

# Thrombocytopenia (Not all Thrombocytopenia is ITP)

Allyson Pishko  
Assistant Professor  
University of Pennsylvania

November 4, 2021

# Disclosures

- ▶ **Research funding:** Sanofi Genzyme and Novo Nordisk
- ▶ **Off-label:** Fondaparinux and direct oral anticoagulants in HIT

# Outline

- 2 cases ( multiple etiologies)
- Work-up
- Diagnosis
- Brief pathophysiology
- Management

# Case #1



## Case # 1

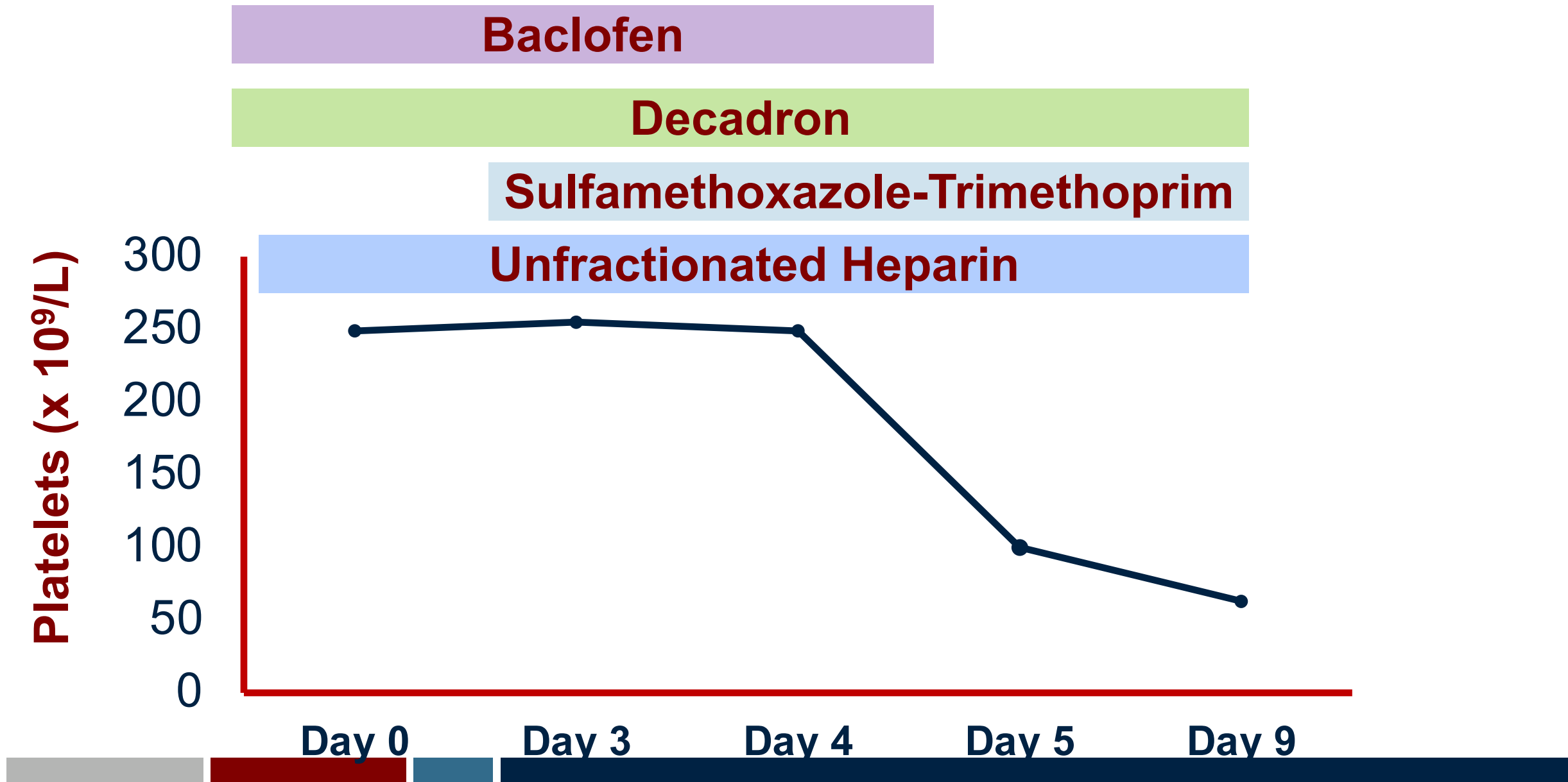
- ▶ 60 yo F with a spinal astrocytoma presents to hospital with worsening neurologic deficits.
- Discharged for trial of rehab while considering surgical options.
- Hematology called 9 days later re: thrombocytopenia

~~10.3  
3.9 53~~

137	107	15
3.8	22	1.06

## Work-up

- Smear review
- Onset of Thrombocytopenia
- Other cytopenias?
- Organ dysfunction?
- Coagulopathy?
- Medications
- Symptoms
  - *Bleeding?*
  - *Thrombosis?*
  - *Fever/chills?*



