Observations on the use of the Becton Dickinson Fibrometer

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SYNOPSIS
An electro-mechanical instrument for use in both Thrombotest and Quick one-stage systems of anticoagulant control is described and the results obtained using it are compared with those obtained in the standard manual method. These figures show a very satisfactory degree of correlation, and it is concluded that the instrument would be of value in laboratories, particularly those controlling anticoagulant therapy by the Owren Thrombotest system.

Clinical experience in the use of coumarin anticoagulants can now be measured in decades. The initial wave of enthusiasm soon settled to a calmer period of careful and critical observation coupled with increasing laboratory evidence of the complexities of the clotting mechanism. Although much criticism of the clinical usefulness of these drugs has recently been made there is certainly no diminution in the number of prothrombin estimations requested in hospital. The control of anticoagulant therapy, then, continues to place upon routine haematology laboratories a considerable responsibility, the acceptance of which implies the need for deployment of skilled and experienced technicians on a task which is both repetitive and tiring. The introduction of anticoagulant control by Owren’s Thrombotest, a method providing distinct technical advantages over the Quick one-stage system, has to some extent accentuated the problem, particularly if the therapeutic desirability of the lower Thrombotest ranges is accepted when the time taken for a specimen to clot may be upwards of 100 seconds.

The automatic measurement of the critical end-point of a coagulation system has for long presented a challenge to the inventive. A photo-electric principle was developed in the prothrombin meter (EEL), described by Toohey and Cook (1960) for use in the Quick one-stage system. The use of the instrument was reported by Jacobs and Freer (1963).

This report describes our experience in the use of a precision coagulation timer, based on electro-mechanical principles, which may be used for both Quick and Owren methods. It is hoped that it will be marketed in the United Kingdom soon, under the name Fibrometer.

MATERIALS AND METHODS
Venous blood was collected in disposal plastic syringes and placed in polystyrene tubes containing 3·1% sodium citrate (Stayne Laboratories). All tests were carried out within three hours of venepuncture. Thrombotest was performed as described by Owren (1959) each sample being tested once. The one-stage method was carried out in duplicate according to the method of Dacie and Lewis (1963).

THE FIBROMETER
The precision coagulation timer is a compact electro-mechanical instrument powered from the mains supply (Fig. 1). Component miniaturization and a transistorized circuit are features of the rugged maintenance-free instrument. A heating block with close thermostatic control and indicator lamp provides seven wells at 37°C ± 0·5°C. Six wells are for preliminary warming of the test specimen and reagents, the seventh or central well is for the mixture under test. Each well holds a disposa plastic cup. In operation the cup containing the Thrombotest reagent is placed in the central well and the citrated blood pipetted into it. The timer bar is pressed simultaneously and the process thereon is completely automatic. Activation of the timing mechanism causes the arm to swing forward and immerse two probes into the blood-Thrombotest mixture. One probe is immobile while the other provides uniform agitation twice per second, moving in two planes. The instant a fibrin thread appears in the mixture the moving probe and the timer stop. The end-point is exact, in relation to the development of fibrin threads in the forming clot, and the time interval is shown to a tenth of a second. The instrument is reset by swinging the arm aside, cleaning the probes, and pressing the reset button to zero the timer. The used plastic cup is removed and the next cup with Thrombotest reagent is transferred to the central well from the preliminary warming well.
In assessing the instrument we compared the results given by the mechanical method with those determined manually by an experienced technician. In this department anticoagulant therapy is controlled by the Thrombotest method and thus we were particularly interested in applying the Fibrometer to this technique.

Table I summarizes all the tests using the Fibrometer for Thrombotest. The number of tests carried out within the specified range of Thrombotest is given, followed by the actual number which fall within the accepted limits of error for that range. From the practical point of view the lower part of this table gives these figures expressed over the range of major importance, for 0-10% Thrombotest a difference of 1% being considered acceptable and over 11-20% the accepted limit is 2%.

