Approach to Coagulopathies, including DIC & HUS

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Presentation Objectives

i. Common aetiologies
ii. Clinical presentations
iii. Investigations
iv. Management in emergency
v. Common complications
vi. Emergency disposition plan

Causes of coagulopathies

Congenital

X-linked

- Haemophilia A and B

Autosomal

- Von Willebrand disease
- Factor II, V, VII, X, XI and XIII deficiencies
- Combined II, VII, IX and X deficiency
- Combined V and VIII deficiency
- Hypofibrinogenaemia
- Dysfibrinogenaemia

Acquired

Underproduction

- Liver failure

Increased consumption

- Coagulation activation
  - Disseminated intravascular coagulation (DIC)
- Immune-mediated
  - Acquired haemophilia and von Willebrand syndrome
- Others
  - Acquired factor X deficiency (in amyloid)
  - Acquired von Willebrand syndrome in Wilms tumour

Drug-induced

- Inhibition of function
  - Heparins
  - Lepirudin
  - Fondaparinux
  - Rivaroxaban
  - Dabigatran
- Inhibition of synthesis
  - Warfarin

Disseminated intravascular coagulation (DIC)

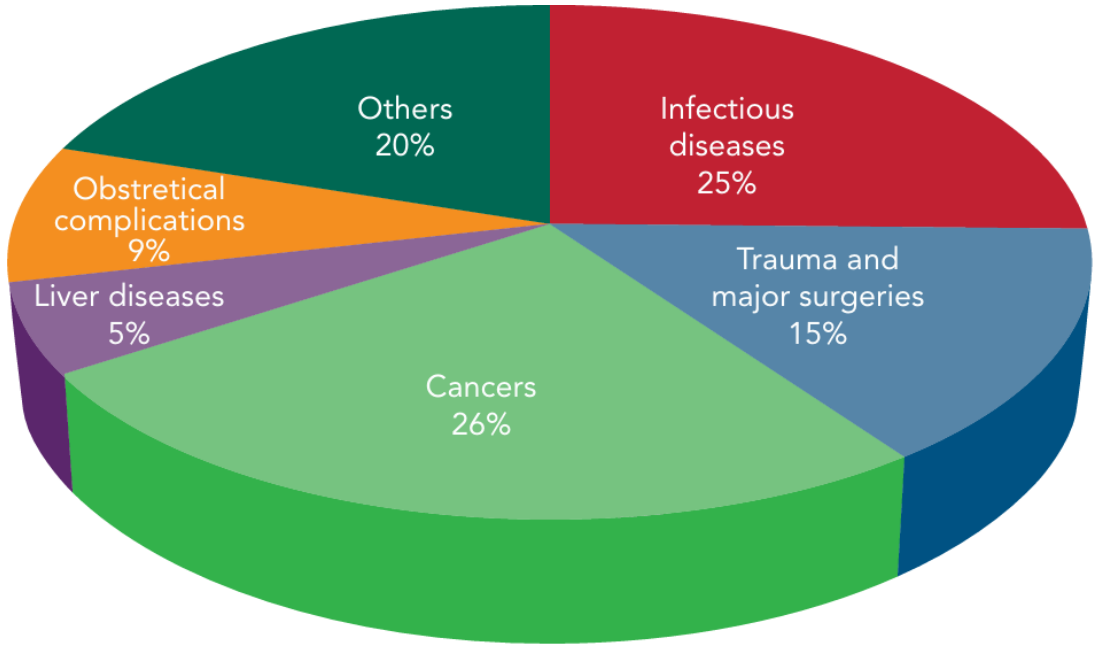
- Acquired syndrome characterized by:
  - Systemic activation of coagulation within the vasculature
  - Leads to microvascular damage, organ dysfunction and haemorrhage
- Triggered by infectious & non-infectious causes
- Infection (sepsis) is the most frequent cause of DIC
- Prevalence of DIC in sepsis varies (18 - 40%) depending on the target cohorts and diagnostic criteria, but mortality >30% generally