# Drug-induced thrombocytopenia

- Immune-mediated thrombocytopenia
- Myelosuppressive





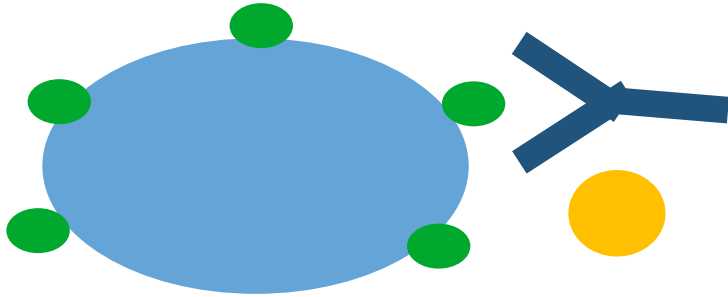
# Drug-induced thrombocytopenia

- **Immune-mediated thrombocytopenia**
- **Myelosuppressive**

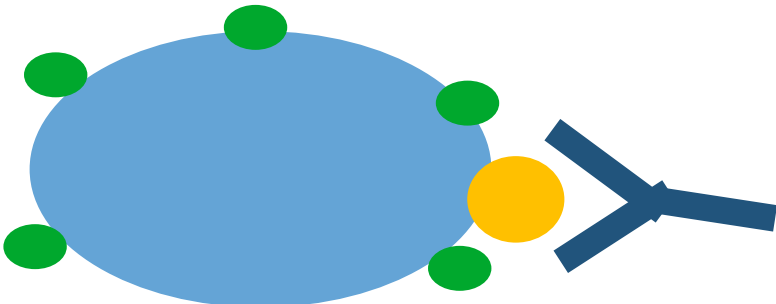


# Drug-induced thrombocytopenia: Immune-mediated

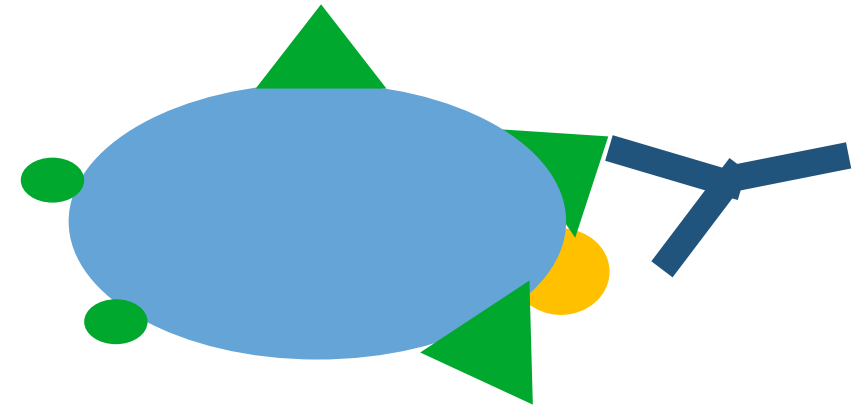
## Drug-specific



## Quinine-type



## Hapten-dependent



Bakchoul et al. Hematology Am Soc Hematol Educ Program (2018) 2018 (1): 576–583.

# Drug-induced thrombocytopenia: Immune mediated

- Lists of offending drugs:
  - <https://www.ouhsc.edu/platelets/ditp.html>
  - Ex. antibiotics (beta-lactams, sulfonamides, vancomycin)
- Usually begins 1-2 weeks after initiation of drug\*
  - \*May be quicker with re-exposure
- Severe thrombocytopenia (median nadir 11k/uL)
- Resolution within several days of drug d/c

George et al. Hematology Am Soc Hematol Educ Program. 2009 ; 153–158

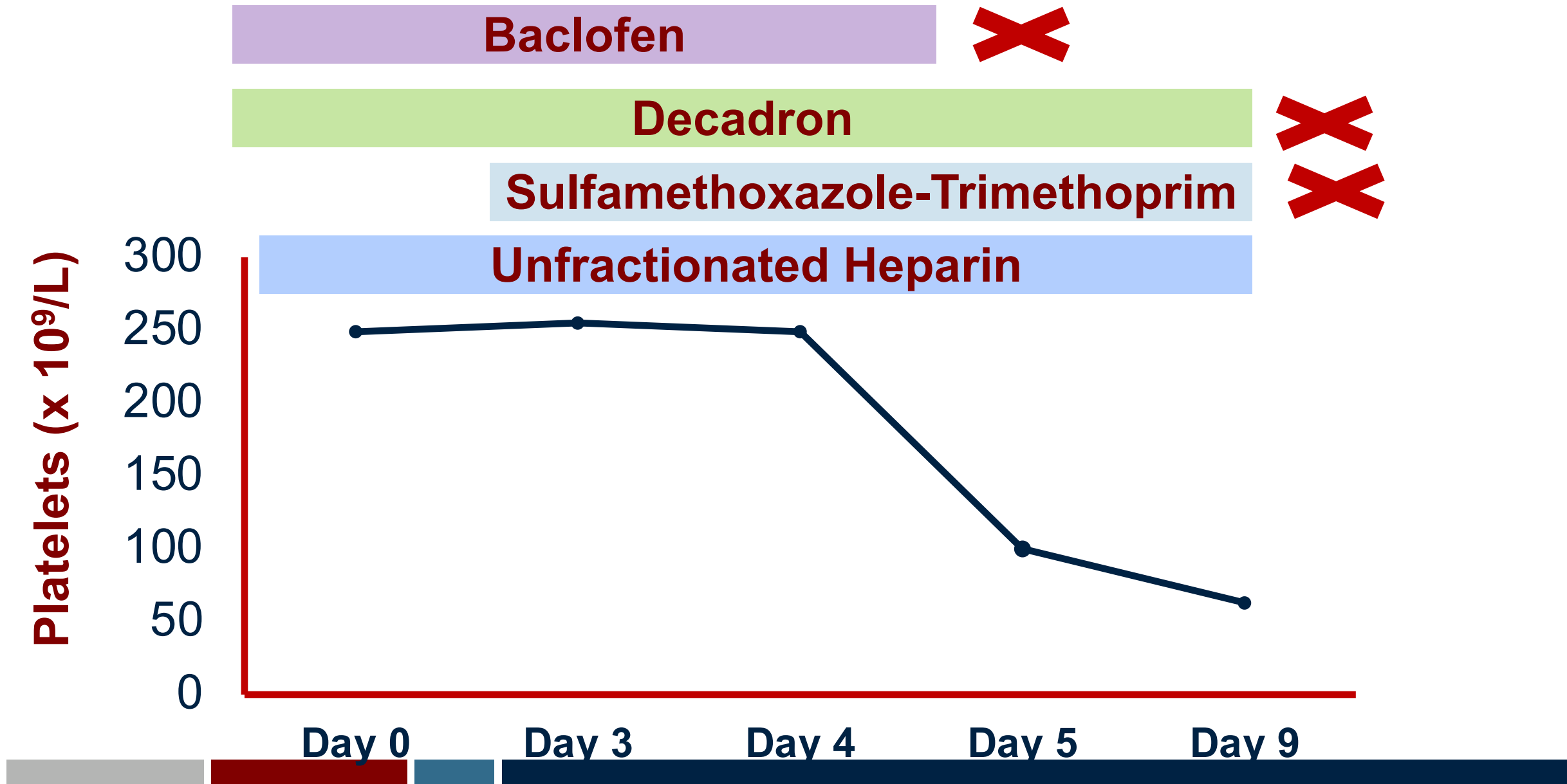
# Drug-induced thrombocytopenia

- Acute, Immune-mediated thrombocytopenia
- **Myelosuppressive**

# Drug-induced thrombocytopenia: Myelosuppressive

- **Impaired platelet production**
  - Chemotherapy
  - Linezolid
  - Thiazide diuretics
  - Ganciclovir
- **Suspected proapoptotic effect**
  - Tamoxifen
  - Methotrexate
  - Cisplatin

Bakchoul et al. Hematology Am Soc Hematol Educ Program (2018) 2018 (1): 576–583.

