Overview of anticoagulants
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Historically anticoagulation involved the use of heparin and its derivatives or warfarin. However, the past few years have seen the introduction of a number of novel direct oral anticoagulants. These drugs are of interest as they require no laboratory monitoring, are relatively easy to use as they have a fixed dose and have demonstrated equivalence and in some cases superiority to warfarin, in the prevention of cardioembolic stroke in individuals with non-valvular atrial fibrillation, in deep vein thrombosis (DVT) prevention in patients undergoing hip and knee replacement surgery and in the treatment of DVT and pulmonary embolism (PE).

This chapter provides an overview of the currently available anticoagulant drugs, their licensed indications, their effects upon the standard laboratory tests and in addition provides guidelines on the management of patients undergoing invasive procedures.

Warfarin
Warfarin is a vitamin K antagonist [VKA] that inhibits γ-carboxylation of Factors II, VII, IX, and X [+ Proteins C, S and Z]. Warfarin has a half-life of 35–45 hours. The other common vitamin K antagonists (VKAs) include:

- Acenocoumarol with a half-life of 8–24 hours; and
- Phenprocoumon with a half-life of 5–6 days.
- Tecarfarin is a novel oral VKA that has been engineered so that it is not metabolized through the Cytochrome P450 [CYP]
pathway. Tecarfarin is metabolized by esterases (mainly human carboxylesterase 2) to a single major metabolite, in rats, dogs, and humans. Tecarfarin is not significantly metabolized by CYP450 enzymes and for these reasons it has a decreased potential to interact with drugs that inhibit CYP450 enzymes. This drug may be of value for the treatment of patients with mechanical and prosthetic heart valves, as well as those with renal dysfunction.

- Phenindione is an inandione derivative but is now rarely used due to a high incidence of adverse events including skin rashes and abnormal liver function tests. Phenindione has a half-life of 5–10 hours.

The use of VKAs is complicated by a narrow therapeutic index and an unpredictable dose-response relationship, giving rise to bleeding complications or insufficient anticoagulation. The inter-individual variability observed with an individual’s response to a VKA is in part due to the genetic variability arising from mutations in the \textit{CYP2C9} and \textit{VKORC1} genes. Mutations in \textit{CYP2C9} have been linked to decreasing activity in metabolising VKA leading to a prolonged half-life and over-anticoagulation [1]. Conversely, mutations in the \textit{VKORC1} gene have been linked to a decrease in requirements for warfarin [1]. An algorithm has been proposed to prevent over- or under-anticoagulation taking into account these two genes [2].

The \textit{VKORC1} gene encodes the VKORC1 enzyme – a small transmembrane unit of the endoplasmic reticulum – and is primarily transcribed in the liver. Various polymorphisms and mutations within the \textit{VKORC1} gene have been reported. The polymorphisms are associated with a reduction in the levels of VKORC1 and therefore a reduction in the amounts of warfarin that an individual requires to achieve a stable international normalized ratio (INR). Mutations within the \textit{VKORC1} gene have been associated with a reduction in the levels of all the vitamin K-dependent clotting factors and are a rare cause of an inherited bleeding disorder [3].

**Heparin**

Several forms of heparin are available for therapeutic use.