Aetiologies of DIC

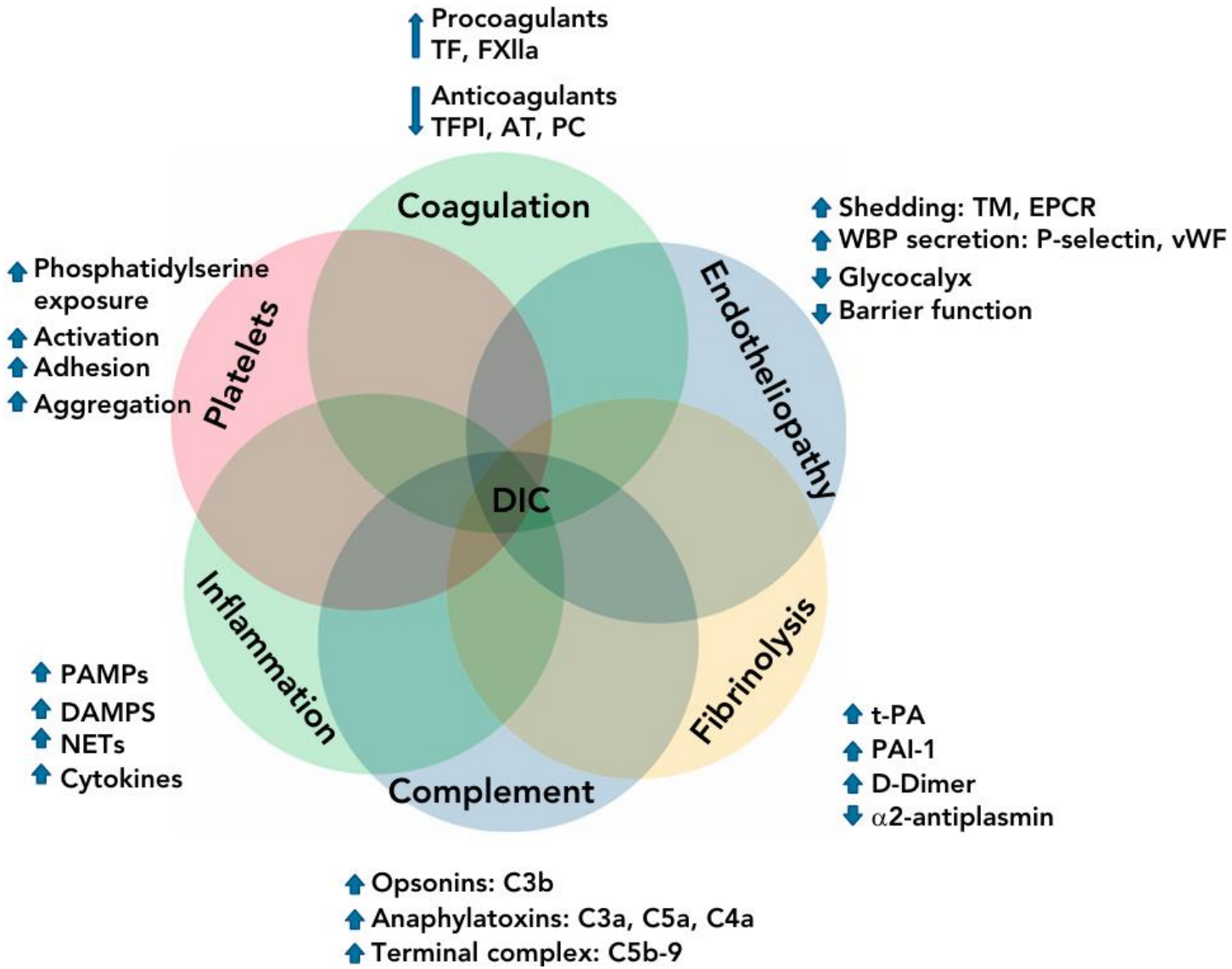
Common aetiologies

- Severe systemic infections
- Malignancy
- Trauma
- Obstetrical complications
- Vascular malformations
- Severe immunological reactions
- Heat stroke