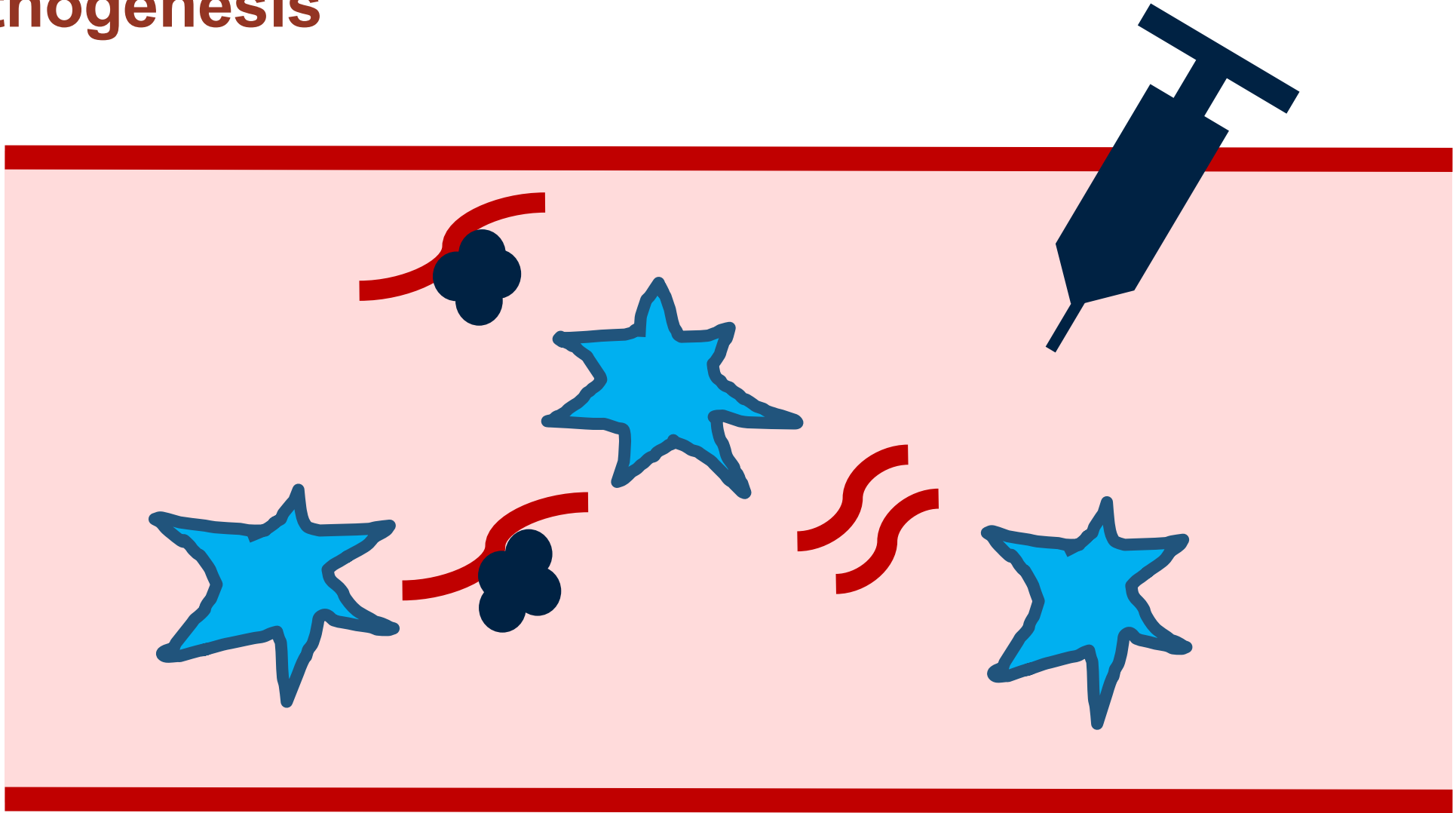


# Heparin-Induced Thrombocytopenia (HIT)

- **Heparin-induced thrombocytopenia (HIT)** is a life- and limb-threatening complication of heparin exposure
- **12- fold increase** relative risk and **50% absolute risk** of thrombosis!
- Incidence of 0.2-5% of all patients that receive heparin  
*.....but suspicion for HIT arises commonly*
- Pathogenesis....

