INFLUENCE OF FLOW PROPERTIES OF BLOOD UPON VISCOSITY-HEMATOCRIT RELATIONSHIPS *

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The influence of the red cell concentration (per cent hematocrit) upon blood viscosity is well known. Some physiology texts (1) portray this relationship by means of a diagram in which relative or apparent viscosity is plotted against the per cent hematocrit (Figure 1). It has been demonstrated that besides the effect of cell concentration the viscosity of blood varies both as a function of the shearing stresses developed within the fluid and the rate at which these forces are distributed between the adjacent fluid elements during flow (2-4). The relationship or ratio of shear stress to the gradient of velocity, or shear rate, defines the viscosity of the fluid in the absolute dimensions of dyne-seconds-cm⁻², or poise. In his original definition of this property of fluids, Newton made the assumption that the ratio of shear stress to shear rate was constant for all fluids. Contemporary studies of the flow properties of various complex fluids have shown that many of these demonstrate a disproportionate change in shear stress as shear rate increases or decreases; in fact, rheological nomenclature is based upon the direction in which this ratio changes with change in shear rate (5, 6). The viscosity of blood has been shown to exhibit this type of shear rate dependence, i.e., viscosity decreasing as shear rate rises (4). At the time Poiseuille made his classic contribution to the dynamics of flow in tubes, it was not known that complex fluids such as blood rarely maintained a constant of proportionality between shear stress and shear rate. The Poiseuillian equation therefore has as its first condition that the fluid under study be a Newtonian fluid, i.e., one with a constant ratio of shear stress to shear rate. Many workers have

values of shear stress over a range of shear rates (10 to 200 sec⁻¹) that are a magnitude less than those of the smaller capillary tube viscometers (4). Such instruments involve the rotation of a bob or cylinder within the fluid at a known rpm. The impedance to rotation (torque) upon the bob itself, or upon an external concentric cyclinder, is a function of the shear stress and thereby of viscosity of the fluid contained between the bob and cylinder or the cylinders (14).

Since blood viscosity is dependent on shear rate, which for cylindrical vessels is a function of the vessel radius and velocity flow, it is apparent that

pointed out that blood is a non-Newtonian fluid

(3, 7, 8), that the law of Poiseuille cannot be di-

rectly applied to the conditions of flow in the capil-

lary circulation (9, 10), and that the viscosity of

blood is anomalous (11-13). In all of these refer-

ences, however, capillary tube viscometers or the

vessels of experimental animals were used as the

testing devices. The use of a capillary viscometer,

which so well imitates the anatomy of a blood

vessel, has certain practical limitations that make

it difficult to derive values of blood viscosity over

the lower ranges of shear rate (below 100 sec^{-1})

(14, 15). The interpretation of the results of viscometry of such fluids in capillary tube viscom-

eters is complicated because the change in shear

rate between a zero value at the central axis and a

maximum value at the tube wall is not linear with

a change in radius (14). To obtain an accurate

estimation of shear rate in tube-type viscometers,

it is necessary to determine the flow rate as a func-

tion of the pressure drop across the ends of the tube at a number of flow rates both greater and

less than the one for which the shear rate is de-

sired. Haynes and Burton have derived shear

rate values for capillary tubes from analysis of the

Viscometers are available that provide accurate

pressure-flow curves of red cell suspensions (3).

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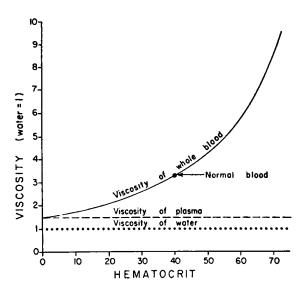


FIG. 1. EFFECT OF HEMATOCRIT ON VISCOSITY. From Textbook of Physiology, A. C. Guyton, Ed. Reproduced through permission of the publishers, W. B. Saunders Co., Philadelphia, Pa.

within the human vascular system there may exist, at any instant of flow, an infinite variety of shear rates. Accordingly, the use of viscosity values in studies of pressure-flow relationships or of related hydraulic phenomena in the human circulatory system would be meaningful only when such values are related to a specific, or point, value of shear rate. This report describes a study of freshly drawn samples of whole blood with many different hematocrit values in which viscosity was measured at various specific rates of shear.

