**Anticoagulants**

**Background knowledge**

- **Haemostasis process:**
  - **Vascular spasm**
  - **Platelet plug formation**
    - Depends on platelet quantity and function
  - **Coagulation**
    - Depends on intrinsic and extrinsic coagulation cascades

- **Coagulation cascade:**
  - **INTRINSIC:** Damaged surface → factor 7 → 11 → 9 → 8
  - **EXTRINSIC:** Tissue damage → Thromboplastin → factor 7 → factor 10 → thrombin → fibrin

- **Clot dissolution:**
  - **tPA**
  - Plasminogen → Plasmin

- **Natural anticoagulants:** protein C&S, heparin, antithrombin
- **Vitamin K dependent 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 memory: **WEPT**
      - **W**arfarin
      - **E**xtrinsic
      - **P**rothrombin
      - **T**ime
  - **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**

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<th>Common uses</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<td><strong>Vitamin K antagonist</strong> (warfarin)</td>
<td>Reduces the synthesis of vitamin K dependent clotting factors</td>
<td>INR - INR adjustment</td>
<td>-AF - FFP - Prothrombin complex concentrate</td>
<td>-Reversible</td>
<td>-Regular INRs required - Under/over coagulation - Interactions</td>
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<tr>
<td>Direct thrombin inhibitor (e.g. dabigatran)</td>
<td>Inhibits thrombin</td>
<td>None</td>
<td>Praxbind</td>
<td>-Quick onset/offset - No monitoring required</td>
<td>-Irreversible - Renally cleared</td>
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<tr>
<td>Direct factor Xa inhibitor (e.g. rivaroxaban, apixaban)</td>
<td>Inhibits factor 10A (the active form of factor 10) directly</td>
<td>None</td>
<td>None</td>
<td>-Quick onset/offset - No monitoring required</td>
<td>-Irreversible - Renally cleared</td>
</tr>
<tr>
<td><strong>Unfractionated heparin IV infusion</strong></td>
<td>Natural anticoagulant that potentiates antithrombin (which inactivates factors 2, 7, 9, 10, 11, 12) and inactivates thrombin</td>
<td>APTT - Protamine sulphate</td>
<td>-Peri-operatively in patients requiring full anticoagulation for a high risk indication (e.g. metallic heart valve)</td>
<td>-Very fast onset - Very fast reversal by stopping infusion - Continuous infusion - Regular APTTs required</td>
<td>-S/C unfractinated heparin may be used in patients with renal impairment instead of LMWH</td>
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<tr>
<td><strong>Low molecular weight heparin S/C (e.g. enoxaparin)</strong></td>
<td>Consists of only short chain heparins therefore only binds to a specific part of antithrombin, which results in inhibition of factor 10A only</td>
<td>Anti-factor 10A (if required)</td>
<td>Protamine sulphate - VTE - VTE prophylaxis</td>
<td>-More predictable effect than unfractionated heparin therefore doesn’t need routine monitoring - Safe in pregnancy</td>
<td>-Renally cleared</td>
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<tr>
<td><strong>Indirect factor Xa inhibitor S/C (fondaparinux)</strong></td>
<td>Synthetic anticoagulant derived from the antithrombin binding region of heparin, which results in indirect inhibition of factor 10A</td>
<td>Anti-factor 10A (if required)</td>
<td>None</td>
<td>-ACS - VTE - VTE prophylaxis</td>
<td>-Safer in ACS than LMWH - Lower risk of heparin induced thrombocytopoena</td>
</tr>
</tbody>
</table>
**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 unavaliable*

*For pre-op warfarin reversal, see pre-op assessment notes*