction - TTP, DIC, Splenomegaly-hypersplenism**



# Immune thrombocytopenia (ITP)



## Secondary ITP:

Infection – HIV, HCV, Helicobacter pylori, + others..

Autoimmune diseases (SLE)

Cancer

Drug-induced

# Therapy

## Immunosuppression

- Corticosteroids, cyclophosphamide
- splenectomy
- rituximab (anti CD20)
- intravenous Ig

## Stimulation of production

- TPO agonists (romiplostim, eltrombopag)

➤ Treat the cause of secondary ITP

# How many is needed

- **Tooth extraction : simple  $\geq 30 \times 10^9/l$ , complicated  $\geq 50 \times 10^9/l$**
- **Small surgery:  $\geq 50 \times 10^9/l$**
- **Big surgery:  $\geq 70 \times 10^9/l$**
- **Neurosurgery:  $\geq 100 \times 10^9/l$**
- **Spontaneous delivery:  $\geq 50 \times 10^9/l$**
- **C-section + epidural anesthesia :  $\geq 70 \times 10^9/l$**
- **Needle biopsy:  $\geq 50 \times 10^9/l$**
- **Bronchoscopy, endoscopy:  $\geq 50 \times 10^9/l$**
- **CVC:  $\geq 30 \times 10^9/l$  – depends on skills and localization**
- **Patient can be released from hospital:  $\geq 10-20 \times 10^9/l$**
- **Infection:  $\geq 20 \times 10^9/l$**
- **Minimal number if patients is w/o other complications:  $\geq 5-10 \times 10^9/l$**

## Case II

- Patient 40 let
- No spontaneous bleeding
- Bleeding after surgery
- Increased time to bleed, coagulation normal, platelets normal

# Trombocytopenia

- **inherited – rare...**
- **Acquired – drug induced (ASA, NSA, clopidogrel, ...)**
  - renal insuf.
  - Cardiopulmonary bypass
  - hematological (MDS, MPD, leukemie)

## Case III

- Patient 38 y.
- Brain hemorrhage
- CBC normal
- increased APTT – 162 s (normal 28-40s)
- PT, TT, Fbg, DD, ATIII normal
- factor VIII levels 0,6% (normal 80-160%)

# Hemophilia

Clinical manifestations (**hemophilia A & B indistinguishable**)

Hemarthrosis (**most common**)

Fixed joints

Soft tissue hematomas (e.g., muscle)

Muscle atrophy

Shortened tendons

**Other sites of bleeding**

Urinary tract

CNS, neck (may be life-threatening)

Prolonged bleeding after surgery or dental extractions

## Case IV

- Patient 56 y.
- Vomiting recently, the stomach content was black



# Lab tests

## Normal values

<b>Time to bleed</b>	<b>19</b>	<b>3-5 min.</b>
<b>PLT</b>	<b>78</b>	<b>150-350 . 10<sup>9</sup>/l</b>
<b>APTT</b>	<b>69</b>	<b>28-40 sec.</b>
<b>PT (INR)</b>	<b>1.88</b>	<b>0.8-1.2</b>
<b>TT</b>	<b>108</b>	<b>&lt; 18 sec.</b>
<b>Fbg</b>	<b>0.45</b>	<b>2-4g/l</b>
<b>FDP</b>	<b>pos</b>	<b>neg</b>
<b>D dimery</b>	<b>281</b>	<b>0-180</b>
<b>ATIII</b>	<b>43</b>	<b>70-140%</b>

## Case IV – cont.

- Ascites, portal hypertension
- Anemic, pale, tachycardia
- Albumin 22 g/l
- Bilirubin high, ALT & AST high
- CBC: Hgb 60 g/l, HCT 18%, WBC 9,4, plt 78

# Case IV - Liver Disease

- Decreased synthesis of II, VII, IX, X, XI, and fibrinogen
- Prolongation of PT, aPTT and Thrombin Time
- Often complicated by Gastritis, esophageal varices, DIC

## Treatment:

Fresh-frozen plasma infusion (immediate but temporary effect)  
Vitamin K (usually ineffective)

