

THE INFLUENCE OF SOME BLOOD FACTORS ON ALTERATION OF CIRCULATION TIME IN MAN

By

B. N. MAZUMDAR AND R.M. VAIDYA

Department of Physiology, B.J. Medical College, Ahmedabad

Measurement of blood flow is regarded as a diagnostic tool in certain morbid conditions, as also it draws one's concern during transfusion. Out of all the methods available, finding of circulation time (1), though it is semiquantitative, is the practice of choice for measuring the velocity of blood for its quickness and accessibility at the bed side level. Circulation time may help us to differentiate dyspnoea of pulmonary origin from that of cardiac origin (7). It is imperative, therefore, that the factors altering it should be taken into account in the interpretation of circulation time. Poiseuille's law cannot be quantitatively applied to the circulatory system (12). Of the multiple factors affecting it, hydraulic and viscosity forces seem to be of major importance and in turn, the viscosity of blood is dependent on the plasma proteins as much as on the red blood cell concentration. The relative contribution of each type of plasma protein has been studied by Roe *et al.* (11) in which they found that the increase in α and β fractions of globulins have been found to increase the viscosity of blood the greatest. The role of red blood cells has been investigated from the point as it affects the haematocrit value (Hct) by Peter *et al* (9) and a rise in viscosity was found along with increase in the Hct value.

With the above correlating factors in view, an attempt has been made to find an inter-relationship between the various blood factors *viz.*, red blood cell-concentration, mean corpuscular volume (MCV), haemoglobin (Hb) concentration and different fractions of plasma proteins and their effect on the alteration of the circulation time in normal healthy individuals.

MATERIALS AND METHODS

Seventy normal subjects of an age group 18 to 21 years from amongst the students of B.J. Medical College, Ahmedabad belonging to both the sexes and including vegetarians and non-vegetarians were chosen. They had a light breakfast 2 hours earlier. 'Arm to throat' circulation time was found by calcium gluconate (13) after sufficient rest in the morning. Venous blood was drawn immediately afterwards for viscosity, specific gravity, red blood cell count, Hb estimation, packed cell volume (PCV), total protein and its fractions. Viscosity of the whole blood was determined by the method of Hess (4) and specific gravity by the method of Phillips *et al.* (10); Neubauer's bright line chamber and Sahli's hemometer were used respectively for red blood cell count and Hb%. The P.C.V. was found by centrifuging in Wintrobe's

tube revolving at the rate of 3000 r.p.m. for 45 minutes. Total plasma protein was determined by the biuret method of King and Wootton (6) and its fractionation was done by the method of Jancks *et al.* (5).

RESULTS

Since most of the factors taken into the present consideration differ according to sex, the values for equal number of male and female subjects have been compiled separately. The relative viscosity (defined as the ratio of the viscosity of blood at a particular temperature to the viscosity of water at the same temperature) and the specific gravity of the whole blood have been shown corresponding to the particular value of the circulation time in Fig. 1 along with