Column A gives the initial results comparing the instrument with the manual technique. In 80 tests 71 (89%) were found to be within acceptable limits of error. On these results the problem of the concept of the 'lag period' was raised, for in the manual method there is recommended a period following the initial mixing of the Thrombotest reagent and the blood during which the test specimen is left in the water bath undisturbed. For a normal or near normal blood period of 30 seconds is suggested, the 'lag period' for an anticoagulated specimen about 50 seconds. For the purposes of our investigation the interval, i.e., lag period, was kept at 45 seconds for all specimens. Since the Fibrometer as used normally does not have a lag period we decided to compare the results of 100 tests done manually with constant agitation with those obtained from the Fibrometer (column B). A correlation of 94% was demonstrated. This apparent improvement was not readily explained and was further investigated by imposing upon the Fibrometer a lag period of 45 seconds thus resembling the classical manual procedure. This was done by pressing the timer bar of the Fibrometer.

**Table I**

**Results for Thrombotest using the Fibrometer**

<table>
<thead>
<tr>
<th>Thrombotest Ranges (%)</th>
<th>Comparison of Paired Manual and Fibrometer Methods</th>
<th>Fibrometer Method Only</th>
<th>Manual Method Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Paired Tests</td>
<td>No. within 'Limits'</td>
<td>No. of Paired Tests</td>
</tr>
<tr>
<td>0-10</td>
<td>28</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>11-20</td>
<td>33</td>
<td>26</td>
<td>33</td>
</tr>
<tr>
<td>21-30</td>
<td>10</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>31-40</td>
<td>4</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>41-50</td>
<td>5</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>50+</td>
<td>80</td>
<td>71</td>
<td>100</td>
</tr>
<tr>
<td>Percentage</td>
<td>0-10%</td>
<td>11-20%</td>
<td>0-10%</td>
</tr>
<tr>
<td>within 'limits'</td>
<td>89</td>
<td>94</td>
<td>97</td>
</tr>
<tr>
<td>Identical</td>
<td>86</td>
<td>30</td>
<td>85</td>
</tr>
<tr>
<td>Within 1% T.T.</td>
<td>100</td>
<td>55</td>
<td>100</td>
</tr>
<tr>
<td>Within 2% T.T.</td>
<td>86</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
exactly 45 seconds after the addition of citrated blood to the Thrombotest reagent with initial mixing.

Used thus, 97% agreement was obtained in comparison with the manual method without lag (column C). A comparison was then made over 100 specimens using the instrument normally and with lag (column D) and a very high degree of correlation was shown. Comparison of the manual procedure with and without time lag showed no difference over 50 tests (column E).

We consider that these results show a very satisfactory degree of agreement between the manual Thrombotest method and the Fibrometer and that this agreement is particularly high over the therapeudic range. The improvement in the figures from the instrument during the study was almost certainly due to increasing experience in its use. The lack of time lag in the instrument appeared to be of no consequence in the accuracy of the results.

Professor Owren in a personal communication (1963) states that a lag time was recommended as it produces a better degree of standardization because frequent agitation throughout the period of the reaction, as might be done by a less experienced operator, can produce agglutination of the red cells in those bloods which take longer to clot, thus giving a false end-point. Steady but slower agitation throughout the reaction time does not, however, affect the clotting time of the system, as our results show.

The Quick one-stage test was performed in duplicate on 50 citrated plasma specimens. The average of two manual results is compared with the average of two Fibrometer results (Fig. 2).

**DISCUSSION**

We have been particularly interested in the use of the coagulation timer for Thrombotest. While it does not, of course, shorten the time for a specimen to clot, it does relieve the operator of all further responsibility from the time of adding the citrated blood to the reagent when the timer bar is pressed. This interval, often considerable, can then be utilized for preparing subsequent tests and entering up results. When large numbers of specimens have to be dealt with one operator can readily use two machines with resultant increase in efficiency. We have found that scrupulous cleanliness of the agitating terminals is essential. Beyond this we experienced no problems in the use of the instrument. It is readily portable and reaches operating temperature in about 10 minutes, making it suitable for use in clinics.

In using the Fibrometer for Quick estimations, the calcium solution had to be separately warmed to 37°C in a water bath. The provision in the heating block of the Fibrometer of one commodious well for this purpose would be a distinct advantage. We consider also that a thermometer should be incorporated in the instrument.

We thank Mr. J. Gibbons, of Shandon Scientific Company Limited, and Becton Dickinson & Company Limited for placing the Fibrometer at our disposal, and Dr. G. A Carnachan, of Evans Medical Limited, for help and advice. We are also grateful to Dr. G. A. McDonald for helpful criticism in the preparation of this manuscript.

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*J Clin Pathol* 1965 18: 372-374
doi: 10.1136/jcp.18.3.372

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