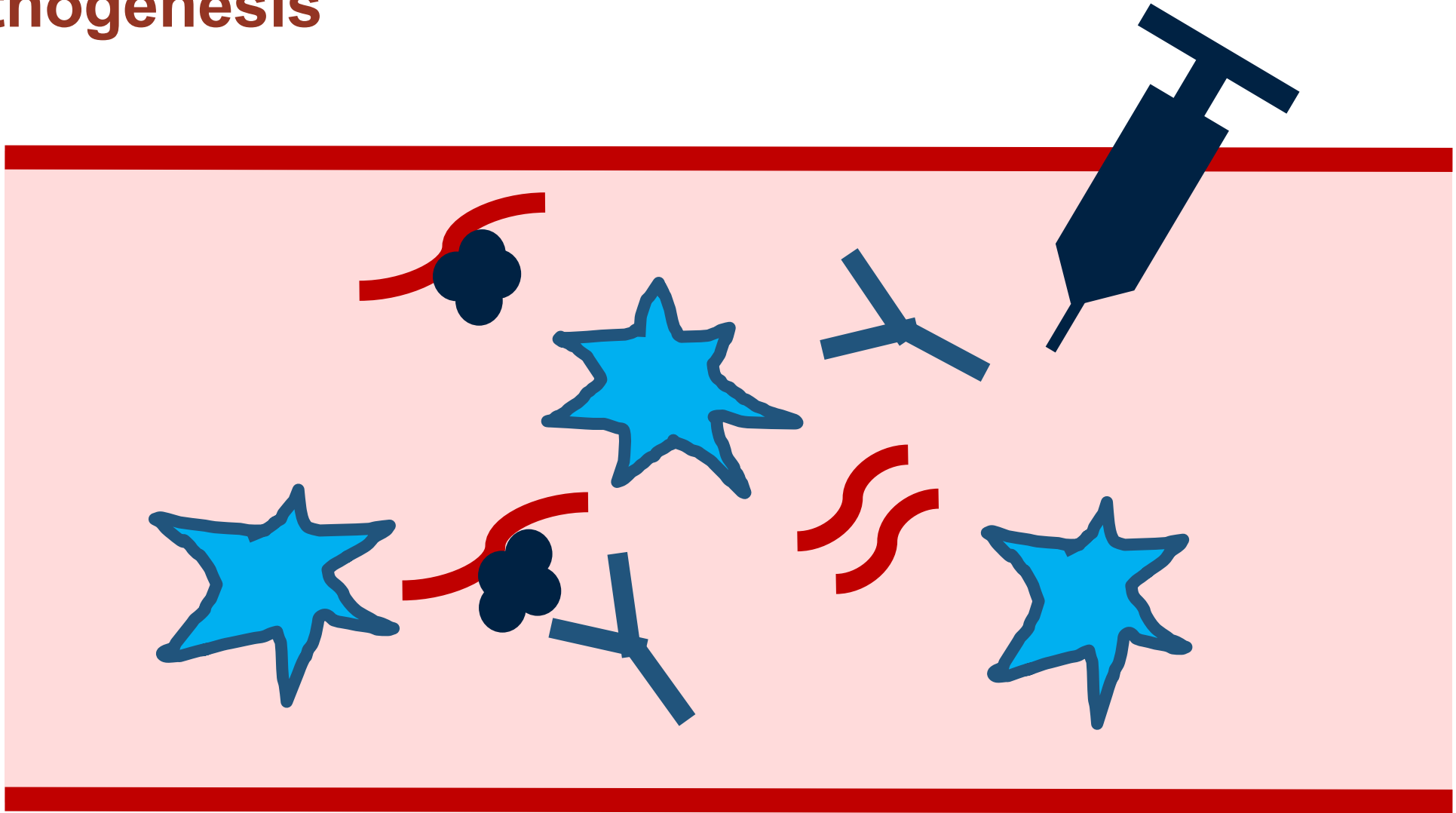


# HIT- Pathogenesis

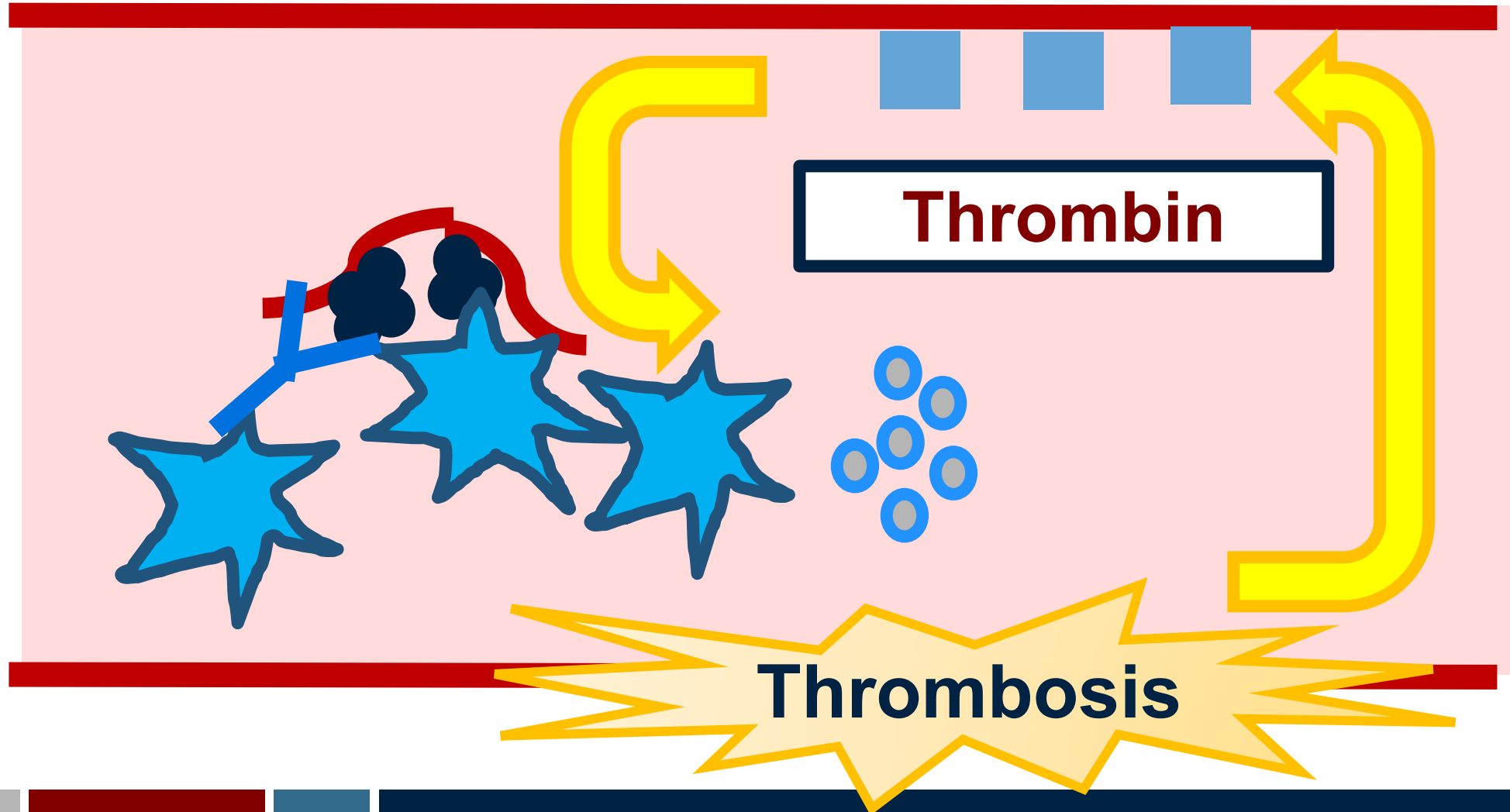




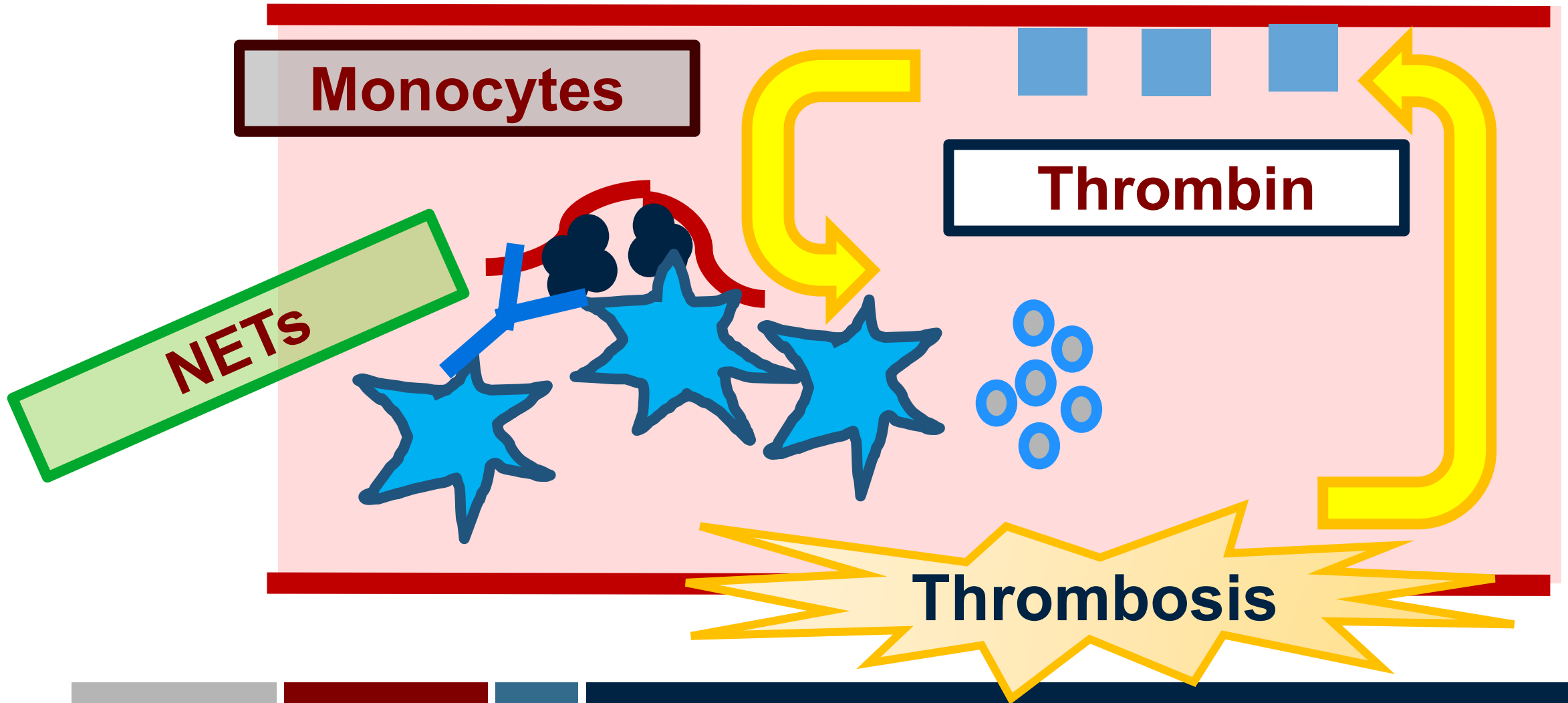
# HIT- Pathogenesis



# HIT- Pathogenesis



# HIT- Pathogenesis



# HIT- Diagnosis & Treatment

## CLINICAL GUIDELINES



American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia

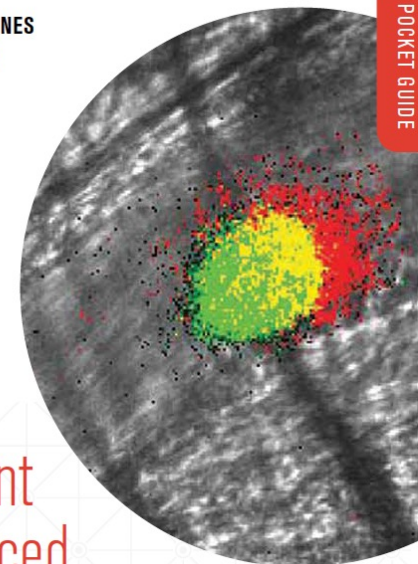
Adam Cuker,<sup>1,2</sup> Gowthami M. Arepally,<sup>3</sup> Beng H. Chong,<sup>4</sup> Douglas B. Cines,<sup>1,2</sup> Andreas Greinacher,<sup>5</sup> Yves Gruel,<sup>6</sup> Lori A. Linkins.<sup>7</sup>

Cuker et al. Blood Advances 2018 2:3360-3392



ASH CLINICAL PRACTICE GUIDELINES  
VENOUS THROMBOEMBOLISM (VTE)

POCKET GUIDE



## Diagnosis and Management of Heparin-Induced Thrombocytopenia (HIT)

A POCKET GUIDE FOR THE CLINICIAN  
DECEMBER 2018

Allyson M. Pishko, MD, *University of Pennsylvania*  
Lori-Ann Linkins, MD, MSc, *McMaster University*  
Theodore E. Warkentin, MD, *McMaster University*  
Adam Cuker, MD, MS, *University of Pennsylvania*

The recommendations in this guide are based on the 2018  
American Society of Hematology (ASH) Clinical Practice  
Guidelines for Management of VTE: HIT