## Case V

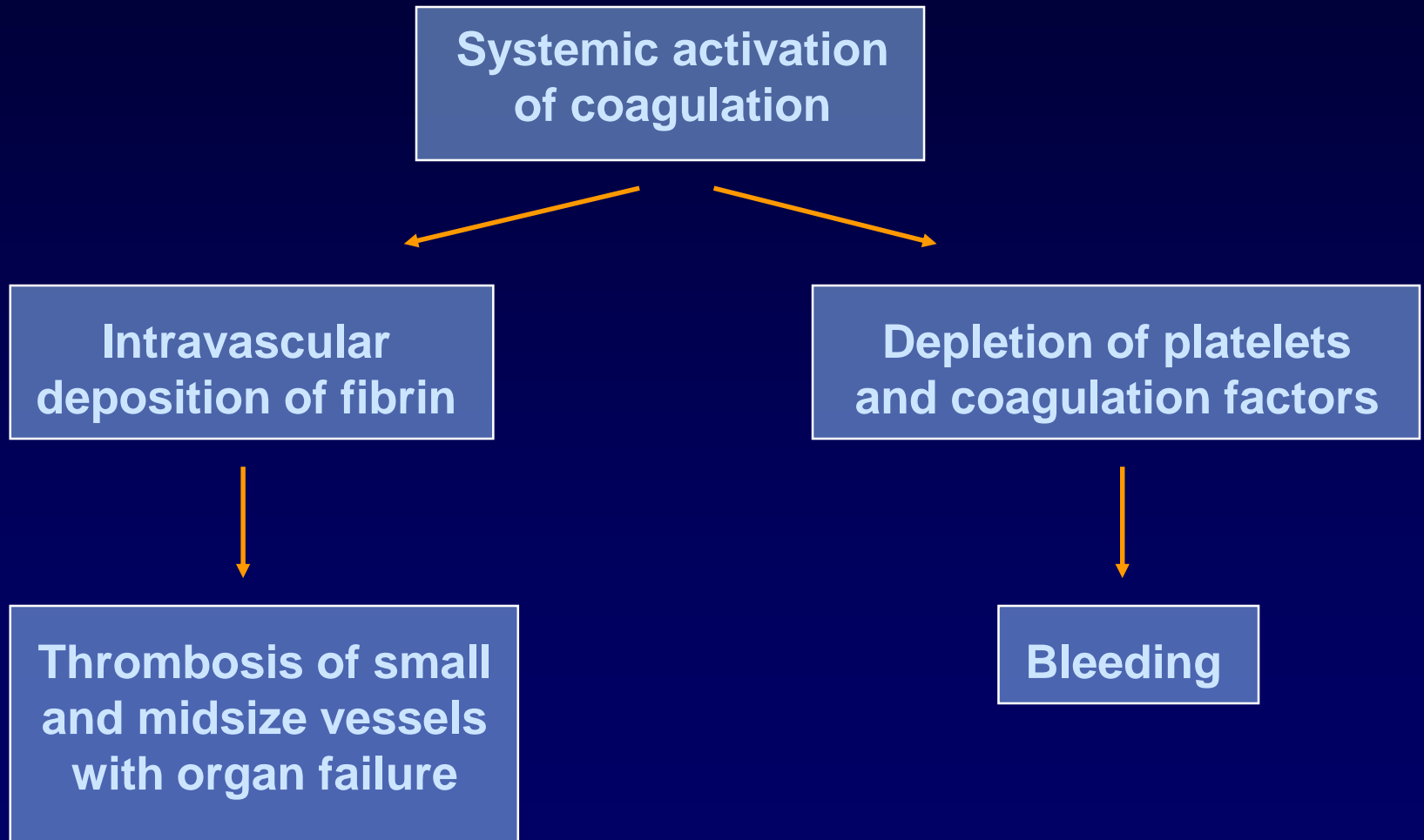
- Patient 25 y.
- AML
- Pneumonia, sepsis
- Bleeding from inserted catheters, petechiae

# Case V – lab tests

## Normal values

Time to bleed	?	3-5 min.
PLT	21	150-350 . 10 <sup>9</sup> /l
APTT	84	28-40 sec.
PT (INR)	1.9	0.8-1.2
TT	>180	< 18 sec.
Fbg	0.2	2-4g/l
FDP	pos	neg
D dimers	6436	0-180
ATIII	32	70-140%

# Disseminated Intravascular Coagulation (DIC) Mechanism



## Case V - therapy

- **Treat the septic shock**
- **Prevent thrombus formation - heparin**
- **Restore coagulopathy – FFP, ATIII, platelets**

## Case VI

- 63 y. old
- Hematuria
- Deep vein thrombosis in the past, takes a lot of pills..
- Our questions?



# Case VI – lab tests

## Normal values

<b>PLT</b>	<b>222</b>	<b>150-350 . 10<sup>9</sup>/l</b>
<b>APTT</b>	<b>74</b>	<b>28-40 sec.</b>
<b>PT (INR)</b>	<b>8.6</b>	<b>0.8-1.2</b>
<b>TT</b>	<b>16</b>	<b>&lt; 18 sec.</b>
<b>Fbg</b>	<b>2.2</b>	<b>2-4g/l</b>
<b>D dimers</b>	<b>150</b>	<b>0-180</b>
<b>ATIII</b>	<b>72</b>	<b>70-140%</b>

# Vitamin K deficiency due to warfarin overdose

## *Managing high INR values*

Clinical situation	Guidelines
INR therapeutic-5	Lower or omit next dose; Resume therapy when INR is therapeutic
INR 5-9; no bleeding	Lower or omit next dose; Resume therapy when INR is therapeutic  Omit dose and give vitamin K (1-2.5mg po)  Rapid reversal: vitamin K 2-4 mg po (repeat)
INR >9; no bleeding	Omit dose; vitamin K 3-5 mg po; repeat as necessary Resume therapy at lower dose when INR therapeutic

# Vitamin K deficiency due to warfarin overdose

## *Managing high INR values in bleeding patients*

Clinical situation

Guidelines

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INR > 20; serious bleeding  
Any life-threatening bleeding

Omit warfarin  
Vitamin K 10 mg slow IV infusion  
FFP ± factor rhVIIa (depending on urgency)  
Repeat vitamin K injections every 12 hrs as needed

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# Acute trombosis - Heparin overdose

## Normal values

PLT	152	150-350 . 10 <sup>9</sup> /l
APTT	>180	28-40 sec.
PT (INR)	3.6	0.8-1.2
TT	>180	< 18 sec.
Fbg	2.8	2-4g/l
D dimers	3862	0-180
ATIII	68	70-140%

# KOAGULAČNÍ KASKÁDA