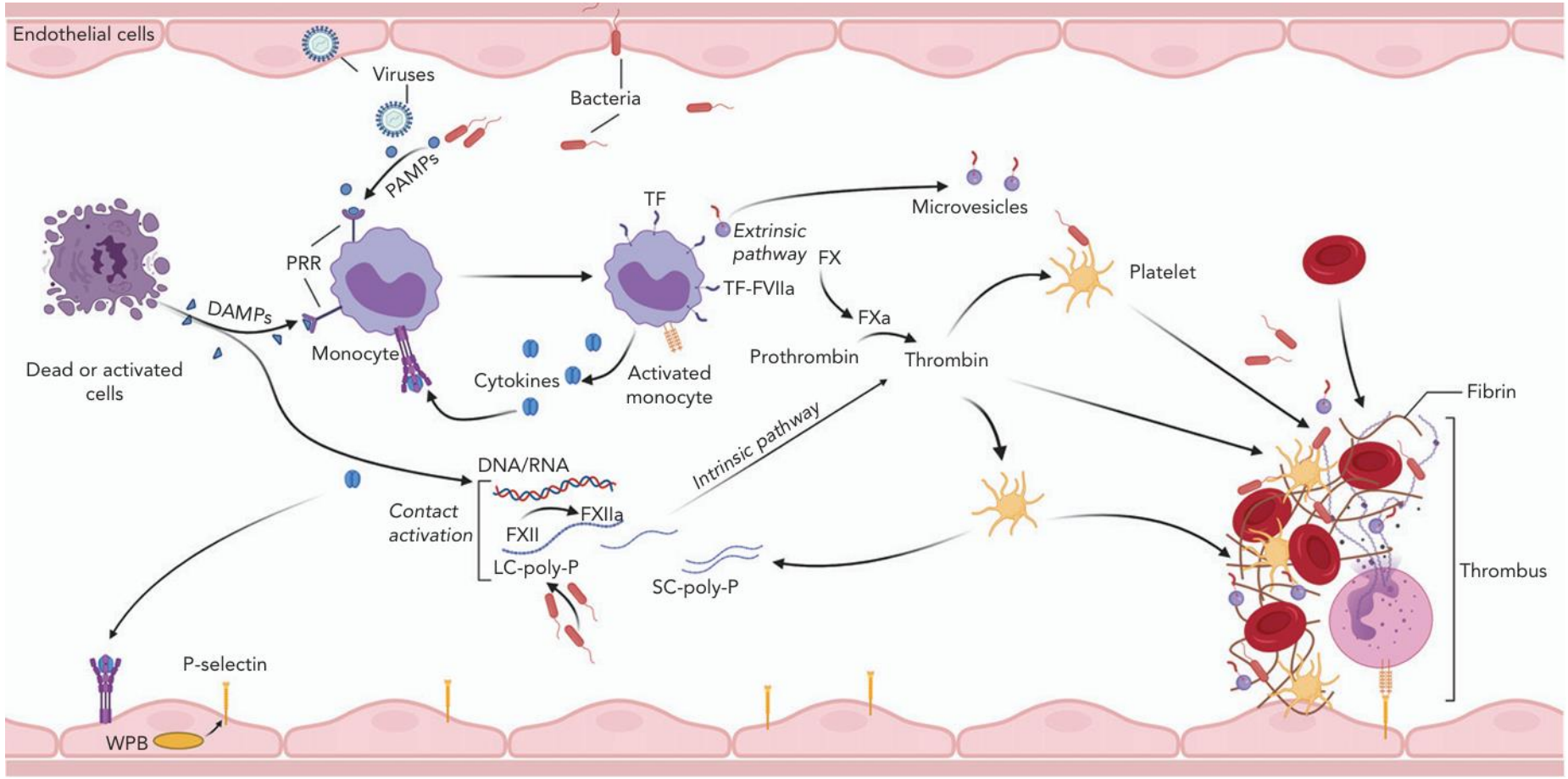
Incidence of DIC in critically ill patients



