Management of Over Anticoagulation with Warfarin

**General Principles**
- The risk of bleeding increases markedly when the INR is >4.5
- What follows is guidance only. The management of over-anticoagulation may vary from patient to patient depending on factors such as:
  - The presence or absence of bleeding
  - Risk factors for bleeding
  - The value of the INR
  - The indication for anticoagulation and the risk of thromboembolic disease
- Intracranial bleeding and significant gastrointestinal bleeding while on anticoagulants are potentially life-threatening.
- An attempt should be made to establish a cause for each episode of over-anticoagulation.

**Products used for reversal of warfarinisation**

**Vitamin K**
Oral or intravenous administration of vitamin K will reverse the effect of warfarin, but takes several hours to do so. Doses up to 2 mg do not prevent re-anticoagulation with warfarin. Doses in excess of 2 mg may make re-warfarinisation difficult. The effect of a given dose of vitamin K is unpredictable, and the INR should always be rechecked the following day.

**Intravenous vitamin K** may be given in 50-100 mls 5% dextrose over 15-30 minutes. There is a small risk of allergic reaction.

**Oral vitamin K:** the intravenous preparation may be given orally – this has been shown to be efficacious in lowering the INR. However, administering vitamin K in the way is **unlicensed** although it is widely practised.

**Prothrombin complex concentrate (DEFIX)**
This contains factors II, IX and X. It is presented as a powder which requires reconstitution with diluent solution. It is plasma derived and virally inactivated. It is virologically safer than fresh frozen plasma, but cannot be considered 100% free of risk of transmission of viral infection. The standard dose for reversal of warfarin is 50 iu/kg, but this may be tailored depending on the INR. As it lacks factor VII, correction of anticoagulation may not be full. Ease of administration, the small volume needed and viral inactivation make it often the preferred product for rapid reversal of warfarinisation. However, it is potentially pro-thrombotic and is probably best avoided in severe liver disease, unstable ischaemic heart disease and severe DIC. It should usually be given along with vitamin K.

**Fresh Frozen Plasma (FFP)**
FFP will result in rapid lowering of the INR. The standard dose is 15 ml/kg. Full reversal of anticoagulation is more difficult to achieve with FFP than with prothrombin complex concentrate (see above). FFP is not virally inactivated. It takes 20-30 minute for the plasma to be thawed ready for use. It should usually be given along with vitamin K.
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INR < 8.0 with no bleeding or minor bleeding
- It is often adequate to discontinue warfarin and restart this when INR < 5.0. The INR should be rechecked daily (and clear arrangements made with the patient for this if the patient is not admitted).
- Reversal of warfarin may be considered if there are significant risk factors for bleeding or if the INR remains > 5.0 despite discontinuation of warfarin. Under these circumstances, vitamin K 0.5 mg iv or orally may be appropriate.

INR > 8.0 with no bleeding or minor bleeding
- Consideration should be given to reversal of warfarin, especially in patients who have risk factors for bleeding such as:
  - Advanced age (>70)
  - Previous bleeding complications
  - Recent surgery (< 4 weeks)
  - Recent haemorrhagic CVA (< 3 months)
  - Poorly controlled hypertension
- A dose of vitamin K between 0.5 and 2 mg iv or oral should be considered, with reassessment of the INR the following day (or sooner if indicated).

Major bleeding
- A major bleed in a warfarinised patient, regardless of the INR, is an indication for urgent reversal of warfarinisation. Although the risks of this must be considered for each individual, in the context of major bleeding, the risk of not reversing the warfarin will usually be greater. GI bleeding, intracranial bleeding or limb-threatening bleeding in particular all call for urgent action.
- If there is a strong suspicion of intracranial bleeding in a warfarinised patient (eg coma, reduced conscious level, focal neurological signs, severe headache) it may be appropriate to reverse warfarin before undertaking definitive investigation – this should be discussed urgently with the consultant responsible for the patient.
- The patient should receive DEFIX 50 iu/kg or FFP 15 ml/kg plus intravenous vitamin K. In this situation a dose of 5 mg is often appropriate, but 2 mg may be given if there is a strong indication to continue anticoagulation in the relatively short term (eg mechanical valve prosthesis). The potential risk of inadequate reversal must be balanced against the possibility of thromboembolic disease.
- Note: major bleeding in a warfarinised patient should normally be discussed with the consultant responsible for that patient (or the on-call consultant at night or weekend). DEFIX and FFP will be issued only after discussion with the on-call haematology consultant (bleep 281 during the day; via switchboard at night or weekend). Haematology medical staff will be happy to advise about overanticoagulation at any time.