Assays for other anticoagulant therapy (3)

Replacement therapy monitoring

Hirudin - desirudin (Revasc®)

A protein produced by the salivary glands of leeches.
Direct thrombin inhibitor.
Recombinant hirudins are currently commercially available.

- **Indications** (depend on drug and country)
  - Treatment of patients with heparin-induced thrombocytopenia (HIT)
  - Prevention of thromboembolic complications after orthopaedic surgery (total hip or knee replacement) in patients with a history of HIT
- **Laboratory tests**
  - **Treatment**
    - aPTT: there is a direct relationship between the aPTT prolongation and the plasma hirudin concentration, except at high concentrations.
    - Ecarin clotting time
    - Ecarin chromogenic assay (ECA): for the quantitative determination of hirudin and its analogues

  - **Prophylaxis**

    No recommendation for monitoring, except in the case of renal or hepatic failure or combined treatment with oral anticoagulants.

Danaparoid Sodium (Orgaran®)

Mixture of heparan sulphate (~ 84%), dermatane sulphate (~ 12%) and chondroitin sulphate (~ 4%). Molecular weight: approximately 5 500 Daltons.
Specific inhibitor of factor Xa.

- **Indications** (according to country)
  - Treatment of patients presenting HIT
  - Prophylaxis of post-operative deep venous thrombosis following total hip or knee replacement surgery (in patients with a previous history of HIT)
- **Laboratory tests**
  - Monitoring not necessary for prophylactic treatments, but recommended for curative treatment.
    - mild effect on time-based assays (PT and aPTT)
    - anti-Xa assays (specific protocol)

New anticoagulants monitoring

Fondaparinux (Arixtra®)

Fondaparinux, a pentasaccharide, is a synthetic and selective inhibitor of factor Xa.
The administration of this drug is simple: 1 subcutaneous injection per day at a fixed dose regardless of patient characteristics.
The half-life varies according to age and is between 17 and 21h, with a peak concentration 2 to 3h after injection

- **Indications**
  - Prevention of thrombosis in orthopaedic surgery
  - Prevention of thrombosis in high-risk abdominal surgery
  - Prevention of thromboembolic events in patients at risk and bedridden for an acute medical problem (cardiac failure, respiratory problems, etc)
  - Curative treatment of acute deep venous thrombosis
  - Curative treatment of acute pulmonary embolism

- **Therapeutic dosage**
  - Preventive treatment: 2.5 mg (or 1.5 mg for renal failure patients) / day
  - Curative treatment: 7.5 mg/day for patients weighing between 50 and 100 kg

- **Laboratory tests**

Although no monitoring is officially recommended, certain clinical situations may require a dosage:
  - Haemorrhagic or thrombotic accidents
  - Additional surgery
  - Renal failure
  - etc.

Anti-Xa activity assay with dedicated controls and calibrator for the monitoring of Fondaparinux (STA® - Fondaparinux Control and Calibrator)
  - Measuring range: 0.1 to 2 µg/mL
    - The assay measuring range covers all doses

Direct factor Xa inhibitors
Rivaroxaban (Xarelto®) - Apixaban (Eliquis®)

Rivaroxaban and apixaban are synthetic direct factor Xa inhibitors.
They have a short half-life and are almost immediately bioavailable upon oral administration.
There is currently no antidote available. It may be necessary to measure anticoagulant activity in certain patients or in certain clinical situations.

- **Indications**
  - VTE prophylaxis after total knee or hip replacement surgery
  - Atrial fibrillation
  - DVT and PE treatment (rivaroxaban)
  - Secondary prevention of VTE (rivaroxaban)
  - Acute coronary events, in combination with antiplatelet drugs

- **Specific test: rivaroxaban anti-Xa activity is assayed using specific controls and calibrators (STA®-Rivaroxaban Control & Calibrator)**
  - For specific determination of rivaroxaban anticoagulant activity:
  - Test to be performed 2 to 4 h after latest intake
  - Working range: 20 to 500 ng/mL

Direct Thrombin Inhibitors (DTIs)

DTIs (Dabigatran -Pradaxa®-, Argatroban®, Bivalirudine®, etc) are direct inhibitors of thrombin with varied therapeutic range.
They have a short half-life and practically immediate bioavailability.
DTIs have no antidotes. It may be necessary to measure anticoagulant activity for certain drugs and in certain patients.

- **Indications** (according to drug and country)
  - Treatment of patients with heparin-induced thrombocytopenia (Argatroban®, Bivalirudine®)
  - Prevention of thrombosis
  - Prevention of stroke in atrial fibrillation
  - Prevention of thromboembolic complications following orthopaedic or cardiac surgery.

- **Laboratory tests**
  - aPTT: there is a direct relationship between the aPTT prolongation and the DTIs concentration in plasma, however:
    - This test is greatly affected by different variables (presence of lupus anticoagulants, factor deficiencies, etc) and concomitant treatments (vitamin K antagonists, heparin, etc)
    - The measuring range is unsuitable for DTIs
    - There is poor linearity with high doses of DTIs
  - Ecarin clotting time (ECT): this is considered as the reference test, but:
    - It is dependent on the patient's thrombin and fibrinogen levels.
    - There is no standardisation
  - Ecarin chromogenic assay (ECA): is a specific and quantitative assay of DTIs levels