THE SERUM VISCOSITY AND THE SERUM PROTEINS

BY

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Equal weights of the various protein fractions in plasma affect the plasma specific gravity equally, whereas weight for weight the fractions exert differing influences on the plasma viscosity. Thus fibrinogen has a greater effect on the plasma viscosity than does globulin, which, in turn, has a greater effect than albumin (Bircher, 1921; Naegeli, 1931; Oberst, 1939; Cowan and Harkness, 1947). Working with mixtures of albumin and globulin, Naegeli (1931) and Nugent and Towle (1935) have shown that at a constant total protein content the viscosity of the mixture falls as the ratio of albumin to globulin rises, and vice versa.

It was considered that perhaps, given the total protein content and the viscosity of a serum, it might be possible to calculate the albumin:globulin ratio. Thus, using the copper sulphate specific gravity method for estimation of the total serum protein level (Harrison, 1947) and a modified Ostwald viscometer for the estimation of the serum viscosity (Lawrence, 1950), the estimation might be completed in under 15 minutes per serum, a much more rapid test than either the Kjeldahl or the Biuret methods. The specific gravity of a serum can be estimated to ±0.0005 (±0.18 g. %), and the serum viscosity ratio is accurate to ±0.2% (Lawrence, 1950). In fact, the estimation of the albumin:globulin ratio by this proposed method was not achieved.

Method

Blood, 7–10 ml., was taken by venepuncture from various patients and normal controls, allowed to clot, and the serum then removed. The total serum protein level and the albumin:globulin level were estimated by the micro-Kjeldahl method described by Harrison (1947). The serum viscosity was estimated by the method described by Lawrence (1950). Each serum was progressively diluted with physiological saline, and the viscosity of each dilution was estimated. From the curve obtained by plotting the total serum protein levels against their respective viscosities it was possible to calculate the viscosity of each serum at a constant total protein level. For convenience, this arbitrary level was taken as 6.5 g.%. Saline was used as diluent so that the various protein fractions should remain in solution (Bingham, 1945).

Also, a normal serum and serum from a case of advanced cirrhosis of the liver were mixed in varying proportions, and the viscosities of the various dilutions of the sera and the mixtures were estimated. Thus both the albumin:globulin ratios and the proportions of the various globulin fractions were varied in the mixtures.

Results

In Fig. 1 the viscosities of the two sera and their mixtures are shown at various dilutions. The results resemble the graphs of Naegeli (1931) and Nugent and Towle (1935), in that as the albumin:globulin ratio rises so the serum viscosity falls.

Thirty-five results are shown in Fig. 2, in which the serum viscosity of each serum at a total pro-
tein content of 6.5 g.% is plotted against its corresponding albumin:globulin ratio. The sera were taken from two normals and from a number of patients with rheumatoid arthritis (nine), congestive cardiac failure (seven), multiple myelomatosis (three), carcinomatosis (two), unexplained anaemia in old age (two), advanced hepatic cirrhosis (one), lymphoma (one), diabetes with nephrosclerosis (one), acute rheumatic fever (one), dermatomyositis (one) and pooled sera (five). Although, in general, the serum viscosity increases as the albumin:globulin ratio falls, there is a wide scatter in the readings of the ratio at any given serum viscosity value. Thus the estimation of this ratio from the serum viscosity and the total serum protein concentration is not feasible.

Discussion

Although the molecular weight of globulin is given as 155,250 by Harkness and Whittington (1947), they state that this is an average estimation. Globulin consists of many fractions, and Wuhrmann and Wunderly (1947) give the molecular weights of alpha-globulin as 500,000, beta-globulin as 2,000,000, and gamma-globulin as 150,000. It is reasonable to suppose that these fractions will have different effects, weight for weight, on the serum viscosity. Harkness and Whittington (1947) showed that a mixture of albumin and globulin also contained a combined (albumin-globulin) complex with a molecular weight somewhere between those of its components, and hence with an intermediate effect on the viscosity of the mixture. This being so, it is obvious that variations in the proportions of the globulin fractions, quite apart from any variations in the albumin:globulin ratio, will affect the serum viscosity. This would account for the wide scatter apparent in Fig. 2, and the resulting gross inaccuracy were the serum viscosity taken as a measure of the albumin:globulin ratio: it has a direct bearing on the erythrocyte sedimentation rate. It is known that the erythrocyte sedimentation rate depends on the aggregating action of the plasma, which is a complex function of the plasma viscosity (Whittington, 1942). Also globulin is known to have a direct effect on the sedimentation rate, although not as great as the effect of fibrinogen (Ley, 1922; Linzenmeier, 1923; Naegeli, 1931; Bendien and Snapper, 1931; Vogt, 1941). Aldred-Brown and Munro (1934) could find no close correlation between the sedimentation rate and the plasma globulin content or the albumin:globulin ratio, and from Fig. 2 it may be concluded that sera with the same viscosity will probably not influence the erythrocyte sedimentation rate to the same degree, since the viscosity may be the result of varying proportions of protein molecules of various sizes.

Ehrström (1939) suggests that euglobulin accelerates the sedimentation rate; also it has been shown that euglobulin has a greater effect on the erythrocyte sedimentation rate than has pseudoglobulin, and that albumin positively depresses the sedimentation rate (Gray and Mitchell, 1942; Gordon and Wardley, 1943). Shedlovsky and Scudder (1942) found a direct qualitative relation to exist between the plasma alpha-globulin and the sedimentation rate, but not between either the beta-globulin or gamma-globulin fractions and the sedimentation rate, while Hardwicke and Squire (1952) found that alpha-globulin and gamma-globulin fractions were the most active of the globulin fractions in increasing both the sedimentation rate and the plasma viscosity. A further complication is suggested by the work of Kunkel and Tiselius (1951); using a two-way electrophoresis technique, they found that some plasma protein fractions, in particular the gamma-globulins, may often be heterogeneous. Thus, while the serum viscosity in conjunction with the total protein content will indi-
cate a qualitative change in the serum proteins, an accurate assessment of the nature of the globulins present or the albumin:globulin ratio is not possible.

Summary

Although sera with a high albumin:globulin ratio are less viscous than those sera in which the ratio is low, no simple relation has been found to exist between these two variables. Thus it is not possible to calculate the albumin:globulin ratio accurately from the total serum concentration and the serum viscosity.

This lack of correlation is probably explained by the different effects of the various globulin fractions on the serum viscosity, and by the possibility that some of these fractions may be heterogeneous.

The significance of these findings is discussed with relation to the effect of the plasma globulin on the sedimentation rate of erythrocytes.

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References

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