<http://ashpocketguides.hematology.org/#/app/home>



Penn Medicine

# HIT: Clinical Diagnosis

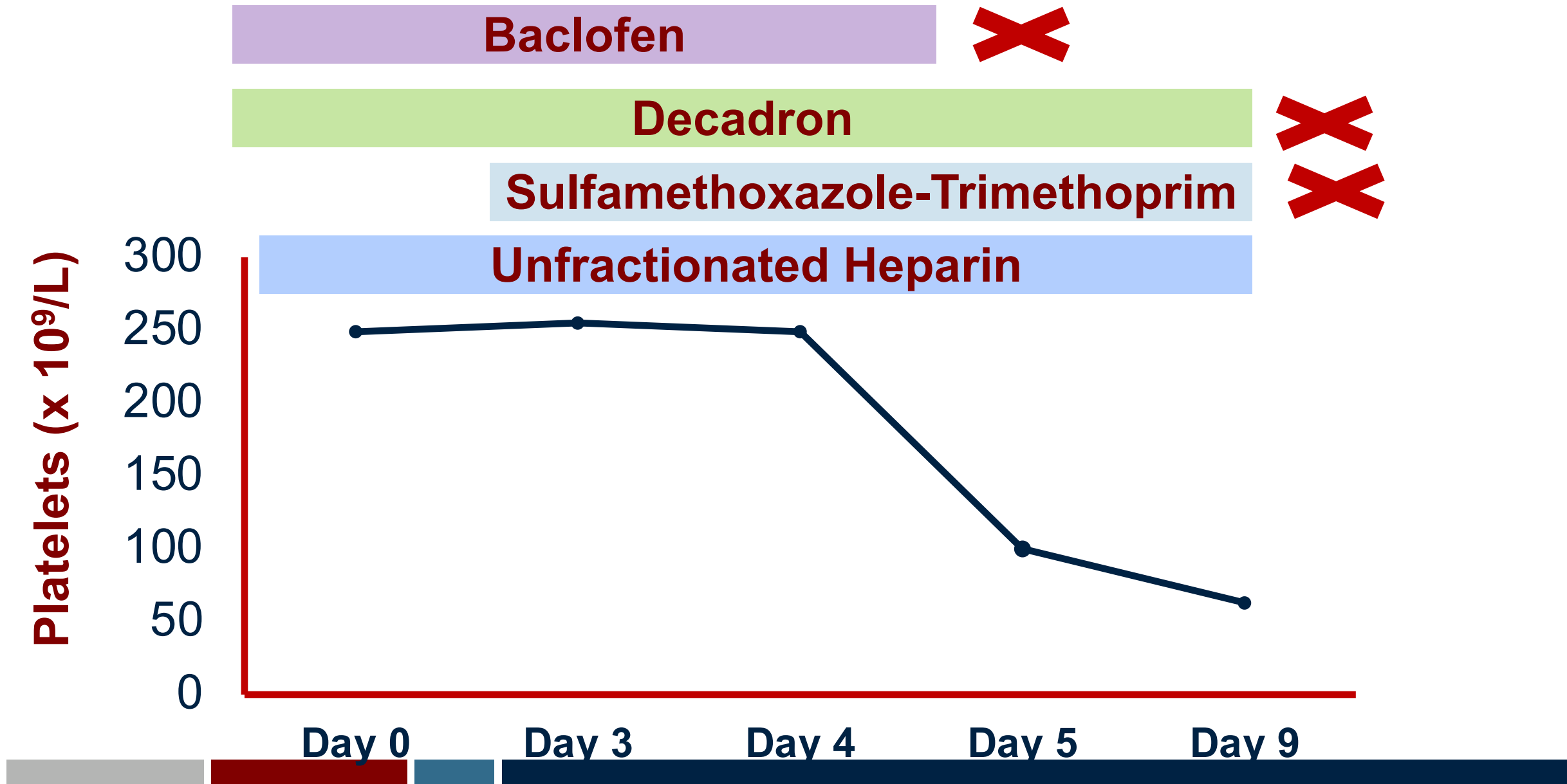
4 T's	2 points	1 point	0 points
<b>T</b> hrombocytopenia	>50% and nadir $\geq 20$	Fall 30-50% or nadir 10-19	Fall <30% or nadir <10
<b>T</b> iming of platelet fall	5-10 days or $\leq 1$ day (prior exposure last 30 days)	After day 10 or $\leq 1$ day (prior exposure 30-100 days ago)	<4 days w/o recent exposure
<b>T</b> hrombosis	New events on heparin	Progressive or recurrent thrombosis	None
<b>O</b> ther causes	None	Possible	Definite

## Total Score

**Low: 0-3**

**Intermediate: 4-5**

**High: 6-8**



# HIT: Clinical Diagnosis (case #1)

4 T's	2 points	1 point	0 points
<b>T</b> hrombocytopenia	>50% and nadir $\geq 20$	Fall 30-50% or nadir 10-19	Fall <30% or nadir <10
<b>T</b> iming of platelet fall	5-10 days or $\leq 1$ day (prior exposure last 30 days)	After day 10 or $\leq 1$ day (prior exposure 30-100 days ago)	<4 days w/o recent exposure
<b>T</b> hrombosis	New events on heparin	Progressive or recurrent thrombosis	None
<b>O</b> ther causes	None	Possible	Definite

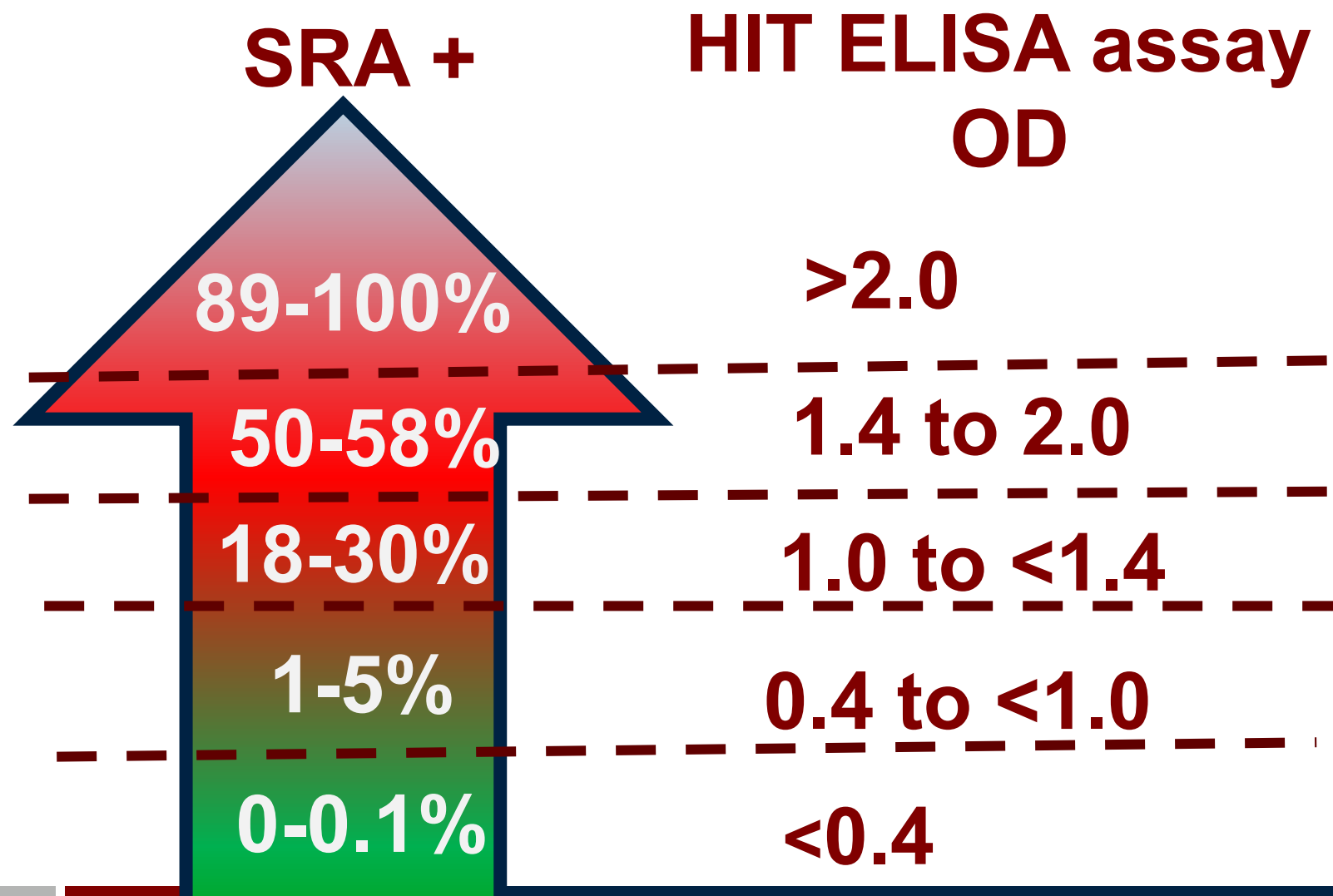
## Total Score

**Low:** 0-3

**Intermediate:** 4-5

**High:** 6-8

# HIT: Laboratory Diagnosis





## Case # 1 (continued)

- Unfractionated Heparin stopped
- Started on fondaparinux 2.5 mg once daily
- HIT confirmatory lab testing is sent
- **PF4/H ELISA 2.32 OD, Serotonin release assay positive**