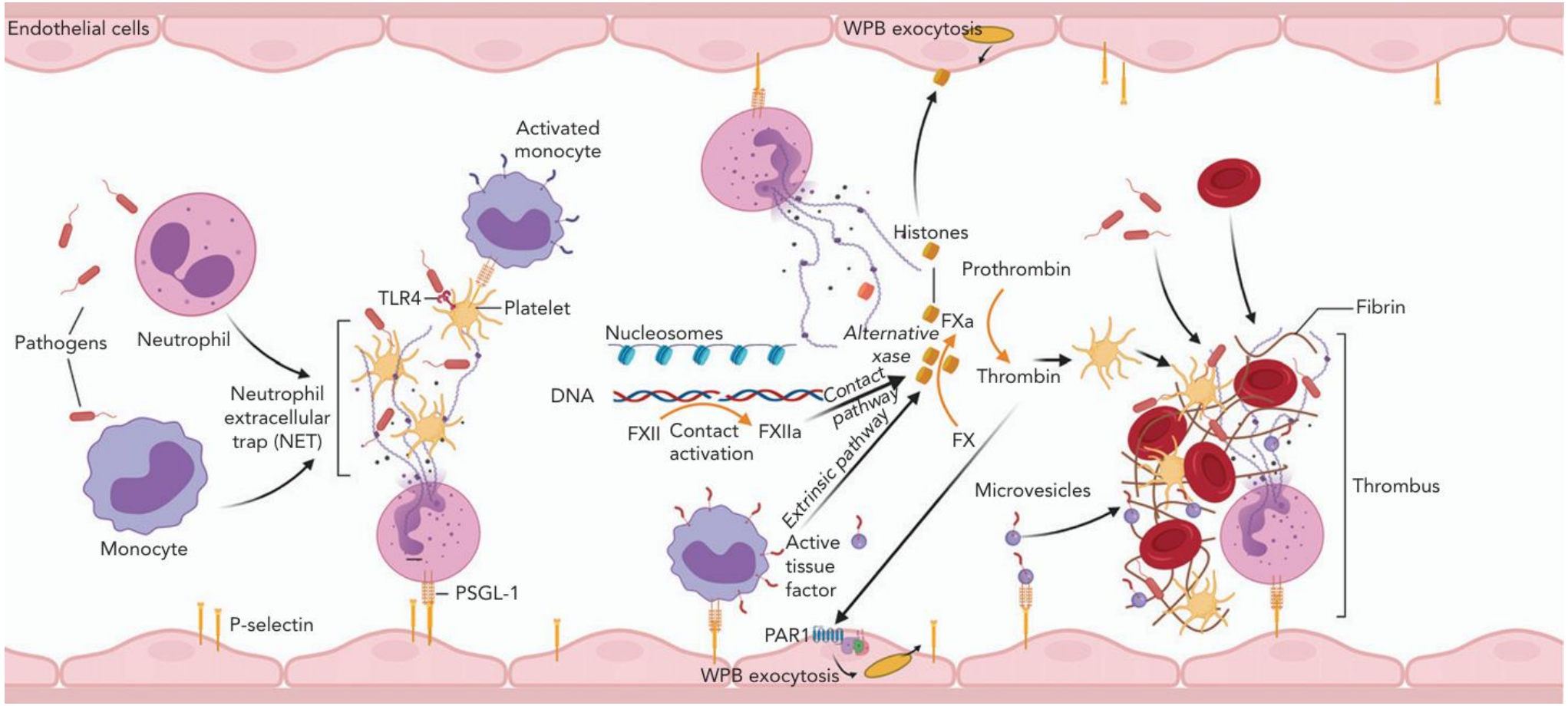
Pathophysiology of DIC



