Anticoagulant therapy monitoring (1)

Oral anticoagulant therapy with vitamin K antagonists (VKA*)

● **Vitamin K antagonists** reduce synthesis of both vitamin K-dependent coagulation factors (factors II, VII, IX, X) and some proteins (Protein C and Protein S). The deficiency in factors II, VII, IX and X induced by the absorption of vitamin K antagonists results in prolongation of PT and of aPTT.

● **The Prothrombin Time** is the reference test of choice for monitoring of vitamin K antagonist therapy. It is expressed as a coagulation time, using the ratio between the patient and a control, or as % prothrombin time, leading to wide inter-laboratory result variability due to the use of different analysers/reagents combination.
In order to standardise the results obtained for patients on vitamin K antagonists, results are expressed as INR.

● **PT results expressed as INR (International Normalized Ratio)**

■ The INR is the ratio of PT to the power ISI (International Sensitivity Index).
It represents the ratio of PT that would have been obtained if an international thromboplastin reference material had been used for the test.

■ The ISI is a value calculated for each batch of thromboplastin reagent and varies according to the type of analyser used. ISI values are specific for pairs of reagents and instruments. The international recommendations suggest the use of a reagent with an ISI value of less than 1.7.

■ The control time is the geometric mean of PT values measured on at least 20 fresh plasma samples from healthy subjects (with no pathology or treatment that might interfere with coagulation).

$$INR = \left(\frac{\text{Patient Time (sec)}}{\text{Control Time (sec)}} \right)^{ISI}$$

● **Anticoagulant therapy monitoring**

■ Heparin followed by vitamin K antagonists

- Monitoring of treatment with vitamin K antagonists with the INR (using a reagent insensitive to heparin at therapeutic doses)
- Monitoring of heparin treatment
  - aPTT (indicates the combined effect of vitamin K antagonists and unfractionated heparin)
  - Specific anti-Xa assay (specific monitoring of anti-Xa activity)
- Treatment with heparin and vitamin K antagonists may be given concomitantly for 4 to 5 days until the desired therapeutic range is achieved in terms of INR (i.e. two consecutive INR of two consecutive days unchanged and in the therapeutic range).

■ Stable patients on vitamin K antagonists treatment
The INR value should be checked weekly then monthly, and more frequently in the event of a dose change, unbalanced assay results or suspected interference by other factors.

- **N.B.:**
  - Wide inter-patient variability
  - Interferences due to:
    - Other treatments (many drugs can interfere with vitamin K antagonists)
    - Other diseases
    - Food and drinks rich in vitamin K

- **Recommended therapeutic ranges (expressed in INR)**

INDICATION	INR	
	ACCP[1], BCSH[2], GEHT[3]	
	Range	Target
Prophylaxis of venous thrombosis.	2.0 - 3.0	2.5
Treatment for deep venous thrombosis (DVT) and pulmonary embolism (EP). Cardiac valve disease. Myocardial infarction. Atrial fibrillation.	2.0 - 3.0	2.5
Antiphospholipid syndrome associated with recurrent DVT or additionnal risk factors.	2.5 - 3.5	3.5

[1] ACCP: American College of Chest Physicians
[2] BCSH: British Committee for Standards in Haematology
[3] GEHT: Groupe d'Etude sur l'Hémostase et la Thrombose

*Antivitamins K or vitamin K antagonists

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