# Selecting Alternative (non-heparin) Anticoagulant

## Clinical Feature

**Critical Illness, Increased Bleeding Risk, or High Potential for Procedure**



**Argatroban or Bivalirudin**

**Clinically Stable**



**Fondaparinux or DOAC**

**Moderate or Severe Hepatic Dysfunction**



**Avoid argatroban or use reduced dose. Avoid DOACs**

## Anticoagulant

## Case # 1 (continued)

- Found to have lower extremity swelling on day 9
- U/S revealed right lower extremity DVT
- Switched to apixaban 10 mg twice daily x 7 days (with platelet recovery) then apixaban 5 mg twice daily for at least 3 months

## Case #2



## Case #2

60 yo M with metastatic prostate cancer presented with

▶ incontinence and bilateral lower extremity weakness.

▶ MRI revealed cord compression.....

▶ Underwent urgent laminectomy for tumor decompression

**Pre-op:**

**POD 4:**



## Case #2 (continued)

### ► Medications:

► Dexamethasone 6 mg q6h

► Oxycodone 10 mg q8h

### ► Vitals:

afebrile, pulse ox 95%, HR  
110 bpm, bp 90/60

### ► Imaging:

► CT scan- hematoma in  
epidural space and in  
paraspinal soft tissues

## Case #2 (continued)

~~26.1 8.2 75~~  
Cr 1.2 ng/mL

Alk phos 418 U/L, AST 15 U/L, ALT 10 U/L

Tbili 0.5 mg/dL

**INR 1.4, PT 15.6 s (nl 9.4-12.5s)**

**PTT 29.9 s (25.1-36.5s)**

**Fibrinogen 86 mg/dL (nl 170-410)**

**D-dimer 59.9 ug/mL (nl 0-0.5)**

# Work-up

- Smear review
- Onset of Thrombocytopenia
- Other cytopenias?
- Organ dysfunction?
- Coagulopathy?
- Medications
- Symptoms
  - *Bleeding?*
  - *Thrombosis?*
  - *Fever/chills?*



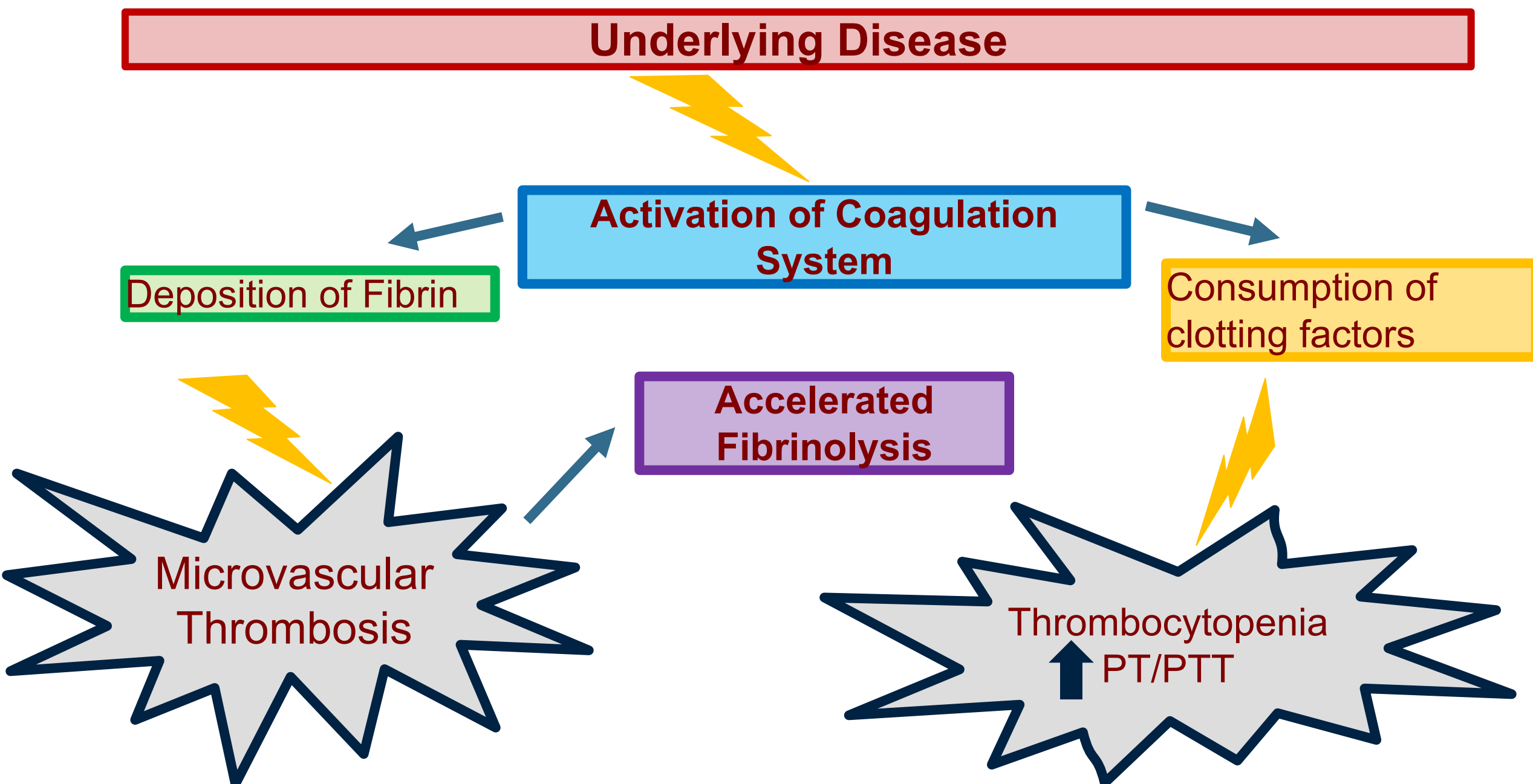
# Primary Hyperfibrinolysis/ Disseminated Intravascular Coagulation (DIC)

