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Focus
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Actions to taken when faced with a long aPTT result

What is aPTT?

The aPTT (activated partial thromboplastin time) is the clotting time of a platelet poor plasma sample once in the presence of calcium ions, phospholipids and a contact activator from the clotting system. Cephalin acts as a phospholipid reagent (originally a platelet substitute of variable composition and concentration) and the activator could be silica, ellagic acid or kaolin (i.e. kaolin activated partial thromboplastin time).

This clotting time is expressed in seconds in reference to a control plasma sample (i.e. 45/30 sec). A patient/control (P/C) ratio of ≥ 1.20 is considered as normal. When faced with a high aPTT result further and thorough investigation is required, such as:

Age, gender (if female: pregnancy?), consanguinity, current treatment, known pathologies and previous history of haemorrhages (patient or familial and whether spontaneous or provoked). The action to be taken for any given patient should be in line with the context: preoperative (type of intervention, hemorrhagic risk, anticoagulant postoperative treatment required), investigation of a hemorrhagic syndrome (type of haemorrhage – spontaneous / provoked).

Difficulties faced: aPTT

1. The sample: The sample should be collected via venous puncture into Vacutainer citrate tubes (0.109 M citrate i.e. 3.2%, or if possible 3.8%), under vacuum and transported in an upright position at a temperature between 18 - 22°C. The dilution of 1 part anticoagulant to 9 parts blood is a necessary requirement; therefore please ensure that the tube is sufficiently filled. If the packed cell volume of the patient is ‹ 35% or › 55%, it is advisable to adjust the volume of the anticoagulant before collecting the sample. If several tubes are to be taken, you must rigorously respect the following order: plain tubes(s) › citrate tubes › other coagulant tubes (EDTA, Heparin) › tubes containing a coagulation activator.

If the sample is referred or testing is delayed for over 2 – 4 hours after collection, double centrifugation (2 x 2500 g for 15 mins) in a temperature controlled centrifuge (but not refrigerated) is recommended, followed by decanting of the sample into a polypropylene tube. Finally the plasma sample must be free from residual platelets (‹ 10 x109 /l) and frozen immediately at -20°C or ideally at -80°C. All syringes, catheters, pots or other tube samples will be refused.

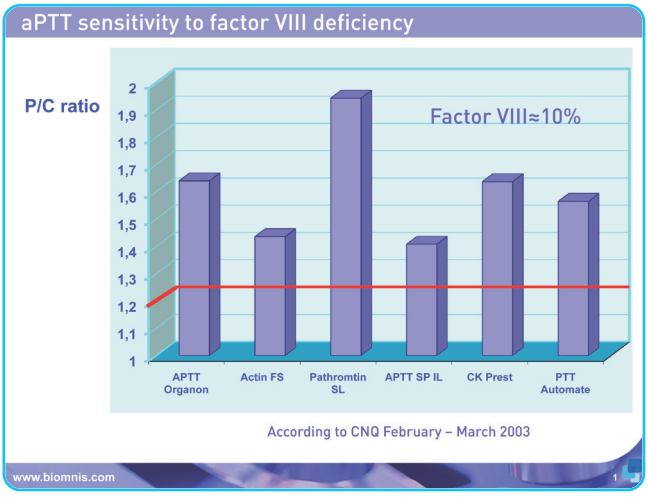
2. The difficulty of choosing the reagent

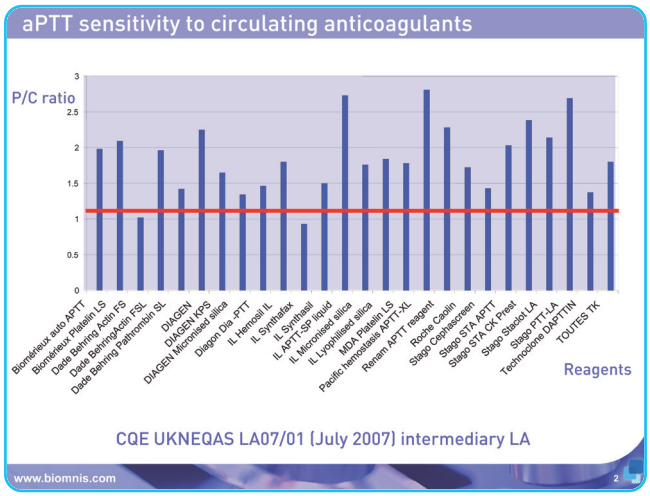
An extensive number of aPTT reagents are available and each industrial company has several types on offer. The activated thromboplastin time test is dependent upon the reagent. Therefore in order to choose the correct reagent one must take into account the clinical context of the patients being tested. In the case of preoperative screening or in haemorrhagic syndrome investigations it is better to choose a reagent that is sensitive to factor deficiency. In the case of thrombosis screening, repeated miscarriage or auto-immune disease, the choice leans towards a reagent sensitive to circulating anticoagulants (ACC).

