

# ANTI-FACTOR Xa ASSAY

Compiled by Dr R Singh

4<sup>th</sup> Quarter 2017

Anticoagulants prevent blood from clotting through a variety of mechanisms, including activation of anti-clotting factors and direct inhibition of thrombin (see Figure 1).

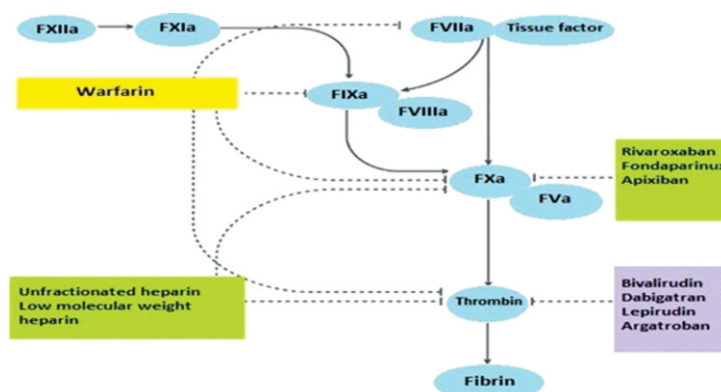


Figure 1. Mechanisms of action of anticoagulants

## Assay principle

The anti-factor Xa assay is designed to measure the concentration of anticoagulants that inhibit factor Xa as a means of monitoring anticoagulant therapy. These anticoagulants include:

- Low molecular weight heparin (LMWH)
- Unfractionated heparin (UFH)
- Fondaparinux
- Rivaroxaban (Xarelto®)

The most commonly used methodology is the chromogenic assay, which uses a chromophore-linked synthetic substrate of factor Xa. Endogenous factor Xa that is not complexed with anticoagulant molecules will be able to cleave the chromophore from the substrate, resulting in a colour change. If the patient is taking one of the anticoagulants mentioned above, there will be less factor Xa available to cleave the chromophore, and less colour change. Thus the strength of the colour change is inversely proportional to the concentration of anticoagulant in the blood sample. An appropriate standard curve, using known amounts of the specific anticoagulant, is used to convert the colour reading into drug concentration. Therefore the laboratory needs to know the specific anticoagulant being monitored.

## Indications for anti-factor Xa testing

Many newer anticoagulants have been designed to require no or less frequent monitoring, and therefore anti-factor Xa (Anti-FXa) testing is not routinely used for monitoring of these anticoagulants. Anti-FXa testing may be indicated in certain specialised clinical situations:

### UFH

- aPTT is used preferentially to measure the response to UFH
- Anti-FXa testing should be used where aPTT is prolonged by factors unrelated to UFH therapy e.g. lupus anticoagulant, deficiency of intrinsic clotting factors (VIII, IX, XI, prekallikrein, high molecular weight kininogen), heparin resistance

### LMWH

- Pregnancy
- Infants
- Patients with a body weight > 120 kg or < 50 kg may require dose-adjustment based on anti-FXa testing
- Patients with renal impairment with CrCl < 30 mL/min

### Rivaroxaban

- Prior to urgent surgery or during the peri-operative period
- Thromboembolic or bleeding events
- Potential overdose and/or compliance issues
- Renal impairment

## Sample requirements for anti-FXa testing

LMWH	RIVAROXABAN
Citrated plasma	Citrated plasma x 2 tubes
Taken on 2 <sup>nd</sup> day of therapy	Dose and duration of treatment must be indicated
3 – 4 hours after administration of last dose	Peak level taken 3 hours after last dose Trough level taken 1 hour or less before next dose

## Reference ranges for anti-FXa levels

Type Of Heparin	Therapeutic Range (anti-FXa activity/mL)	Prohylactic Range
LMWH	0.5 - 1.0	0.25 - 0.5
UFH	0.3 - 0.7	0.1 - 0.4

Rivaroxaban Dose	Trough (ng/mL)	Peak (ng/mL)
10 mg daily	1 - 38	91 - 196
15 mg daily	18 - 136	178 - 313
20 mg daily	6 - 87	189 - 419

## Interpretation

- Results are reported in drug concentration – a high anti-FXa level indicates high or supratherapeutic anticoagulation; low anti-FXa levels indicate low or subtherapeutic anticoagulation.
- The anti-FXa assay measures the drug concentration (quantitative assessment) and not the intensity of the drug's anticoagulant activity (qualitative assessment), therefore a higher than expected drug level does not necessarily indicate a greater risk of bleeding complications. One needs to interpret the test results in relation to the drug pharmacokinetics and clinical context (e.g. other risk factors for bleeding).
- Possible causes of erroneous/unreliable results include:
  - Haemolysed, icteric or lipaemic samples
  - Incorrect time of sample collection
  - Delayed specimen transportation
  - Heparin contamination
  - Antithrombin deficiency if reagent does not contain antithrombin

## References

- Gehrie E, Laposata, M. Test of the Month: The chromogenic antifactor Xa assay. Am J Hematol 2012; 87(2): 194 – 196.
- Noll A. Coagulation Assays and the New Oral Anticoagulants. American College of Cardiology, Jun 22, 2015. Available at: <http://www.acc.org/latest-in-cardiology/articles/2015/06/22/12/06/coagulation-assays-and-the-new-oral-anticoagulants>
- Samama MM, et al. Laboratory assessment of rivaroxaban: a review. Thromb J 2013; 11(1): 11.

Johannesburg | 0861 LANCET

Polokwane | (015) 294 0400

Cape Town | (021) 673 1700

Pretoria | (012) 483 0100

Rustenburg | (014) 597 8500

Bloemfontein | (051) 410 1700

Durban | (031) 308 6500

Nelspruit | (013) 745 9000

Kimberley | (053) 836 4460



@LancetLab



LancetLaboratories



[www.lancet.co.za](http://www.lancet.co.za)

