A METHOD FOR MEASURING PLASMA VISCOSITY AND A COMPARISON OF PLASMA VISCOSITY WITH BLOOD SEDIMENTATION RATE IN RHEUMATOID ARTHRITIS

BY

A. WOODMANSEY

Spa Research Department, Harrogate

and

J. V. WILSON

Pathologist to Harrogate General Hospital and Royal Bath Hospital, Harrogate

In the study of the rheumatic diseases the measurement of blood sedimentation rate has an established value in estimating the activity of the disease and in evaluating the effects of treatment. It is generally agreed, however, that the erythrocyte sedimentation rate is not always a reliable index even if a correction is made for anaemia.

The study of the viscosity of blood was first described over a hundred years ago. Hess in the early part of the present century used a well-known type of viscometer. Evans (1942) gave a detailed survey of the subject. Whittington (1942) called attention to the measurement of plasma viscosity as a clinical index and claimed diagnostic value for it. Miller and Whittington (1942), Houston and others (1945), and Harkness and others (1946) applied the test in pulmonary tuberculosis and reached the conclusion that plasma viscosity is a reliable laboratory test in assessing the clinical condition and prognosis in tuberculosis and certain other diseases.

In the present paper a simplified method of measuring plasma viscosity is described, and its application in comparison with the erythrocyte sedimentation rate in interpreting cases of rheumatoid arthritis is discussed.

Viscosity is a physical property of fluids which, in the case of pure liquids, may be treated mathematically. Protein and similar colloidal solutions show slight divergencies from the equation, probably due to deformation of the large molecules or to adsorption effects. For practical purposes these slight anomalies are unimportant, and it is sufficient to compare the rate of flow of plasma through a capillary tube with the rate of flow of distilled water

under the same conditions. Strictly speaking, as the plasma is slightly heavier than water the specific gravity should be taken into account, but this factor may be omitted for simplicity.

Method for Measuring Viscosity

The viscometer (Fig. 1) is made as follows. A small bulb is blown in a piece of thermometer tubing. The tube is drawn out to form a constriction some two inches below the bulb. The lower end is cut off flat, and marks are made just above and below the bulb and a third mark one-eighth of an inch from the lower end. The capacity of the original viscometer is 0.085 ml., and the time of outflow of distilled water is 43 seconds. In order to compare the performance of similar viscometers, a number of tubes were made with capacities of from 0.070 to 0.100 ml., and times of outflow of distilled water from 40 to 53 seconds. The ratios, $\frac{\text{time of plasma outflow}}{\text{time of water outflow}}$ with these tubes were not identical but were sufficiently close to enable anyone with elementary glass-blowing experience to carry out confirmatory work.

The viscometer is held by a cork perforated to allow equalization of pressure, in a half-inch diameter test-tube so that the lower end of the viscometer is immersed a fixed distance (to the eighth-inch mark) below the surface of the plasma. It is important to maintain this same adjustment in every test. About 1 ml. of plasma is usually used, although determinations may be made with much less. The test-tube and contents are supported vertically in a large glass water-bath adjusted to 20° C., provided with electric heater, stirrer, and thermostat. These refinements are not essential if the highest degree of accuracy is not sought. When the plasma has assumed the right temperature (about three minutes is required) it is drawn by suction above the upper mark. The suction is released, and the time of outflow between the upper and lower marks is measured

FIG. 1.—The viscometer as described in the text.

by stopwatch. Three runs are taken, and they are usually in agreement.

The viscosity of a plasma (PV) is then recorded as the ratio of the number of seconds to the number of seconds taken by distilled water under the same conditions. The figure is multiplied by a hundred to avoid the decimal.

Plasmas from a series of healthy subjects vary from 160 to 180. From patients with rheumatoid arthritis the figures vary from normal to 250 or more.

The viscometer is cleaned by drawing through it first cold, then hot water, then alcohol followed by drying. Chromic acid is used at intervals as required.

In the work to date the specimen of blood is taken from a cubital vein and oxalated in the usual way. Five ml. are placed in a conical centrifuge tube, and the erythrocyte sedimentation rate is read after one hour according to the method of Collins and others (1939). The tube is centrifuged and about 1 ml. of the plasma is withdrawn for the viscosity determination. It does not appear as important to do the PV within an hour or two of taking the sample as it does the erythrocyte sedimentation rate.

Clinical Results

The plasma viscometer described above has been in use in the Royal Bath Hospital for the past eighteen months, and during that time we have performed over a thousand tests on cases of rheumatoid arthritis, at the same time carrying out the customary erythrocyte sedimentation rate (ESR) tests.