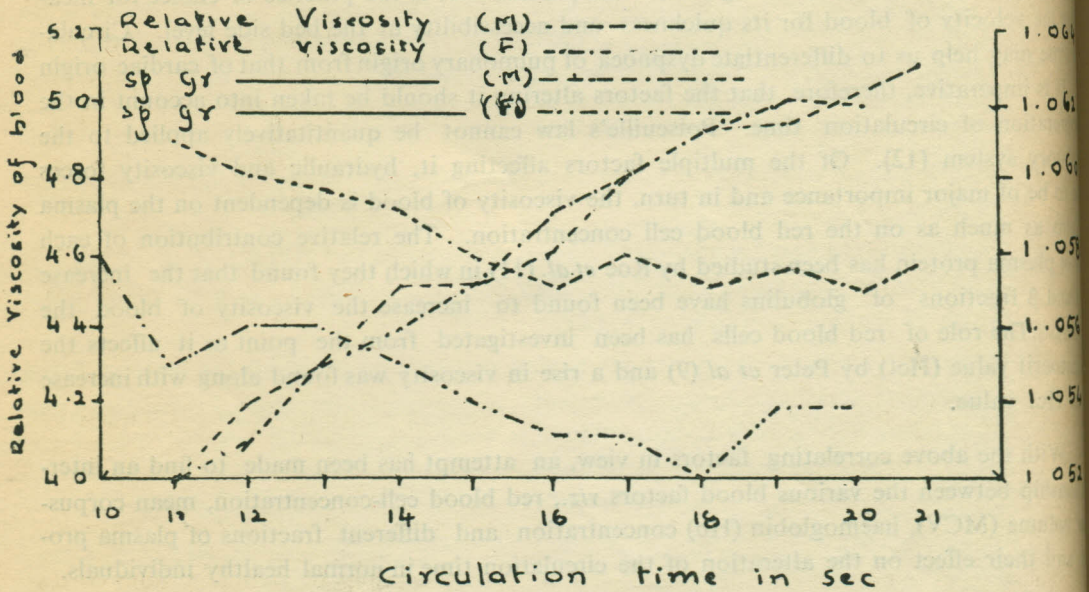


Fig 1

relative contribution of viscosity and the specific gravity in altering the circulation time in different sexes. The average viscosity of blood was found to be 4.71 ± 0.46 in males and 4.60 ± 0.65 in females and it showed a corresponding rise with the rise in the circulation time. The specific gravity of the whole blood showed a wide difference in the two sexes; the males showing an average specific gravity of 1.058 ± 0.18 while the females had 1.054 ± 0.004 . The figure showed a gradual fall in the specific gravity with the rise of circulation time upto 18 seconds in males and 18 sec. in females, further record showed either a steady level or a slight rise with the increase in the circulation time.

TABLE I

Relationship between circulation time, relative viscosity and specific gravity of the whole blood in normal adult males and females.

35 males			35 females		
<i>Circulation time in secs.</i>	<i>Relative viscosity</i>	<i>Specific gravity of whole blood</i>	<i>Circulation time in secs</i>	<i>Relative viscosity</i>	<i>Specific gravity of whole blood</i>
10	10	4.0 (3)	1.058 (3)
11	4.0 (1)	1.061 (1)	11	4.0 (2)	1.058 (2)
12	4.2 (2)	1.060 (2)	12	4.1 (5)	1.056 (5)
13	4.3 (2)	1.059 (2)	13	4.3 (4)	1.056 (4)
14	4.5 (2)	1.059 (2)	14	4.4 (3)	1.055 (3)
15	4.6 (2)	1.058 (2)	15	4.5 (4)	1.054 (4)
16	4.6 (6)	1.057 (6)	16	4.7 (3)	1.053 (3)
17	4.8 (5)	1.058 (5)	17	4.8 (8)	1.053 (8)
18	4.9 (5)	1.057 (5)	18	4.9 (1)	1.052 (1)
19	4.95(7)	1.057 (7)	19	5.0 (1)	1.057 (1)
20	5.0 (2)	1.057 (2)	20	5.0 (1)	1.054 (1)
21	5.1'(1)	1.057 (1)
Mean 16.7	4.71	1.0581	14.5	4.6	1.054
S.D.±4.14	±0.46	±0.0187	±5.09	±0.65	±0.004
C.V.24.7	9.7	17.0	35.10	15.0	1.30

Note: Figures in bracket denote the number of cases. S.D. Standard deviation. C.V. Coefficient of Variation.

Since, from the above results, the circulation time seemed to be changing more corresponding to the viscosity of blood than to its specific gravity, the viscosity was regarded as a determining factor and so some of the factors, supposed to change the viscosity have been investigated. Thus P.C.V., MCV, MCHC and the value for different protein fractions of the plasma were found and the results recorded in Table II and Table III for the males and the females respectively. The average values for the same viscosity have been taken into record. The relative contributions of packed cell volume and mean corpuscular hemoglobin concentration on the viscosity of blood have been shown in Fig. 2. Other factors presented in the table did not show much co-relationship with the viscosity and hence were not shown in the graph.

