

### Reptilase and Thrombin Clotting time of Plasma from Patients Treated with Streptokinase

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Increasing clinical experience has gradually diminished the number of laboratory tests required for monitoring thrombolytic therapy. Still wider and wider use of plasminogen activators, often without a specialized laboratory basis, makes it imperative that some easily performed and reproducible tests should be at our disposal. Such conditions seem to be fulfilled by a simple assay of plasma clotting time. Usually thrombin was used as the clotting agent for this purpose. The test could not, however, be applied or would give erroneous results if heparin had been given simultaneously or following treatment with thrombolytic agents. The use of reptilase instead of thrombin is therefore proposed.

In contrast to the observations made by some others, our previous studies (Latallo and Teisseyre, 1971) indicated that the addition of fibrinogen degradation products (FDP) to normal plasma resulted in parallel prolongation of both the thrombin and the reptilase clotting times. A comparison of both types of clotting tests was made on plasma samples from four patients obtained at various stages of treatment with Kabikinase (Kabi, Stockholm). Plasma was obtained from blood taken into a mixture of EACA and sodium citrate with the following assay system: 0.2 ml of plasma and 0.1 ml of enzyme, 37°, pH = 7.8. Thrombin was dissolved in the same carrier solution as reptilase to a concentration which gave an identical clotting time of normal plasma for both enzymes. Standardized preparation Reptilase R (Pentapharm, Basel) was used.

Very good agreement was observed in values for clotting times produced by either enzyme. Both equally depend upon the concentration of fibrinogen and/or FDP. Comparison of clotting times of undiluted plasma samples and on samples mixed in a 1:1 ratio with normal plasma allowed workers to distinguish whether the observed prolongation was due to a very low content of fibrinogen or to a high concentration of fibrinogen degradation products.

### Preliminary Results of the Reptilase Clotting Time and Protamine Test in Patients Undergoing Open Heart Surgery with Extracorporeal Circulation

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Extracorporeal circulation is usually accompanied by a marked decrease in fibrinogen level of

plasma. This may be due simply to dilution of blood in the apparatus but also to the activation of intravascular coagulation and/or fibrinolysis. The changes may occur quite suddenly and appropriate therapeutic measures have to be undertaken as soon as possible.

The protamine test and reptilase clotting time have been already proposed for the detection and evaluation of the intravascular formation of fibrin and fibrinogen degradation products respectively (Latallo, Wegrzynowicz, Teisseyre, and Kopec, 1971). Previous work (Palester-Chlebowczyk, Strzyzewska, Sitkowski, Olender, Wegrzynowicz, and Latallo, 1971)<sup>1</sup> indicated that the protamine test, if run under proper conditions (at 37°, 0.1-0.2% final concentration of protamine sulphate, pH around 7.8), may serve as a rapid method for detection of intravascular fibrin formation. Further results confirm these observations.

Since heparin given during surgery seriously interferes with many clotting tests, the reptilase clotting time (which is not affected by the presence of the drug) seemed to be particularly convenient for detection of active products of fibrinogen proteolysis (Latallo and Teisseyre, 1971).

Clotting time measurements were performed at 37°, pH = 7.8 in a system: 0.2 ml of citrated plasma and 0.1 ml of standardized preparation of reptilase (Reptilase R, Pentapharm, Basel). The test was repeated at short intervals before, during, and after surgery, and the results were compared with assays of the euglobulin lysis time and fibrinogen content in plasma.

In all cases in which the euglobulin lysis time was significantly shortened, the clotting time was prolonged. Some prolongation was observed also in samples with prolonged euglobulin lysis time. This might indicate that the fibrinogen degradation products remain in circulation for some time after the activation of the fibrinolytic system.

It is concluded that the two tests described here might be conveniently applied as simple screening tests during open heart surgery.

### Methodology for the Control of Thrombolytic Therapy

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Methods required for the control of thrombolytic therapy include (1) methods for measuring the intensity of the induced plasma thrombolytic state, (2) methods for assay of other plasminogen-plasmin system components altered by therapy, (3) methods for determining the secondary effects of the treatment

<sup>1</sup> *Scand. J. Haemat.*, 1971 (In press).