- Metastatic cancer (ex. adenocarcinoma)
- Acute promyelocytic leukemia or monocytic leukemia
- Sepsis
- Trauma
- Vascular malformations (localized activation of coagulation factors)



- Obstetric Complications

# DIC



## DIC Diagnosis: DIC score

	0	1	2	3
Platelet Count	>100	<100	<50	-
Fibrin markers (D-dimer)	No increase	-	Increased but <5 X ULN	≥ 5 X ULN
Prolonged PT	<3s	≥ 3 but <6s	>6s	-
Fibrinogen	>1.0 g/L	≤1.0g/L	-	-

**Score ≥ 5 consistent with DIC**

Taylor et al. *Thromb Haemost.* 2001;86(5):1327-1330

## Case #2 (continued)

~~26.1 8.2 75~~

Cr 1.2 ng/mL  
Alk phos 418 U/L, AST 15  
U/L, ALT 10 U/L

Tbili 0.5 mg/dL

**INR 1.4, PT 15.6 s (nl 9.4-12.5s)**

**PTT 29.9 s (25.1-36.5s)**

**Fibrinogen 86 mg/dL (nl 170-410)**

**D-dimer 59.9 ug/mL (nl 0-0.5)**

## DIC Diagnosis: DIC score (case #2)

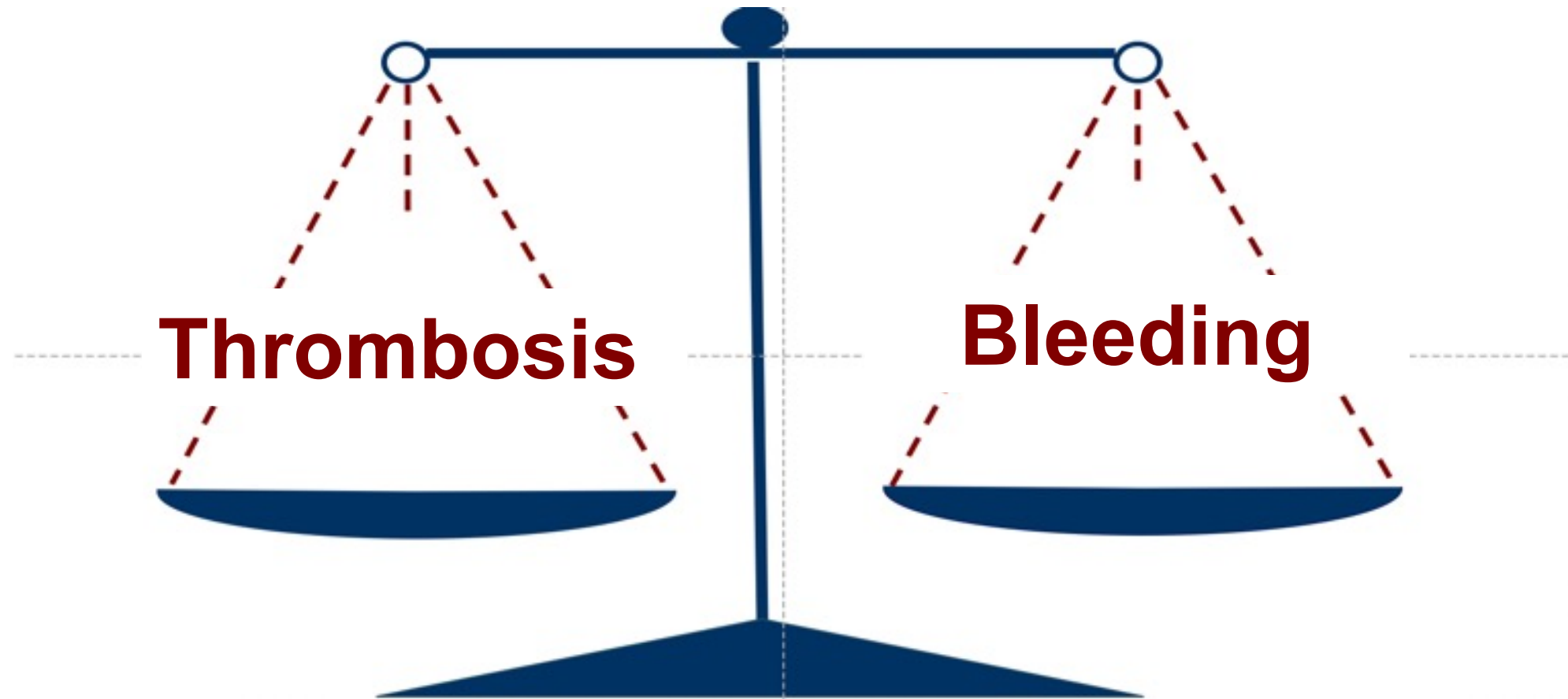
	0	1	2	3
Platelet Count	>100	<100	<50	-
Fibrin markers (D-dimer)	No increase	-	Increased but <5 X ULN	≥ 5 X ULN
Prolonged PT	<3s	≥ 3 but <6s	>6s	-
Fibrinogen	>1.0 g/L	≤1.0g/L	-	-

Score ≥ 5 consistent with DIC

# DIC- Treatment

- Treat underlying cause
- Supportive care for bleeding
  - Platelet transfusion  $>30\text{-}50\text{k/uL}$
  - Plasma and/or cryoprecipitate to keep PT $<3$  s  
prolonged and fibrinogen  $>1.5$  g/L
  - Vitamin K supplementation

# DIC- Treatment



# DIC- Treatment

Unfractionated  
heparin or  
LMWH

**Thrombosis**

**Bleeding**



# DIC- Treatment



**Thrombosis**

**Bleeding**

? Tranexamic  
acid  
(hyperfibrinolysis)

*Blood* (2018) 131 (8): 845-854

## Case #2 (continued)

- Active bleeding → transfused with cryoprecipitate, platelets, FFP.
- Close labs monitoring q6h + repletion
- Tranexamic acid in the OR
- Initiated on treatment for prostate cancer
- Stabilized bleeding & decreasing transfusion requirements

# Recap: Key Points

- Not all thrombocytopenia is ITP
- Medications, medications, medications....
- Clinical setting/onset is important
- **HIT:** ASH VTE HIT guidelines for updates in management
- **DIC:** Management in addition to treating underlying cause depends on dominant symptoms

# Thank you!

► Questions?

► allyson.pishko@pennmedicine.upenn.edu



@PishkoMD