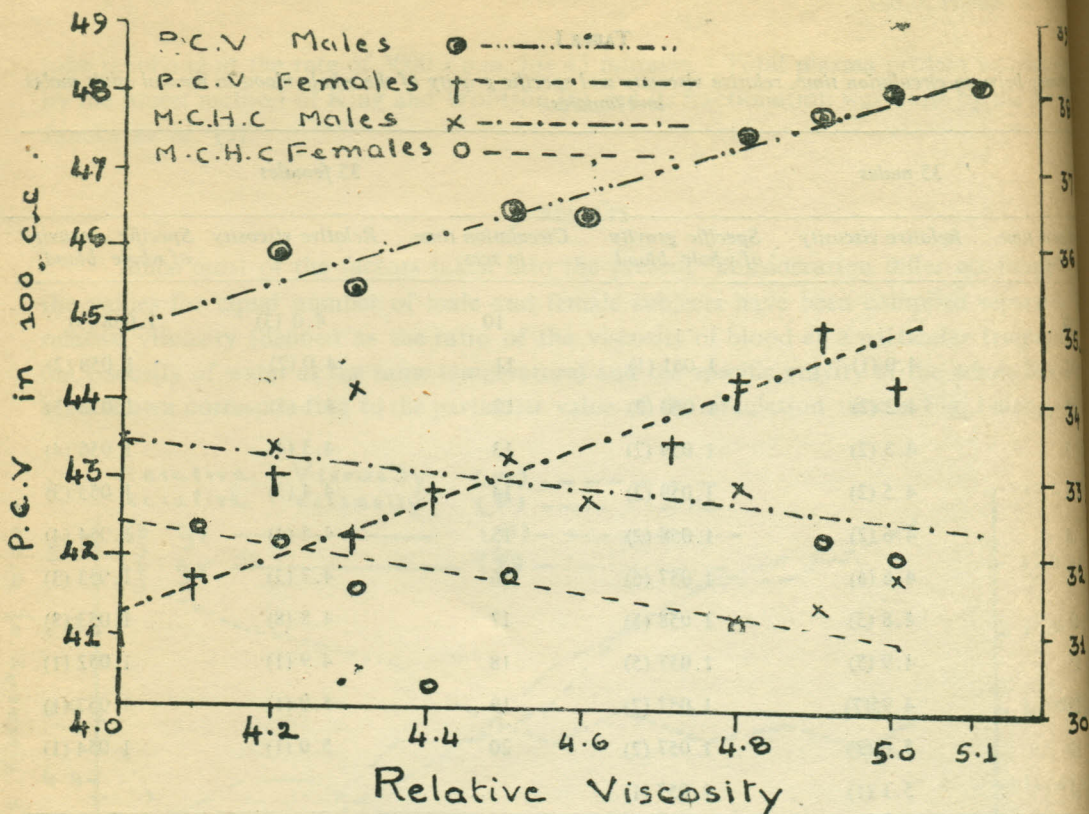


Fig. No. 2

TABLE II

Showing PVC, MCV, MCHC and total and differential protein fractions against relative viscosity in thirty five male

Relative viscosity	PCV %	MCV μ^3	MCHC %	Total protein	Albumin in	α Globulins	β Globulins	γ Globulins gm
4.0 (1)	45.8	84.2	34.06	7.9	4.6	0.83	0.80	1.57
4.1 (—)
4.2 (2)	45.8	92.5	33.80	7.2	3.6	0.87	0.98	1.75
4.3 (2)	45.5	91.0	34.70	7.2	3.8	0.78	1.05	1.57
4.4 (—)
4.5 (2)	46.4	93.3	33.2	7.7	3.9	0.36	1.03	1.80
4.6 (8)	46.8	92.6	32.7	7.1	3.7	0.84	1.02	1.54
4.7 (—)
4.8 (5)	47.4	96.6	32.4	7.3	4.0	0.89	0.83	1.40
4.9 (5)	47.6	92.6	31.3	7.3	3.9	0.76	0.88	1.70
4.96 (7)	47.7	94.8	31.9	7.2	4.2	0.85	0.71	1.45
5.00 (2)	48.0	96.2	31.3	7.4	4.2	0.98	1.32	1.10
5.1 (4)	48.1	90.0	32.3	7.3	4.0	0.95	0.00	1.40
Mean	47.0	93.4	32.4	7.27	3.94	0.85	0.92	1.55
S.D.	1.60	3.96	1.65	0.355	0.49	0.38	0.84	0.91
C.V.	3.4	4.2	5.1	4.72	12.6	45.0	91.01	58.7

TABLE III

Showing packed cell volume, mean corpuscular volume, mean corpuscular haemoglobin concentration, total and differential protein fractions against relative viscosity in thirty five females.

