Coagulopathy in Intensive Care

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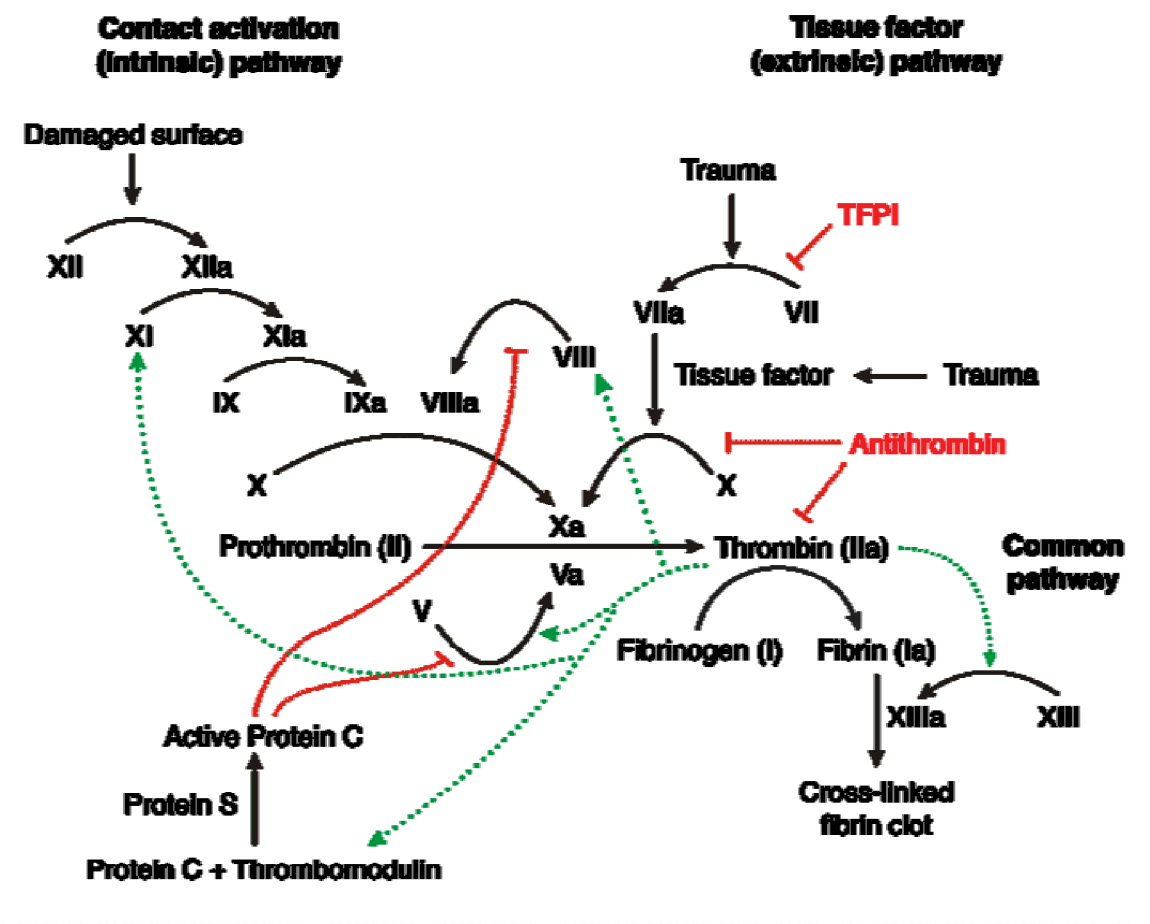
- Overview of coagulation
- Testing coagulation
- Coagulopathy in ICU
  - Incidence
  - Causes
  - Evaluation
  - Management