Lastly, reagents with variable sensitivity to heparin should have their reference ranges adapted in relation to the cephalin used (see the example below). It is essential that physicians are reminded of the precautions and reservations linked to the use of aPTT and that the gold standard for treatment monitoring is quantification of anti-Xa activity.

- **aPTT sensitivity to recent anticoagulants**

	Silimat® Biomérieux		aPTT® Organon	
	aPTT (sec)	ratio	aPTT (sec)	ratio
0.30 - 0.70 UI antiXa/ml	63 - 178	1.90 – 5.40	53 - 127	1.70 – 4.10





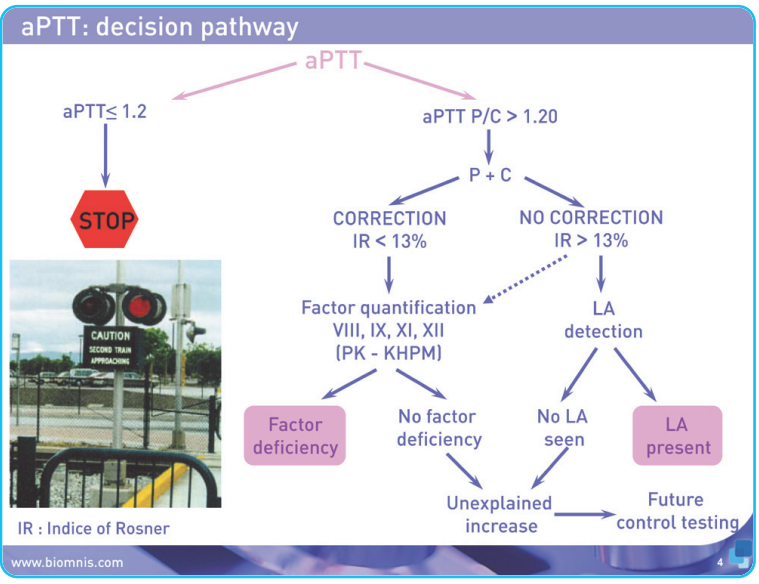
Rivaroxaban (XareltoR) is a direct anti-Xa treatment. It increases the aPTT and the Prothrombin Time (PT) in a dose dependent fashion. At a therapeutic dose, the P/C ratio is between 1.30 and 1.70, which is variable according to the reagent used.

All the same, Dabigatran (Pradaxa®), a direct thrombin inhibitor increases the aPTT at therapeutic doses (the increase varies according to the reagent used).

In patients on Hirudin treatment (also a direct anti thrombin treatment), the aPTT also increases but quickly levels off. Therefore, this test cannot be used for treatment monitoring as there is a risk of being unaware of an overdose. The quantification of the ecarin clotting time (ECT) allows for a more precise follow-up whereas the thrombin time (TT) is too sensitive and should not be used.

3. The right control

It is a mixture of so called 'normal' plasma samples with their platelets properly removed by double centrifugation, mixing, aliquoting and freezing. Lyophilised commercial control pools should not be used. However, more appropriate commercial lyophilised or frozen standard pools do exist (normal plasma pools).



Main uses of aPTT

- **Diagnosis of haemorrhagic syndrome:** haemophilia A and B, Willebrand disease, factor XI deficit (factor XII deficiency, prekallikrein or PK and high molecular weight kininogen (HMWK) or HMWK increasing aPTT but not haemorrhagiparous) and acquired deficiency (specific inhibitor of a factor: anti-VIII, anti-IX or anti- XI).
- **Circulating anticoagulant screening:** lupus screen (anti-phospholipids)
- **Anti thrombotic treatment monitoring:** unfractionated heparin etc

Factor deficits and aPTT

Reagents are generally not sensitive enough for factor VIII and IX deficiencies but are more sensitive to factor XI and XII deficiencies. Sensitivity for factor deficiencies in the contact phase (prekallikrein and HMWK), without clinical symptoms, is variable. Reagents containing ellagic acid are not sensitive. To confirm a factor deficiency in the contact phase, aPTT testing with 1 min incubation and aPTT with 10 mins incubation must be performed. In the case of a PK deficiency the P/C ratio is largely corrected after 10 minutes in comparison to those obtained after only 1 minute of incubation. There is only a slight correction in the case of HMWK deficit.

When the patient aPTT is lower than that of the control

It could be:

- A coagulation activation problem at the time of sample collection,
- A 'hypercoagulability': raised levels of factor VIII, fibrinogen etc.
- Activated protein C resistance.

aPTT in children

Generally the aPTT is higher than in adults:

In the newly-born: P/C ≈ 1.3. However, they are generally compared to those of an 'adult' control (child controls create errors) and we do not have the exact reference values for each reagent. Ultimately, the same attitude should be used as those for adults: investigate if P/C › 1.20. Finally, in children circulating anti coagulants are frequent and often transitory with no clinical consequence. They often resurface during repetitive ENT infections and infections.

Conclusion

The aPTT test is simple and routine, but badly standardised. It can be used as a screening test to detect various anomalies, but further investigation of abnormal results is required to characterize and determine their clinical significance.

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