Relative viscosity	PCV	MCV in;	MCHC	Total proteins	Albumins in	α Globulins	β Globulins	γ Globulins gms.
	%	μ^3	%					
4.0 (5)	40.8	90.6	32.3	6.8	3.9	0.72	0.80	1.38
4.1 (3)	41.6	88.2	32.3	6.9	4.2	0.76	0.63	1.31
4.2 (2)	42.9	88.0	32.0	7.0	4.1	0.66	1.00	1.24
4.3 (3)	42.3	95.8	31.6	7.1	3.8	0.70	1.03	1.57
4.4 (3)	42.8	101.0	30.3	7.3	3.9	0.75	1.05	1.60
4.5 (4)	43.0	104.0	32.1	7.2	4.0	0.94	1.00	1.26
4.6 (—)
4.7 (3)	43.5	97.6	32.0	7.1	4.1	0.71	1.21	10.09
4.8 (8)	43.75	96.2	31.2	7.4	4.2	0.83	1.20	1.17
4.9 (1)	44.0	90.0	32.2	7.3	4.0	0.90	1.25	1.15
4.95(—)
5.0 (2)	44.3	96.3	32.0	7.4	4.2	0.92	1.25	1.03
5.1 (—)
Mean	42.8	95.7	31.7	7.1	4.0	0.81	1.03	1.25
S.D.	± 2.32	± 9.3	± 1.15	± 0.53	± 1.10	± 0.51	± 0.38	± 0.17
C.V.	5.4	9.6	3.6	7.4	2.6	63.0	37.00	13.00

DISCUSSION

The rheological character of the blood depends on its viscosity and the relationship looks to be almost linear—(Fig. 1) Individuals having a particular viscosity were found to have not much different a circulation time. The viscosity found in our subjects falls within the normal range of 3.5 to 5.4 (17). On the average, the viscosity of blood in males was found to be higher than that in females and that it is in conformity with the findings of Hess (4).

The specific gravity of blood did not show such a perfect correlation with the circulation time. On the whole, they seemed to keep an inverse relationship between each other upto the circulation time of 16 seconds.

Thus the viscosity being found to be a more determining factor, than the specific gravity in regulating the rate of flow of blood (Circulation time), the factors affecting it drew further considerations. The viscosity of the whole blood depends on the cellular elements as well as

the fluid elements in it. Of the cellular elements, the white blood cell concentration is significant only when their number is abnormally high, while the role of platelets is doubtful.

According to Nygard (8), within the range of 15-50 ml. PCV, the viscosity shows a linear relationship with it. The same has been found to be true in our cases both for males and females (Fig. 2). The PCV for female subjects being found to be low compared to those of males for the same relative viscosity of blood. Gregersen and his associates (3) have shown an increase in viscosity with increase in cell size. This could not be corroborated by our study. The reason for this may be, that, they had found it in different mammalian species with same hematocrit value, while those of our cases had variable blood factors including hematocrit value. Moreover small crenated cells may increase the viscosity due to its increase in intracellular viscosity. Again, for the same reason MCHC by virtue of its property of changing intracellular viscosity can affect the viscosity of the whole blood as shown by Erslev *et al.*, (2). In all the cases studied here, both males and females showed a regular fall in MCHC with the rise in the viscosity of the whole blood. This can be correlated with the specific gravity of the whole blood which has been found to have, in general, an inverse trend with the viscosity as shown in Table I. Thus MCHC has been found to change in the same direction as the specific gravity of blood and this is understandable from the fact that hemoglobin content of blood can be calculated, from its specific gravity (14), which vary directly with each other. So, from our study, it seems, that the intracellular viscosity plays a minor role compared to the extra-cellular viscosity of blood as affected by the packed cell volume.

Of the plasma elements of the blood, the protein is supposed to form an important factor altering its viscosity and hence flow. As worked out by Wells *et al.* (16), dilution of protein reduces the whole blood viscosity by lowering the plasma viscosity and by decreasing protein induced red cell aggregation. Other group of workers as Wells, Cox and Shahviar (15) had noted an increased blood viscosity with hypotonic dilution. We have not been able to find any change in the viscosity of the whole blood in relation to that of plasma protein, not even to that of any particular fraction of protein as advocated by workers reported in this paper earlier.