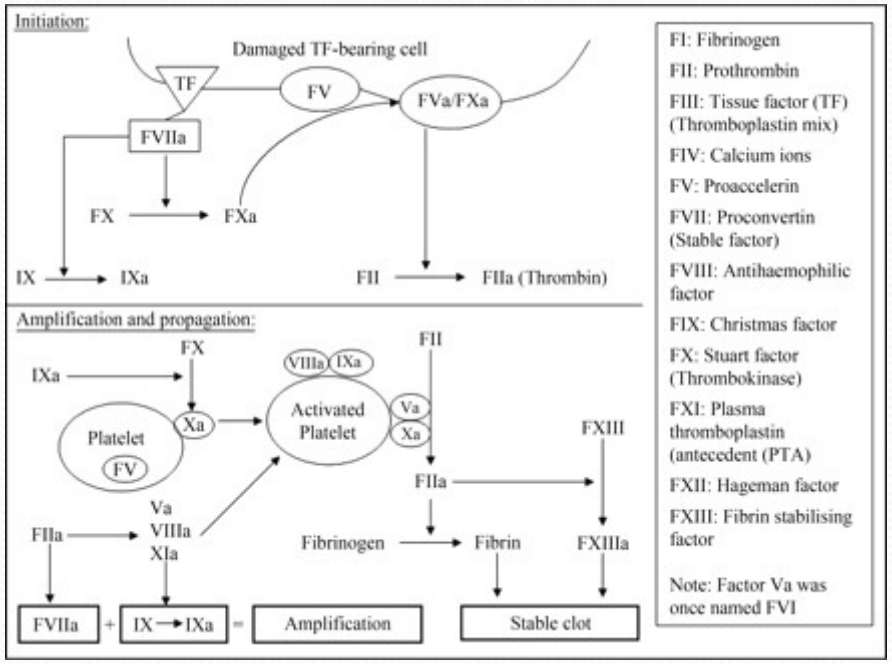
Cascade model



Cell-based model coagulation

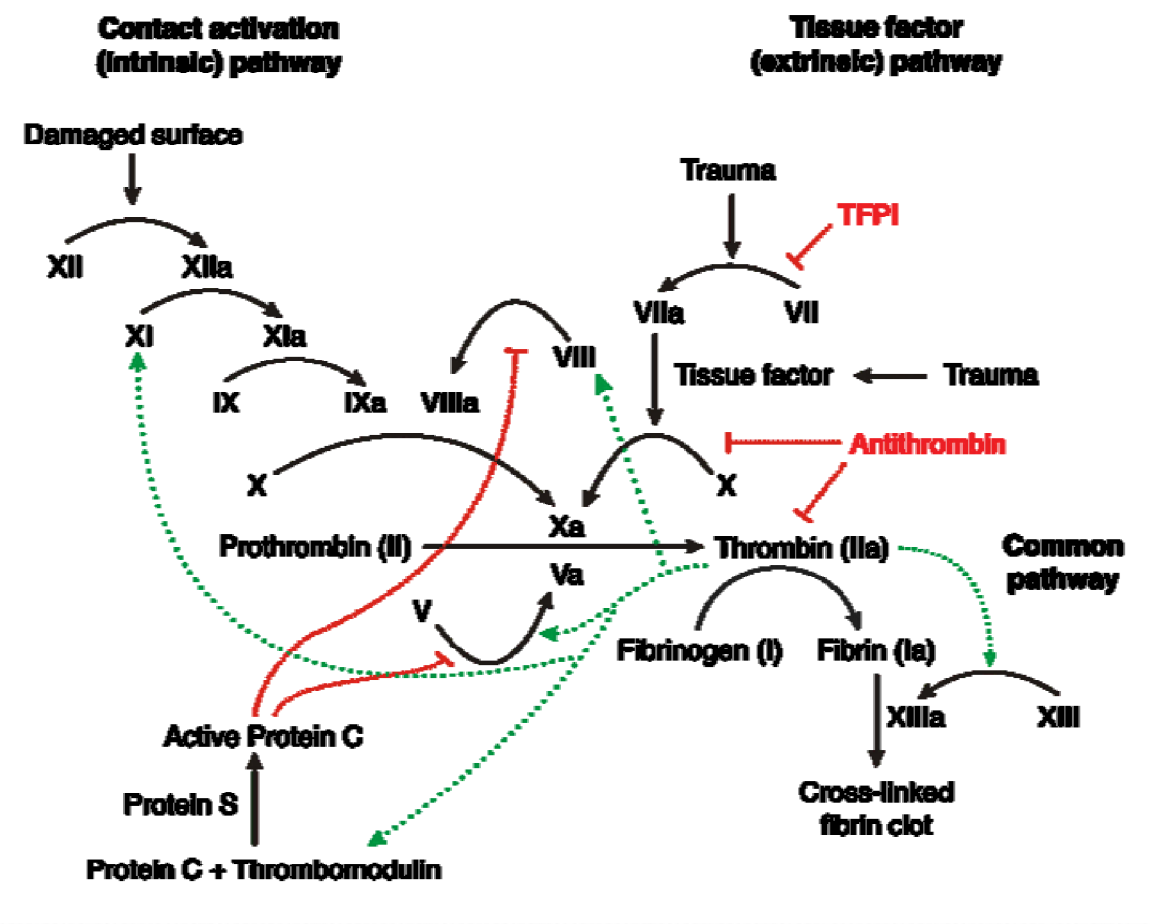
- Coagulation must be localised to site of tissue injury
- Cell injury leads to reconfiguration of cell membrane
- Procoagulant proteins moved to outside of cell
- Tissue factor binds FVIIa
- Amplification and propagation leads to formation of clot

Cell-based model



- Prothrombin time
- Activated partial thomboplastin time
- Platelet count
- Platelet function testing
- Thromboelastogram