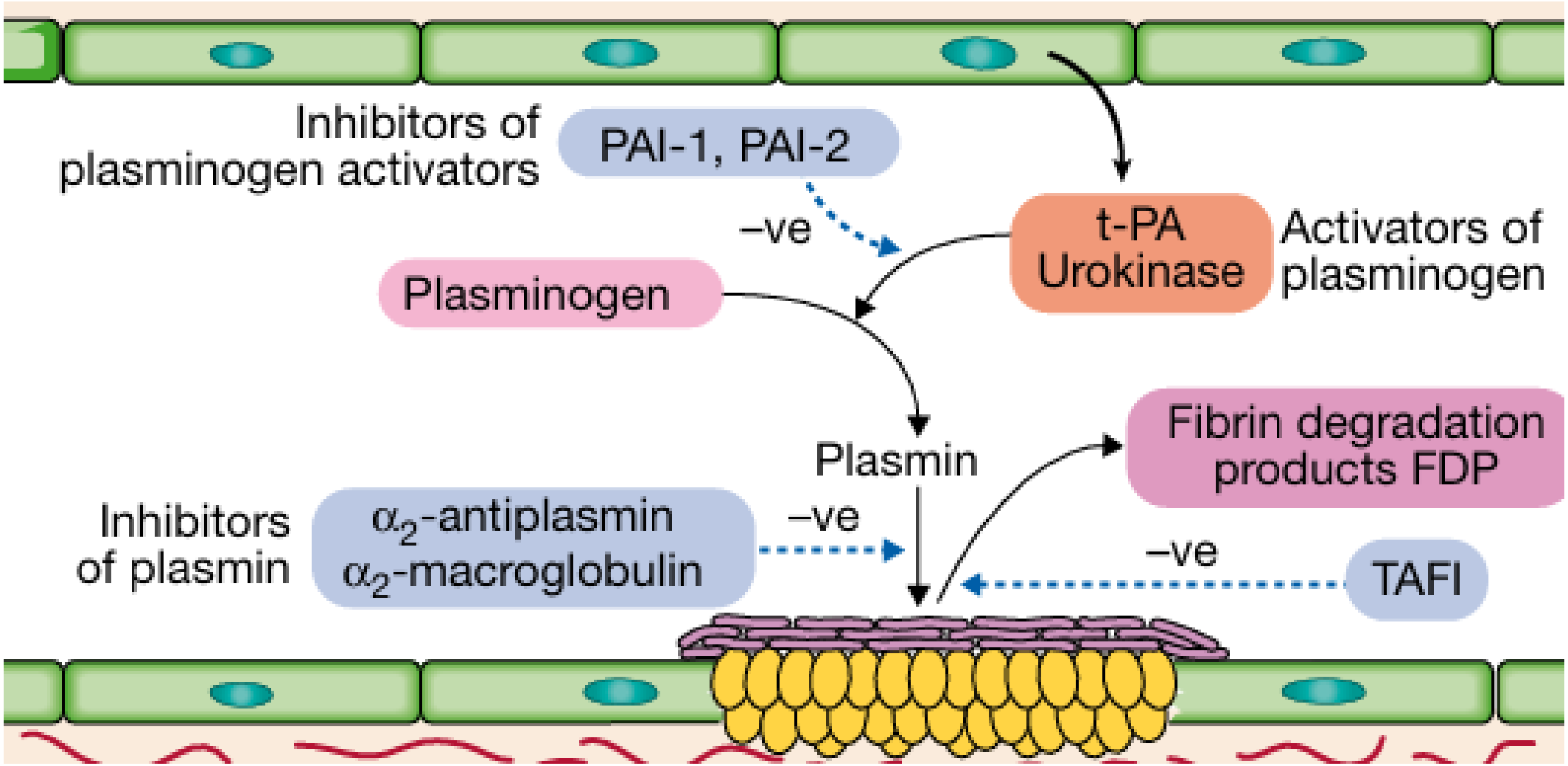
Initiation of coagulation in DIC



