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Title:	Anticoagulation: Warfarin Reversal Guidelines
Author:	Dr Bridgham
Speciality / Division:	Haematology
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Warfarin Reversal in Cases of Over-anticoagulation or in Preparation for Emergency Procedure

- **Once appropriate treatment is underway (see below), determine the reason for over anticoagulation, e.g., interacting medicine, alcohol, incorrect dose of warfarin taken.** Examine patient's own warfarin medication packs to ascertain exactly what dose has been taken and exclude overdose. If the patient does not present with their own warfarin medication packs, all reasonable attempts should be made to inspect these as soon as possible, including out of hours, by contacting for example, next of kin, other relatives, nursing home to obtain the medication packs. Medical and nursing staff will need to obtain and examine these packs when pharmacy staff is not available. If an overdose has occurred, the extent of the overdose may significantly alter the degree of reversal treatment. If there has been a substantial overdose, discuss with the Consultant Haematologist on call.

- **Consider <u>embolic risk</u> of indication for anticoagulation prior to reversal.**

1. **Major haemorrhage or strong clinical suspicion of major haemorrhage, e.g.**
   Intracranial, peritoneal, intraocular (not conjunctival), muscle bleed and compartment syndrome, pericardial, active bleeding with hypotension or 2g/dl fall in Hb.

   - Urgent INR; it is not necessary to wait for result if bleeding is life threatening (e.g. intracerebral). Treatment plan can be amended when result is available
   - Urgent radiology. In patients with rapid onset of neurological signs and INR > 4.5, consider reversal with Prothrombin Complex Concentrate (PCC) (see below) without waiting for CT scan. NB. Ensure CT scan is reported and acted on immediately
   - Stop warfarin
   - Give:
     - phytomenadione (vitamin K_1) 5mg by slow intravenous bolus injection (dilute dose in 20ml glucose 5% and give over 3-5 minutes), and
     - PCC, e.g. Octaplex®, Beriplex®

Octaplex®	30 units/kg if INR >4: approx. 70 kg person, 2000 units (4vials)
	15 units/kg if INR <4: approx. 70 Kg person, 1000 units (2vials)

Request appropriate number of 500unit vials from blood bank or if patient is in ED, use the supply kept in 'Resus' in a red labcold blood box. (To track use of the product and replenish the supply, it is essential that the documents provided in the box are completed fully and returned to blood bank.)

Reconstitute each vial with the diluent provided. Administer initially at 1ml per minute increasing slowly so total dose is given slowly by IV bolus over 5 minutes (experience shows that it is safe to give faster than SPC indicates). Monitor pulse as you give injection and if a marked increase in the pulse rate occurs the infusion speed must be reduced or the administration must be interrupted.

- Involve senior medical staff (ST3 Grade and above) in decision making.
- Check INR and APTT immediately post infusion and in 4-6 hours. If INR >1.5, discuss with Haematologist.
- PCC may induce a prothrombotic state; use with caution in patients with disseminated intravascular coagulation, decompensated liver disease and thrombosis. If possible, delay surgery (see below) and thereby avoid use of PCC for emergency procedure. PCC must not be used to facilitate elective procedures.

2. **Emergency surgery that cannot be delayed for 6 to 12 hours.**

- Urgent INR
- Stop warfarin
- Give:
    - phytomenadione (vitamin K_1) 5mg by slow intravenous bolus injection (dilute dose in 20ml glucose 5% and give over 3-5 minutes), and
    - PCC, e.g. Octaplex®, Beriplex®

Octaplex® 30 units/kg if INR >4: approx. 70 kg person, 2000 units (4vials)
15 units/kg if INR <4: approx. 70 Kg person, 1000 units (2vials)

- Recheck INR at least 1 hour before procedure, aiming for an INR < or = 1.4

3. **Emergency procedure that <u>can be delayed for at least 6 hours</u>, preferably longer and will take place within 24 hours.**

- Give:
    - phytomenadione (vitamin k_1) by slow intravenous injection (dilute dose in 20ml glucose 5% and give over 3 -5 minutes):

If INR <4, give phytomenadione (vitamin k_1) 3mg
If INR >4, give phytomenadione (vitamin k_1) 5mg

- Recheck INR at least 1 hour before procedure, aiming for an INR < or = 1.4
- Intravenous phytomenadione (vitamin k_1) has maximum effect at 6 hours after injection.

4. **Minor Bleeding, INR >8**

- Stop warfarin
- Give phytomenadione (vitamin K_1) 1-3mg by slow intravenous injection or 5mg if complete reversal required
- Check INR in 24 hours or sooner if clinical deterioration
- Repeat dose if INR still too high after 24 hours
- Restart warfarin when INR <5

5. **Minor bleeding, INR 5-8**

- Stop warfarin
- Give phytomenadione (vitamin K_1) 1-3mg by slow intravenous injection. Check INR in 24 hours or sooner if clinical deterioration. Restart warfarin when INR <5

6. **No bleeding, INR >8**

- Stop warfarin
- Give phytomenadione (vitamin K_1) 1-5mg by mouth*; dose depends on patient's bleeding and embolic risks
- Check INR in 24 hours or sooner if clinical deterioration
- Repeat dose if INR still too high after 24 hours
- Restart warfarin when INR <5

7. **No bleeding, INR 5-8**

- If the patient has a low / moderate risk of bleeding:
  - stop warfarin for two days and recheck INR or reduce warfarin dose from day 3 and recheck as soon as possible
- If the patient is at high risk of bleeding:
  - stop warfarin and give phytomenadione (vitamin K_1) 1mg by mouth* and check INR in 24 hours. Restart warfarin when INR <5

8. **Bleeding with therapeutic or sub-therapeutic INR or INR <5:**

- Investigate possible underlying causes
- If major bleeding, treat as above
- If minor bleeding, consider stopping warfarin and giving phytomenadione (vitamin K_1)

*NB: The most effective oral preparation of phytomenadione (vitamin K_1) is Konakion MM® Paediatric Injection 2mg/0.2ml given orally. Draw up the appropriate amount in the oral syringe provided with the preparation and then dilute in juice/water to drink.
After IV phytomenadione, INR will show maximum response at 6 hours.

References:

1. BMJ Group and Pharmaceutical Press. British National Formulary No 69 (September 2015), Section 2.8.2.
2. Burbury KI et al. Short-term warfarin reversal for elective surgery - using low dose intravenous vitamin k: safe, reliable and convenient. BJH 2011; 154: 626-634.
3. Keeling D et al. Guidelines on oral anticoagulation with warfarin - fourth edition. BJH 2011; 154: 311-324.

Prepared by Dr H K Boyd and Mrs Sinead Doyle: October 2010
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