Cascade model



Pre-test variables

Variable	Effect
Overfilled sample	Prolong PT/APTT
Underfilled sample	Prolong PT/APTT
Venepuncture •Frothing •Syringing through sample tube lids •Not flushing heparinised lines	Prolong/shorten PT/APTT
Haematocrit <20%	Prolong PT/APTT
Haematocrit >50%	Prolong PT/APTT
Raised CRP/fibrinogen	Prolong APTT
Drugs	Shorten or prolong PT/APTT
Anticoagulant in sample tube	Prolong PT/APTT

Coagulopathy in ICU

- Definition
- Incidence
- Causes
- Investigation
- Management

Definition

- When the blood is too slow (or too quick) to coagulate
- Thrombocytopenia
  - Platelet count $<150 \times 10^9/L$
- Prolonged PT or aPTT >1.5x normal

Incidence

- Common
- Thrombocytopenia
  - <150 35-44%
  - <100 20-25%
  - <50 12-15%
- Prolonged PT/aPTT
  - 14-28%

Consequences

- Increased risk of bleeding
- Thrombocytopenia
  - <50 4-5x risk of bleeding
  - Intracerebral haemorrhage
- Predictor of mortality

Thrombocytopenia

- Impaired production
- Increased consumption or destruction
- Sequestration in the spleen

Thrombocytopenia

• Sepsis	52%
• DIC	25%
• Drug-induced	10%
• Massive haemorrhage	8%
• Immune thrombocytopenia	3%
• Heparin-induced thrombocytopenia	1%
• Thrombotic microangiopathy	1%

Sepsis

- Impaired production
- Increased consumption

DIC

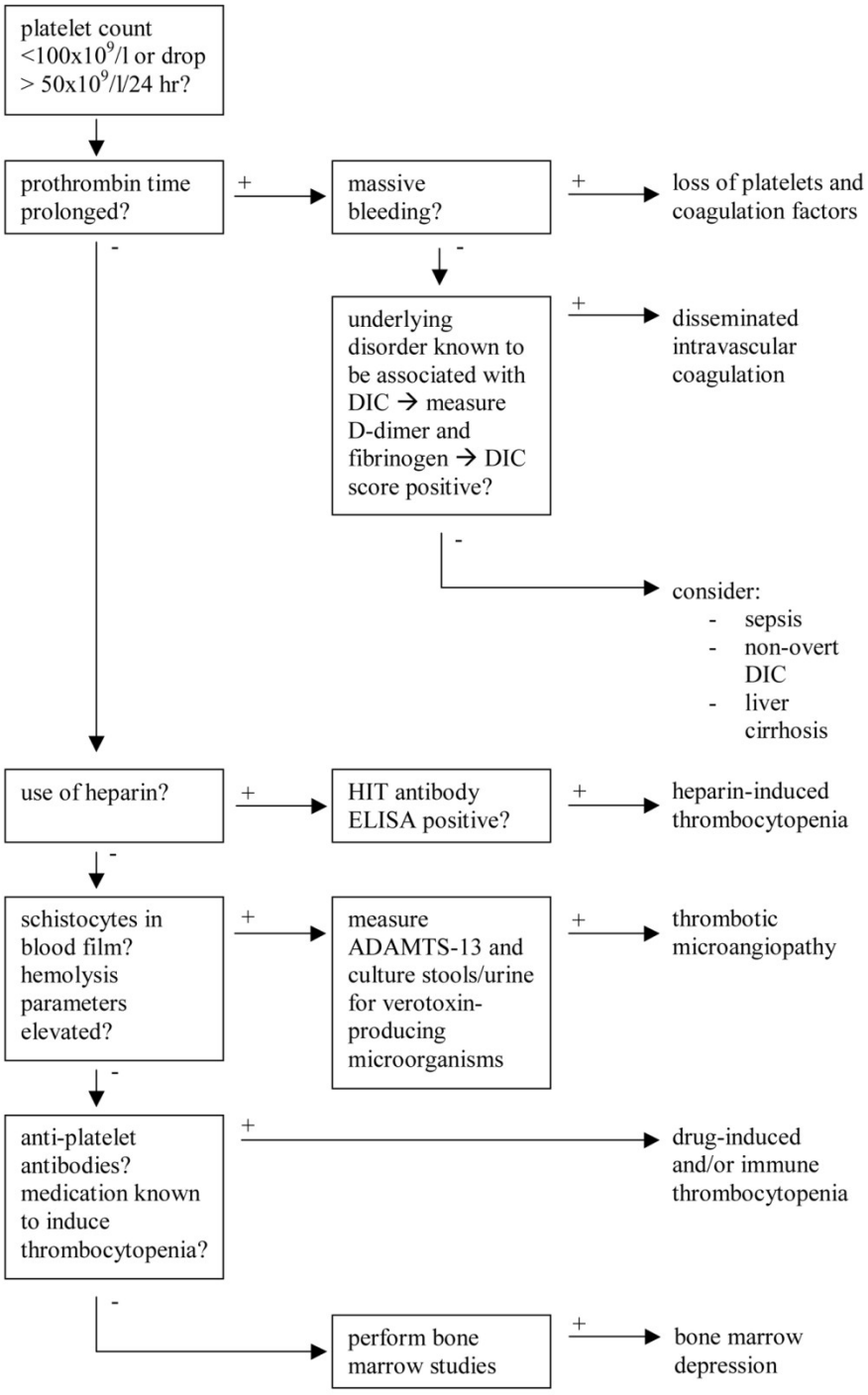
- Systemic intravascular activation of coagulation
- Causes include sepsis, trauma, malignancy
- Consumption of platelets and coagulation factors