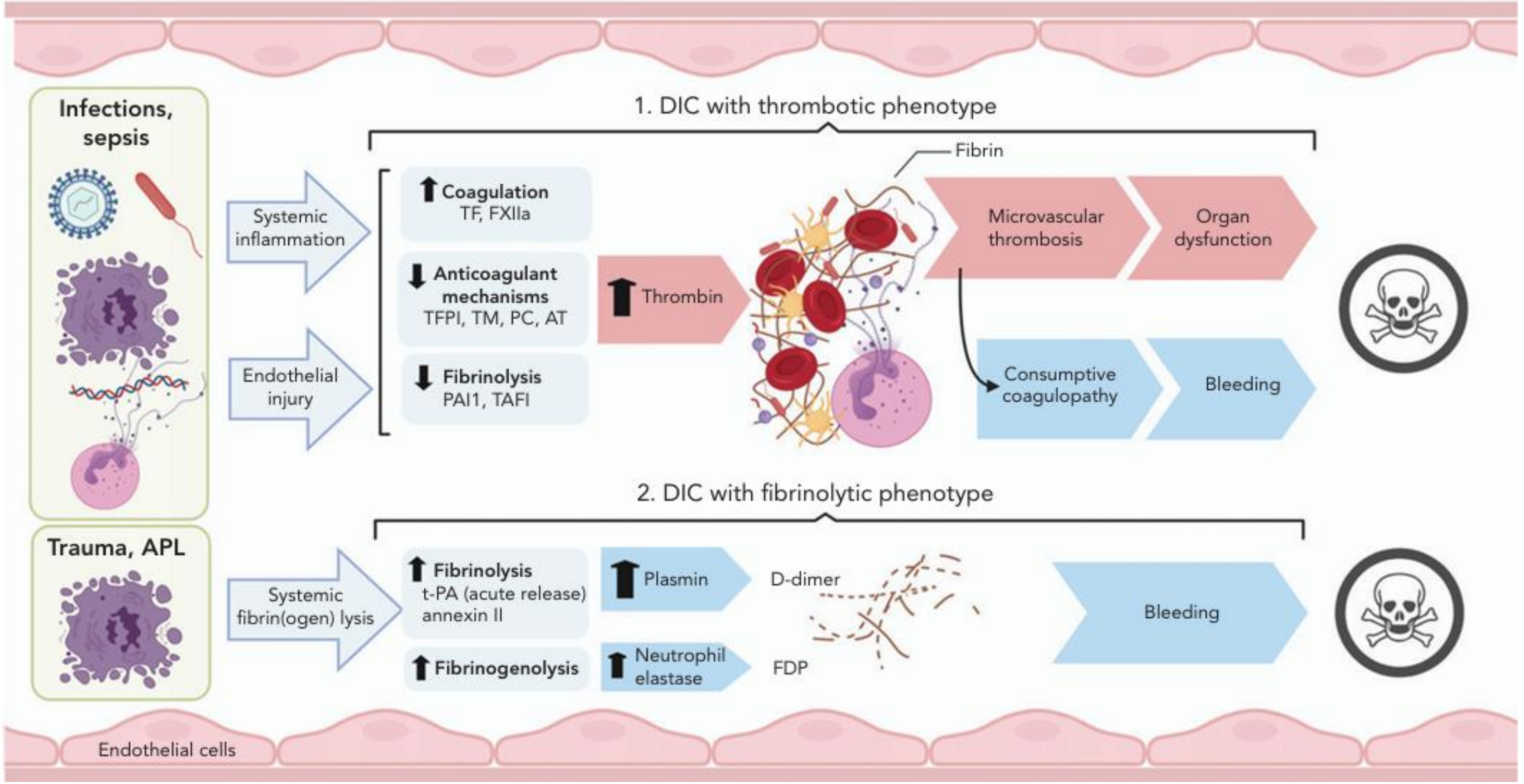
Immune mechanisms & propagation of coagulation in DIC