On the whole, it seems, that PCV is the most dominant factor altering the viscosity of the whole blood and hence the circulation time. The role played by other factors is inconclusive and controversial and the role of plasma proteins can not be definitely known unless other parameters are kept constant, for example, just dilution of protein may change the fluidity of the plasma as also the shape and size of the cells which will bring other factors into play masking the effect of low protein concentration.

SUMMARY

Seventy normal subjects of age group 18 to 21 years belonging to both the sexes of equal distribution were investigated.

Their 'arm to throat' circulation time found by calcium gluconate method was compared with the relative viscosity and the specific gravity of blood. The viscosity of blood was found to alter the circulation time.

The viscosity, in turn, was found to increase with the increase in PCV of blood.

The different protein concentrations of the plasma failed to show any corresponding change in viscosity while the specific gravity of the whole blood and MCHC showed an inverse relationship with the viscosity.

REFERENCES

1. Best, C.H., and M.B. Taylor. *The Physiological Basis of Medical Practice*, The Williams and Wilkins, Baltimore, 7th Edn., 225, 1961.
2. Erslev, A.J. and J. Atwater. Effect of mean corpuscular haemoglobin concentration on viscosity. *J. Lab.Clin.Med.* **62**: 401, 1963.
3. Gregersen, M.I., B. Peric, S. Chier, D. Sinclair, C. Chang and H. Taylor. The influence of erythrocyte size on the viscosity of blood at low shear rates. *Abstr. of the fourth international congress of Rheology*. Brown University. 279, 1963.
4. Hess, W.R. Viscositatdes Blutes and Herzarbeit, Viertelshrsschr. D. *Natuff-Cosellsch, Zurich* 1906.
5. Jancks, W.P., M.R. Jilton, and R. Durram. Paper electrophoresis as a quantitative method. *Biochem. J.* **60**:205, 1955.
6. King, E.J. and J.D.P. Wootton. *Microanalysis in Biochemistry*, J. and J. Churichill Ltd., London 3rd Edn., 30, 1956.
7. Musser, J.H., M.G. Wohl. *Internal Medicine*, Lea and Febiger, Philadelphia, 5th Edn. 758, 1951.
8. Nygaard, K.K., R.M. Wilder, and J. Berkson. The relation between viscosity of blood and relative volume of erythrocyte. *Am. J. Physiology.* **114**:128, 1935.
9. Peter, W. Rand and Eleanor Lacombe,. Hemodiluation, Tonicity and blood Viscosity. *J. Clin Invest.* **43**:2214, 1964.
10. Philips, R.A., D.D. Van Slyke, P.B. Hamiltor, V.P. Dole, K. Emerson, Jr. and R.M. Archibald. Measurement of specific gravities of whole blood and plasma by standard copper sulphate solution. *J. Bio. Chem.* **183**:305, 1950.

11. Roe E. Wells, Jr., R.D. Perera, Thomas Gawronski and A.A. Shawriari. Effect of plasma proteins upon rheological character of blood in the microcirculation. *J. Clin. Invest.* **142**:991 1963.
12. Rushmer, R.F. *Cardio-Vascular Dynamics*, W.B. Saunders Co., London, 2nd Edn. 7, 1958.
13. Spier, L.C., I.S. Wright, and L. Saylor. *Am. Heart J.* **12**:511, 1936.
14. Van Slyke, D.D., R.A. Philips, V.P. Dole, P.B. Hamilton, R.M. Archibald and J. Palmer. Calculation of Haemoglobin from Blood specific gravity. *J. Biol. Chem.* **183**:349, 1950.
15. Wells, R.E. Jr., P.J. Cox, A.A. Shahariari. Effects of pH and osmolarity upon blood viscosity. *Clin. Res.* **11**:176, 1963.
16. Wells, R.E., Jr. E.W. Merrill and H.G. Gabelnick. Shear rate dependence of viscosity of blood. Interaction of red blood cells and plasma proteins. *Trans. Soc. Rheology.* **6**:101, 1962.
17. Wintrobe, M.M. *Clinical Haematology*, Lea and Fabiger, Philadelphia, 5th Edn., 325, 1962.