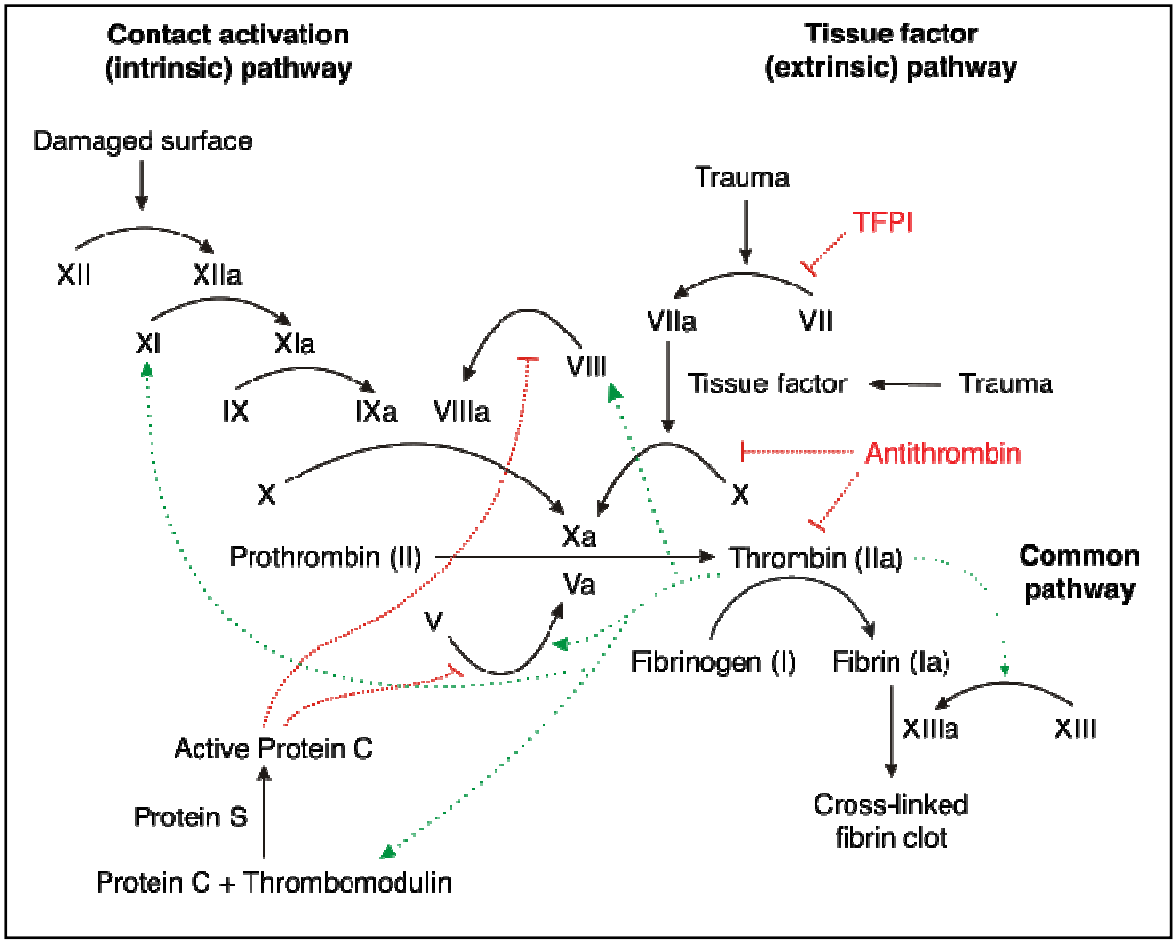
Haemostasis & Coagulation

Haemostasis

Normally, when endothelial cells lining blood vessels are breached, plts interact with vWf via the membrane glycoprotein Ib complex to help seal the breach. Glycoprotein IIb/IIIa complex attracts other plts, which form aggregates. Platelet granules release fibrinogen, vWf, platelet-derived growth factor, ADP, Ca^{2+} & 5HT. All → haemostatic plug (**primary haemostasis**). Activated platelets also synthesise TXA_2 from arachidonic acid as well as presenting negatively charged phospholipids on the outer leaflet of the platelet membrane bilayer. This provides binding sites for enzymes and cofactors of the coagulation system. The total effect is therefore to stimulate the coagulation system to form a clot (**secondary haemostasis**).

Coagulation cascade

- Converts a loose aggregation of platelets in a plug to a fibrin-bound thrombus (clot).
- Fibrin results from complex interlinked cascade of activated coagulation factors.
- Two pathways meet with factor X, but only extrinsic pathway physiologically important.



Fibrinolytic System

Plasmin (formed by thrombin and TPAacting on plasminogen) lyses fibrin/fibrinogen to FDPs. D dimers are derived from fibrin.

Anticoagulant Systems

Balance coag systems – **Endothelium PGI_2**, **Tissue Factor Pathway Inhibitor (TFPI)**, **Antithrombin** (inhibits thrombin, (VIIa), IXa, Xa, XIa & XIIa) which is augmented by heparin, **Thrombomodulin** (circulating protein that when bound to thrombin activates Protein C). **Protein C** & co-factor **Protein S** (form an anticoagulant complex that inactivates Va, IIIa and TPA inhibitor).