Fibrinolytic modulation of DIC

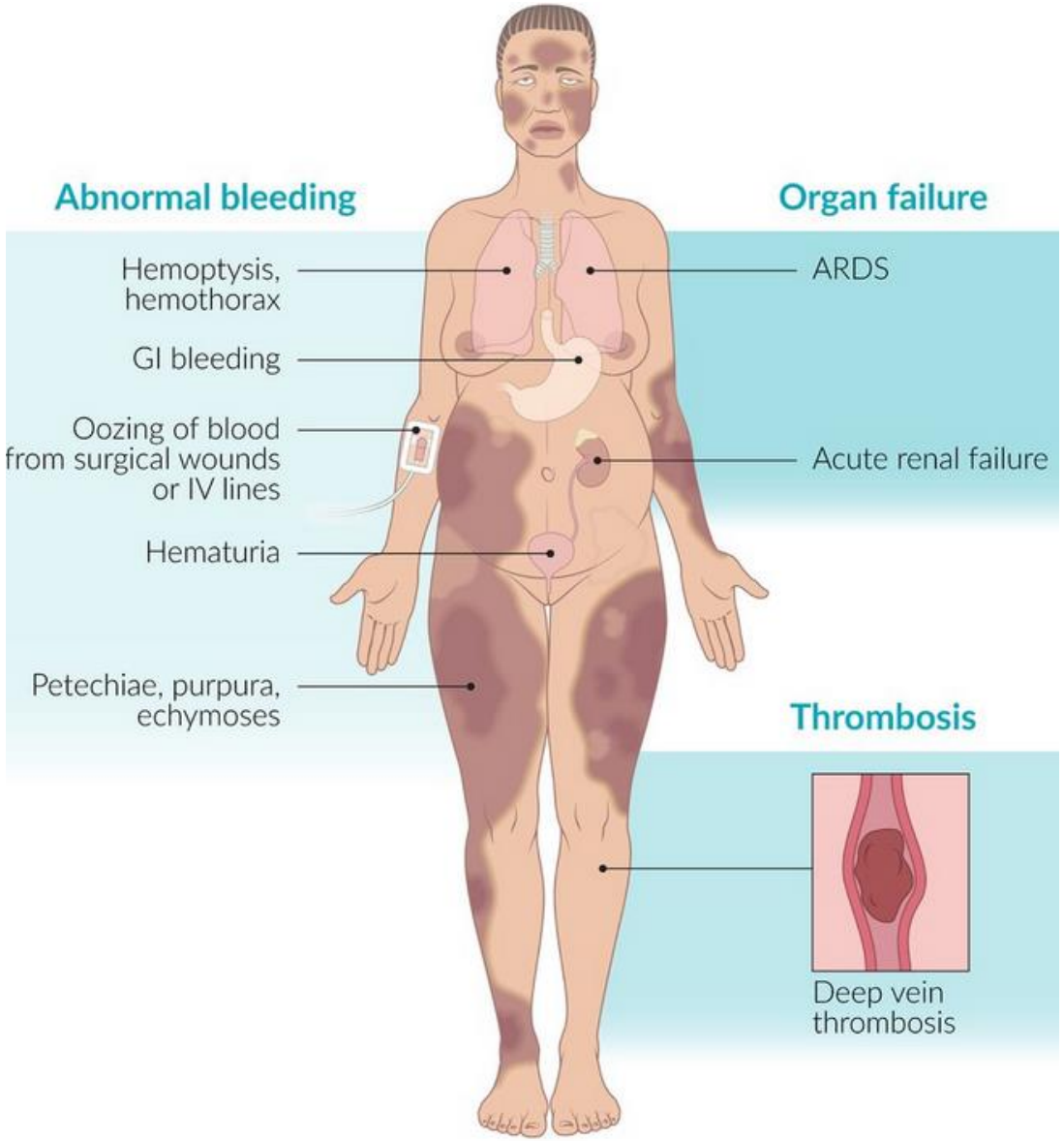


Pathogenesis of the phenotypes of DIC



Clinical presentations

- Microvascular thrombosis
  - Organ dysfunction,
  - Gangrenes
  - Acute kidney injury
  - Pulmonary & cerebral thrombosis
- Bleeding
  - Petechiae/ecchymoses
  - Necrotizing purpura
  - Vascular access sites
  - Mucosal
  - Organs e.g. adrenals & CNS
- Other features
  - Hypotension
  - Shortness of breath
  - Confusion



Investigations for DIC

- CBC
- Peripheral blood smear exam
- PT/aPTT
- **Fibrinogen**
- **D-dimers**

- Findings not highly sensitive or specific
- To be evaluated in context
- No single lab. test can accurately confirm or eliminate the diagnosis

Scoring systems for DIC

Item	Score	ISTH overt DIC Range	JAAM DIC Range	ISTH SIC Range
Platelet count ($\times 10^9$/L)	3	–	< 80 or ≧ 50% decrease within 24 h	–
	2	< 50	–	< 100
	1	≧ 50, < 100	120 >, 80 ≦ or ≧ 30% decrease within 24 h	≧ 100, < 150
FDP (D-dimer)	3	strong increase	≧ 25 μg/mL (use convert chart)	–
	2	moderate increase	–	–
	1	–	≧ 10, < 25 μg/mL (use convert chart)	–
Prothrombin time	2	≧ 6 s	–	> 1.4
	1	≧ 3 s, < 6 s	≧ 1.2 (PT ratio)	> 1.2, ≦ 1.4 (PT-INR)
Fibrinogen (g/mL)	1	< 100	–	–
SIRS score	1	–	> 3	–
SOFA score	2	–	–	≧2
	1	–	–	1
Total score for DIC or SIC		≧ 5	≧ 4	≧ 4

Total SOFA score is the sum of 4 items (respiratory SOFA, cardiovascular SOFA, hepatic SOFA, and renal SOFA)

ISTH International Society on Thrombosis and Haemostasis, *DIC* disseminated intravascular coagulation, *JAAM* Japanese Society for Acute Medicine, *SIC* sepsis-induced coagulopathy, *SIRS* systemic inflammatory response syndrome, *SOFA* Sequential Organ Failure Assessment

DIC vs other thrombotic microangiopathies

- Other TMAs generally present with thrombocytopenia and normal coagulation studies unlike DIC.
- In some cases, other TMAs are caused by clearly defined endothelial defects:
  - TTP is caused by deficiency of the ADAMTS13 protease,
  - Complement-mediated HUS
- Both DIC and other TMAs can produce microangiopathic hemolytic anemia (MAHA)

Discussion of Management…