ANTICOAGULANTS

WARFARIN:

DELIBERATE SELF-POISONINGS ARE USUALLY ASYMPTOMATIC AT PRESENTATION

THE APPROACH TO THERAPY IS DETERMINED BY BOTH THE MAGNITUDE OF OVER-ANTICOAGULATION AND THE INDICATION FOR TREATMENT, IN ADDITION TO THE PRESENCE OR ABSENCE OF BLEEDING

RISK ASSESSMENT:

- The risk of bleeding increases progressively as the INR rises above 5
- In patients not on therapeutic warfarin who overdose:
    - Acute ingestion <0.5mg/kg unlikely to cause a clinically significant increase in INR
    - Acute ingestion >2mg/kg can produce a significant increase in INR within 72 hours

TOXIC MECHANISM:

- Warfarin inhibits vitamin K metabolism, leading to depletion of the active reduced form, which is required as a cofactor for the synthesis of clotting factors II, VII, IX, X as well as the anticoagulant factors proteins C and S
- Peak effects by 72 hours
- Toxicity renders patients coagulopathic and vulnerable to haemorrhage

TOXICOKINETICS:

- Rapidly and completely absorbed, 100% bioavailability
- 99% protein bound and small volume of distribution, 35 hour half life

CLINICAL FEATURES:

- Over-anticoagulated patients are usually asymptomatic
- Severe coagulopathy usually manifests as bruising, petechial or purpural rashes, bleeding

INVESTIGATIONS:

- INR → in the patient hat is not previously anticoagulated, the INR is normal for the first 6 hours and a normal INR at 48 hours excludes warfarin overdose
    - In the patient with excessive anticoagulation, but a therapeutic requirement, the INR is measured at presentation and at six hourly intervals thereafter

MANAGEMENT:

- Resuscitate along standard lines
- If there is active, uncontrolled haemorrhage, administer prothrombin complex concentrate (25-50 units/kg), FFP 10-15mL/kg (if PCC unavailable) and vitamin K 10mg IV
- Give charcoal if presents within 1 hour of ingestion/deliberate self-poisoning

- ANTIDOTES:
    - Vitamin K is administered PROPHYLACTICALLY (10-20mg)to patients who have ingested a potentially anticoagulating dose but have no therapeutic requirement → check INR at 48 hours as an outpatient
    - In patients with therapeutic requirement for anticoagulation, the dose of vitamin K is titrated in an effort to maintain an INR in the optimal range
    - High doses of vitamin K overcome impairement of vitamin K epoxide reductase and restores normal levels of clotting factors

ANTICOAGULANT RODENTICIDES:

AKA SUPERWARFARINS → VERY LONG-ACTING

MASSIVE OR REPEATED DOSING LEADS TO PROFOUND AND PROLONGED ANTICOAGULATION → WEEKS TO MONTHS

RISK ASSESSMENT:

- 0.1mg/kg of BRODIFACOUM will cause anticoagulation, but this equates to 2g/kg of standard bait (or 3 50g packets for a 75kg adult)
- Anticoagulation is usually associated with repeated ingestion → anticipate weeks of anticoagulation requiring massive doses of vitamin K

TOXIC MECHANISM:

- Works in similar way to warfarin, but several mechanism confer increased potency and duration of action → hepatic accumulation, greater affinity for enzyme, disruption of enzymatic activity at several sites

CLINICAL FEATURES:

- Coagulopathy usually delayed 72-96 hours
- Manifests as bleeding diathesis

INVESTIGATIONS:

- Serial INR 12 hourly for 48 hours to rule out toxicity → withhold vitamin K until anticoagulation is documented. Normal INR at 48 hours excludes toxic ingestion

MANAGEMENT:

- If there is active, uncontrolled haemorrhage → administer prothrombinex, FFP if PCC not available) and vitamin K 10mg IV
- Very large daily doses of vitamin K (titrated to INR of <4) needed for weeks or months → DO NOT GIVE PROPHYLACTIC VITAMIN K