Drug-induced thrombocytopenia

- Diagnosis based on timing of initiation of agent and thrombocytopenia
- Exclude other causes
- Can be due to marrow suppression or immune-mediated mechanisms

Heparin-induced thrombocytopenia

- Antibody binds heparin-platelet factor 4 complex on surface of platelets
- Immune-mediated platelet consumption
- Activation of platelets leads to procoagulant state


platelet count <100x10^9/l or drop > 50x10^9/l/24 hr?
prothrombin time prolonged?
+
massive bleeding?
+
loss of platelets and coagulation factors
-
-
underlying disorder known to be associated with DIC → measure D-dimer and fibrinogen → DIC score positive?
+
disseminated intravascular coagulation
-
consider:
- sepsis
- non-overt DIC
- liver cirrhosis
use of heparin?
+
HIT antibody ELISA positive?
+
heparin-induced thrombocytopenia
-
schistocytes in blood film? hemolysis parameters elevated?
+
measure ADAMTS-13 and culture stools/urine for verotoxin-producing microorganisms
+
thrombotic microangiopathy
-
anti-platelet antibodies? medication known to induce thrombocytopenia?
+
drug-induced and/or immune thrombocytopenia
-
perform bone marrow studies
+
bone marrow depression

Prolonged PT/aPTT

- These tests poorly reflect in vivo coagulation
- Mostly due to factor deficiencies
  - Impaired synthesis
  - Massive loss
  - Increased turnover (consumption)
- Inhibitor may be present

- Impaired synthesis
  - Liver impairment
  - Vitamin K deficiency
- Clotting factor loss
  - Massive haemorrhage
- Consumption
  - DIC
- Dilution

Test result	Causes
PT prolonged, aPTT normal	Factor VII deficiency Mild vitamin K deficiency Mild liver insufficiency Low dose vitamin K antagonists
PT normal, aPTT prolonged	Factor VIII, IX, XI deficiency Unfractionated heparin Inhibiting antibody ± anti-phospholipid antibody
PT and aPTT prolonged	Factor X, V, II or fibrinogen deficiency Severe vitamin K deficiency Vitamin K antagonists Global clotting factor deficiency Synthesis – liver failure Loss – massive haemorrhage Consumption – DIC

Coagulopathy with normal routine coagulation tests

- Platelet dysfunction - common
  - Uraemia
  - Liver failure
  - Drugs eg aspirin, clopidogrel
- Hyper-fibrinolysis – rare
  - Malignancy eg prostatic ca.

Management of coagulopathy

- Main focus is to treat underlying cause
- Diagnosis critically important
- Correction of defects may be required

Thrombocytopenia

- <50 if bleeding or at high risk of bleeding
- <10 regardless of presence or absence of bleeding

- Treatment should be initiated if bleeding or at high risk of bleeding and not based on laboratory abnormalities alone
- FFP
- Cryoprecipitate
- Prothrombin complex (Beriplex)
- Antifibrinolytics
- Recombinant Factor VIIa

FFP

- Single donor
- What's left after red cells removed
- 15 ml/Kg
- Usually ≈ 300ml/unit

Cryoprecipitate

- Contains Factor VIII, fibrinogen, von Willebrand factor
- Give at direction of Haematologist

Beriplex

- Factors II, VII, IX, X
- Reverses the effect of warfarin
- Dose 30 units/kg
- Supplied in 500 unit vials
- Maximum dose 3000 units

Antifibrinolytics

- Tranexamic acid
- Inhibits the production of plasmin
- Plasmin degrades fibrin
- Trauma
- Elective surgery – esp orthopaedics

Recombinant Factor VIIa

- Licensed for use in haemophilia patients with severe bleeding
- Off-label use in uncontrollable haemorrhage

Summary

- Coagulopathy is common
- Not all coagulopathy needs treating
- Cause will guide treament
- Liaison with Haematology will aid diagnosis