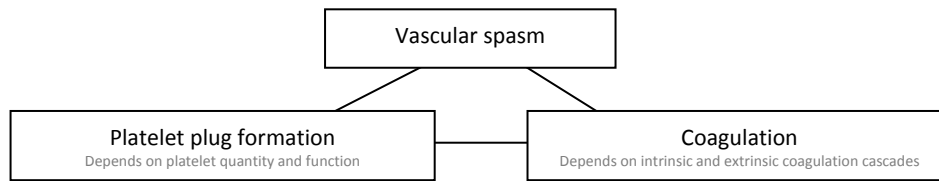
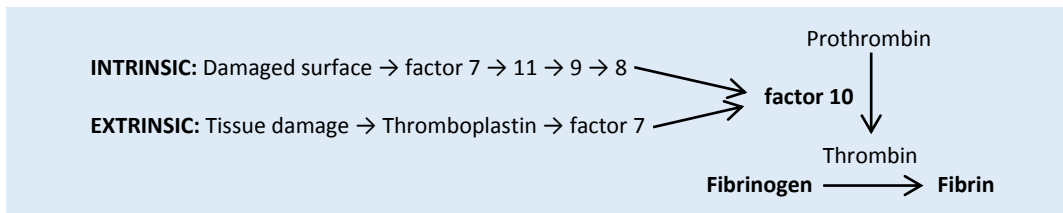


Background knowledge

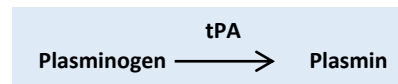
- Haemostasis process:



- Coagulation cascade:



- Clot dissolution:



- Natural anticoagulants: protein C&S, heparin, antithrombin
- Vitamin K dependant clotting factors: 2, 7, 9, 10 (+ protein C&S)
- Tests
 - PT and INR = EXTRINSIC:** thromboplastin is added to blood to activate the extrinsic pathway. Clotting time is measured in seconds (PT). This is compared to the normal value (12-13s) to get the INR for ease of comparison (normal 0.8-1.2).
*Aid to memoire: **WEPT** Warfarin Extrinsic Prothrombin Time*
 - APTT = INTRINSIC:** phospholipid, a contact activator and calcium are added to blood to activate the intrinsic pathway. Clotting time is measured in seconds (normal = 30-50s). Involves the same clotting factors as the extrinsic pathway PLUS some others (8, 9, 11)

Types of anticoagulant

	Action	Monitoring	Reversal	Common uses	Advantages	Disadvantages
Oral anticoagulants						
Vitamin K antagonist (warfarin)	Reduces the synthesis of vitamin K dependant clotting factors	INR	-Vitamin K -FFP -Prothrombin complex concentrate	-AF -VTE -Metallic heart valves	-Reversible	-Regular INRs required -Under/over coagulation -Interactions
Direct thrombin inhibitor (-tran's e.g. dabigatran)	Inhibits thrombin	None	None	-AF -VTE -Post-op VTE prophylaxis	-Quick onset/offset -No monitoring required	-Irreversible -Renally cleared
Direct factor Xa inhibitor (-xaban's e.g. rivaroxaban, apixaban)	Inhibits factor 10A (the active form of factor 10) directly	None	None	-AF -VTE -Post-op VTE prophylaxis	-Quick onset/offset -No monitoring required	-Irreversible -Renally cleared
IV and S/C anticoagulants						
Unfractionated heparin IV infusion	Natural anticoagulant that potentiates antithrombin (which inactivates factors 2, 9, 10, 11, 12) and inactivates thrombin	APTR	Stop infusion Protamine sulphate	-Peri-opertively in patients requiring full anticoagulation for a high risk indication (e.g. metallic heart valve)	-Very fast onset -Very fast reversal by stopping infusion -S/C unfractionated heparin may be used in patients with renal impairment instead of LMWH	-Continuous infusion -Regular APTRs required
Low molecular weight heparin S/C (e.g. enoxaparin)	Consists of only short chain heparins therefore only binds to a specific part of antithrombin, which results in inhibition of factor 10A only	Anti-factor 10A (if required)	Protamine sulphate	-VTE -VTE prophylaxis	-More predictable effect than unfractionated heparin therefore doesn't need routine monitoring -Safe in pregnancy	-Renally cleared
Indirect factor Xa inhibitor S/C (fondaparinux)	Synthetic anticoagulant derived from the antithrombin binding region of heparin, which results in indirect inhibition of factor 10A	Anti-factor 10A (if required)	None	-ACS -VTE -VTE prophylaxis	-Safer in ACS than LMWH -Lower risk of heparin induced thrombocytopenia	-Renally cleared -Irreversible

Warfarin reversal

Therapeutic targets

- Warfarin therapy is monitored using the INR
- Aims:
 - INR 2-3: DVT/PE, hypercoagulable states, AF
 - INR 2.5-3.5: aortic metallic heart valves (higher pressure blood flow reduced embolic risk)
 - INR 3-4: mitral metallic heart valves

Reversal guidelines

- Major bleeding → stop warfarin, prothrombin complex concentrate, 5-10mg IV vitamin K
- Non-major bleeding
 - INR >8 → stop warfarin, PLUS 0.5-2.5mg PO vitamin K if other risk factors for bleeding
 - INR 6-8 → stop warfarin
 - INR 3-6 → reduce/stop warfarin

Stop warfarin for 2-4 days to see effect

Oral vitamin K takes 24-48 hours, IV vitamin K takes 6 hours, prothrombin complex concentrate takes 15 minutes

FFP may be used instead of prothrombin complex concentrate if this is unavailable

For pre-op warfarin reversal, see [pre-op assessment](#) notes