As a general rule it was found that the PV and ESR readings tended to correspond, that is, when one was high so also was the other. This correlation, however, was by no means absolute. Fig. 2 is a scatter diagram of two hundred consecutive cases in which the general trend of the PV to rise with the ESR is clearly shown. It is only a trend, however, as there are instances where the two readings do not correspond at all.

Followed over the course of the disease in the individual patient this correlation is also very general, as is shown in the case of No. 20 (Table 1).

TABLE 1

MRS. L. (CASE 20): SEVERE RHEUMATOID ARTHRITIS FOR THREE YEARS *

	ESR	PV
On admission	36	215
1st week	35	222
2nd week	38	223
3rd week	41	223

* Both PV and ESR indicate the condition to be still very active

In this patient both tests confirm the clinical findings.

There are instances where the indications provided by the PV and ESR are conflicting. These

FIG. 2.—Scatter diagram of plasma viscosity and erythrocyte sedimentation rates in two hundred consecutive cases of rheumatoid arthritis seen at the Royal Bath Hospital.

are shown by the outlying points on the scatter diagram, and they also occurred in individual cases during their stay in hospital. In these cases the physician in charge of the patient was invited to give his report of the clinical condition on discharge compared with the condition on admission. He had full knowledge of the ESR but was unaware of the PV results. The reports, therefore, were quite unprejudiced. Reference may be made to two cases (Table 2).

TABLE 2
COMPARISON OF ESR AND PV IN TWO CASES

		On admission	On discharge
No. 42: Mrs. A.	ESR PV	45 229	43 208
No. 62: Miss S.	ESR PV	23 180	37 181

In No. 42 the ESR remained relatively constant but the PV showed a fall towards normal. The physician reported improvement. In No. 62 the ESR for some unknown reason rose sharply but the PV remained stationary. The physician found no evidence of increased activity in the disease process, no respiratory trouble, and she was not menstruating. Such cases are interesting, and their investigation has led us to the view that where there is such disagreement the PV is a more reliable guide than the ESR.

Discussion

The ESR depends on the degree and rapidity with which the cells aggregate into "rouleaux" and the size of these aggregations. Gordon and Wardley (1943) have built up artificial pathological plasmas and have studied sedimentation rates in these. They conclude that the power of sedimentation of blood is not controlled by the absolute concentration of plasma proteins but by the inhibition of one protein by another.

The tendency to give that property of plasma causing aggregation a specific name, "sedimentin" (Day, 1940), is to be deprecated as it lends support to the idea that a specific substance exists capable of exerting this influence. No such substance has been isolated, and there is no experimental evidence of its existence.

Plasma viscosity, like ESR, is a function of the

plasma proteins, and similarly it is not proportional to the total plasma protein present.

Proteins may be broadly divided into two classes, fibrillar and globular (Astbury, 1937). These are named according to whether the molecule exists as a long chain, albeit with foldings and side groups, or whether it has a more or less spherical form. It is considered that the former type presents greater frictional contacts in solution, and that it therefore leads to increased viscosity. It is thus easy to understand how a qualitative change in the plasma proteins brought about by disease processes could influence viscosity.

Summary

1. A simple method of measuring plasma viscosity is described.

2. We believe that the plasma viscosity gives a more accurate figure than the erythrocyte sedimentation rate for estimating the activity of rheumatoid arthritis.

We wish to thank the staff of the Royal Bath Hospital, Harrogate, for their kind co-operation, and to express our indebtedness to Mr. A. Steel, B.Sc., who performed the ESR estimations and made viscometer tubes to our design.

REFERENCES

- Astbury, W. T. (1937). *Nature*, **139**, 641.
 Collins, D. H., and others (1939). *Annals of the Rheumatic Diseases*, **1**, 333.
 Day, G. (1940). *Lancet*, **1**, 1160.
 Evans, P. (1942). *Ibid.*, **1**, 162.
 Gordon, C. M., and Wardley, J. R. (1945). *Biochem. J.*, **37**, 393.
 Harkness, J., and others (1946). *Brit. med. J.*, **1**, 268.
 Houston, J., and others (1945). *Acta tuberc. scand.*, **19**, 153.
 Miller, A. K., and Whittington, R. B. (1942). *Lancet*, **2**, 510.
 Whittington, R. B. (1942). *Proc. roy. Soc. B.*, **131**, 183.

Methode de Mesure de la Viscosite du Plasma et Comparaison de la Viscosite du Plasma et du Taux de Sedimentation Sanguine dans L'arthrite Rhumatismale

RÉSUMÉ

1. Description d'une technique simple de mesure de la viscosité plasmatique.

2. Les auteurs considèrent que la viscosité du plasma donne des indications plus précises de l'activité de l'arthrite rhumatismale que le taux de sédimentation des globules rouges.