A viscometric method of measuring plasma fibrinogen concentrations

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Abstract
A technique based on deducing the viscosity of serum from that of plasma was compared with the commonly used Clauss method. The two methods correlated closely (r = 0.914). The reproducibility of the viscometric method was slightly poorer than the Clauss technique at low fibrinogen concentrations, equal to that at medium fibrinogen concentrations, and marginally better at high concentrations. Fibrinogen can therefore be measured reasonably accurately with the viscometric method, and can be recommended as an alternative for laboratories possessing a viscometer.

The identification of fibrinogen as a major cardiovascular risk factor has increased the demand for a quick, simple, inexpensive and reproducible method to determine its plasma concentration. There are many methods of quantifying plasma fibrinogen; possibly the best and certainly the most common is the Clauss method.

Due to its large size and spherical shape, fibrinogen strongly influences plasma viscosity. It is the only constituent of plasma that...
is missing in serum. Therefore, it should be quantifiable by deducting serum viscosity from plasma viscosity.4 The following is a re-evaluation of this forgotten method.

Methods
For reference the Clauss method (Multifibren, Behring AG, Marburg) was used.4 Plasma and serum viscosities were measured at 37°C.2 One hundred and ten subjects were studied (61 men, 49 women, mean age 52.7, range 19.5–84.5). Eighteen were apparently healthy, 19 had a history of coronary heart disease, 43 patients had been admitted for elective surgery, nine patients had non-inflamatory, and 22 inflammatory disorders. Venous blood samples were taken according to a standardised protocol.6 All measurements were done on fresh samples.

Each sample was tested four times with both methods. The means of these four results were correlated using Pearson’s linear correlation coefficient. A formular was derived to convert the viscometer readings into absolute fibrinogen concentrations (in mg/dl): fibrinogen = 1725 PV−SV + 70 (PV = plasma viscosity, SV = serum viscosity).

Three samples were measured 10 times. Thus three individual coefficients of variation (CV) were calculated. The mean of the three was taken as a measure of accuracy of each method. As precision might vary as a function of plasma concentration, this procedure was repeated at nine different ranges of fibrinogen concentration (as determined by Clauss method).

Results
The correlation of the two methods (figure) was highly significant (r = 0.914, p < 0.000001). The table summarises the CVs obtained at various plasma concentrations for both methods. At low concentrations the viscometric method yielded higher CVs. In the medium range the viscometric technique gave marginally higher CVs; in the upper range it was slightly lower.

Discussion
The results suggest that the viscometric method is a useful approach to measure plasma fibrinogen—particularly in the upper range of normal, where fibrinogen measurements are most meaningful.4

The original description does not detail reproducibility, but merely correlates data from two methods.4 The correlation coefficient was 0.80—slightly lower than the present one. Nevertheless, the author states that his method “offers possibilities of establishing a simple and accurate means for the quantitative measurement for fibrinogen”.

There are three main fibrinogen fractions (340, 305, and 270 kilodaltons).7 These are all clottable and are thus picked up by the viscometric technique. Low molecular weight fibrinogens clot slower and may therefore be underestimated by clotting time methods.3 An official recommendation is published for viscometry,5 but not for measuring fibrinogen. Artefacts can almost totally be excluded for Newtonian viscosity but not for the Clauss method.2 Cheap standards exist for viscometry (distilled water), but not for measuring fibrinogen. The viscometric method is quick (one to two minutes) and easy to handle; there is no need for one way equipment, nor for purchasing reactants (as in the Clauss method). The viscometric technique does not need a dilution step, a notorious source of error in the Clauss method.2

One drawback of the viscometric method is its poorer reproducibility; yet the difference is not large. The viscometric method requires a relatively large sample volume; the Harkness viscometer3 needs 1 ml for three repetitive measurements. This translates into 4 ml of whole blood needed for one fibrinogen test. However, other viscometers use less volume and are equally accurate.5

We do not conclude that the viscometric technique should be universally adopted, but suggest that those who own a capillary viscometer might consider it as a cheap, quick, and reproducible alternative.