Activated partial thromboplastin time (APTT)

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INTRODUCTION

The term partial thromboplastin is used to distinguish the reagent from that used in the prothrombin time, since the APTT reagent lacks the apoprotein component of the complete tissue thromboplastin. The APTT is the main test for screening for intrinsic clotting defects including haemophilia. It is also used for detection of lupus anticoagulant and for laboratory monitoring of heparin administration. The presence of an activator in the test system, to accelerate the PTT test by effecting maximum activation, also increases its precision and reproducibility by eliminating the variable effects of contact with glass surfaces.

APTT PHOSPHOLIPIDS

The partial thromboplastin consists of the phospholipid component of thromboplastin and is prepared from animal tissue or from vegetable sources. The phospholipid acts as a platelet substitute in the intrinsic system. The lipid composition of different APTT reagents, however, varies considerably. The total concentrations of phospholipid and fatty acid in some widely used APTT reagents have been shown to differ by as much as 300 times. These discrepancies markedly affect responses to coagulation defects and inhibitors of coagulation. The requirements for the phospholipids in the test system may also vary according to the nature of the clotting defect being measured. For example, the concentration of negatively charged phospholipids, e.g. phosphatidyl serine, has been shown to be critical.
OTHER COMPONENTS OF THE APTT TEST

Factors which affect the clotting response include the type of activator, length of incubation with the plasma and the presence of buffers\(^3\).\(^4\). Particulate activators include kaolin, celite and micronized silica, whereas a commonly used activator, ellagic acid, is non-particulate. The amount of activator present in the various commercial techniques, and the length of incubation time employed with the plasma, show considerable variation. The effectiveness of an activator in the APTT is governed by many considerations, e.g. its concentration, the incubation time and the composition of the phospholipid. It is the combination of the activator with the other components which appears to determine the reliability of the test\(^5\). The trend is to use less opaque activation to avoid interference with newer types of coagulometers. The use of different types of coagulometer can also have a considerable effect on the clotting time\(^6\).

SENSITIVITY OF THE APTT

A reliable APTT reagent should be sufficiently sensitive to record an abnormal result when the level of any single or combined intrinsic clotting factor deficiency is reduced to a level which may cause spontaneous bleeding, or haemorrhage following a haemostatic challenge. Proctor and Rapaport\(^7\) stated that the APTT should be able to detect factor deficiencies of 30% or less. It should also be sufficiently responsive to low concentrations of heparin whilst giving a linear response to graded concentrations of heparin, spanning a clinically relevant range of 0.05–0.5 units/ml of heparin. The importance of assessing heparin response to patients’ heparin-treated samples rather than normal plasma ‘spiked’ with heparin was emphasized in the ISTH/ICSH Study\(^8\) as the response to heparin-treated patients may be markedly less with some APTT reagents compared with the same concentration of heparin added \textit{in vitro}, particularly after a recent thrombotic episode. The variable effects on heparin response of APTT reagents from coagulometers used to perform the test was observed in the ISTH/ICSH study and a UK survey from the National External Quality Assessment Scheme\(^9\). The sensitivity to lupus-like anticoagulant of an APTT system should be established in comparison with a responsive formulation of the viper venom test.

CLINICAL USE

The main use of the APTT is for the screening of coagulation defects and the presence of inhibitors. The test is prolonged by deficiencies of factors VIII, IX, X, XI and XII and defects of the contact phase, e.g. prekallikrein, high molecular weight kininogen. It also may be prolonged by gross defects of factors II, V and fibrinogen. With reliable APTT systems, specific and non-specific inhibitors of intrinsic clotting factors are detected. The degree of abnormality depends upon the responsiveness of a particular APTT method to a specific defect. When used as a screening test for lupus anticoagulant (LA)