METHODS

Blood samples were obtained by venipuncture from normal subjects and hospitalized patients. A 5-ml sample was gently aspirated into a silicone-coated glass syringe through a no. 18 stainless steel needle. Tourniquets were loosely applied before blood collection and only samples that were quickly and easily obtained were used, i.e., the presence of bubbles or difficulty in entering the vein precluded the use of the sample. A 2-ml volume was placed into the cup of the viscometer and analyzed immediately. Two ml of the remaining sample was mixed with a dry powder of 2.5 mg of ammonium oxalate and 1.5 mg of potassium oxalate, 1 ml of which was placed in a Wintrobe hematocrit tube and centrifuged at 3,000 rpm for 30 minutes. Anticoagulants were not used with the sample placed in the viscometer. Samples were drawn in the fasting state, or no earlier than 12 hours after intravenous fluids or blood transfusions. Patients with abnormal red cell forms were not included in the study. Two of the patients with high hematocrit values had secondary polycythemia, and their arterial blood gases are recorded in conjunction with their viscosity data. Since the factor of time was critical in the viscometry, viscosity studies were carried out at the bedside or with the patient next to the viscometer in the laboratory. Rarely did the maximum time from vein entry to completion of viscometry take more than 5 minutes. Determinations of the viscosity of freshly drawn plasma were also carried out, usually immediately after the whole blood study was completed. Celluloid or plastic tubes used as containers were centrifuged at 3,000 to 4,000 rpm for 3 minutes, and the supernatant plasma was decanted into the measuring cup and analyzed.

The viscometer used in these studies has been described in detail elsewhere (4). In principal, the viscometer is a torque-measuring device capable of analyzing shear stress as a direct function of the torque developed within a fluid at various, preset rates of shear. The instrument is a cone-plate type viscometer requiring 2 ml of fluid placed between a very low angle cone $(1^{\circ} 33')$ and a flat plate. The flat plate is represented as a floor of the cup supported just beneath the cone. Both cone and cup surfaces are rhodium-plated. The cone is rotated by a constant speed motor that can be set at four different rates of speed: 6, 12, 30, and 60 rpm. The degree of torque imposed on the cone and its spindle is registered by a calibrated spring connecting the spindle and the motor. The spring flexion is a linear function of torque, which at maximum contraction equals 673.7 dyne-cm. A pointer attached to the spring overrides a circular dial, numbered from 0 to 100 per cent of maximum spring flexion, that records percentage of maximum deflection and thereby percentage of maximum torque. Since shear rate is a function of the cone angle and rpm, the four speed settings provide shear rates of 12.4, 24.7, 61.8, and 123.6 inverse seconds.¹ The cup and fluid sample are held at a constant temperature by perfusion of water from a constant temperature water bath between the inner wall of the cup and an outer jacket that surrounds both the walls and the bottom of the cup. The cup is approximated to the cone by a threaded groove at its lip that is attached to a cylinder suspended from the motor housing, and the groove is calibrated to allow the cup to rise 0.024 of an inch for each 360° rotation. Contact of the cone tip and cup is determined by motion of the cone when the cup is rotated by hand. The cup is then backed off just to a point at which no impedance on the cone is

¹ The value of inverse seconds is derived from the definition of shear rate, or the velocity gradient that has the dimensions of velocity in centimeters per second per unit distance between fluid elements in centimeters. Hence, centimeters per second per centimeter equals 1/second, or sec⁻¹, or inverse seconds. A more complete exposition of this quantity can be found in references that include the derivations of shear rate for a cone plate viscometer (4, 14, 16-18).

noted. Between each sample analysis, cone and cup are washed with a dilute solution of Alconox, rinsed thoroughly with distilled water, and dried. The cup is brought to 37° C before the collection of a blood sample is begun. Temperature control is such that a variation of $\pm 0.1^{\circ}$ C is not exceeded.

Earlier studies of fluids of constant viscosity included a technique of heating the upper part of the viscometer so that there was no heat loss from the sample to the cone. Subsequent studies revealed that heating of the bottom and walls of the cup by the high perfusion rate from the constant temperature water bath was sufficient to prevent any significant temperature drop within the sample; hence, temperature control of the cone, spindle, and motor housing was not continued. The process of clotting did not appear to influence the results up to the point of clotting, which usually appeared suddenly. This was shown by a sudden erratic motion of the recording pointer to full scale. Readings were reproducible at any shear rate until the moment of clotting. Recordings of readings at the increasing rates of shear followed by similar measurements at decreasing rates of shear showed no evidence of either time dependency (hysteresis) or vield values of any sample tested. Generally, 4 to 6 readings were made at each speed setting. The characteristics of the dial indicator and scale permitted a reading accuracy of from 0.1 per cent at the highest to 2 per cent at the lowest scale values. These values are derived from the relative error on the basis that any reading was accurate to ± 0.1 of the observed scale values.

The problem of being certain that no turbulence had developed within the fluid at the higher speeds was settled as follows. Check runs were made with 0.9 per cent saline solution as a test fluid, and the linearity of the torque with rotational speed was noted over the entire range. Had there been turbulence, the torque would have increased out of proportion to rotational speed. Since the saline remained in laminar flow and there was linearity of the relationship between torque and rotational speed, it was unlikely that turbulence had developed within the sample. Since whole blood is under all conditions more viscous than water, it must have also remained in laminar flow within the rotational speeds used with this viscometer.

A total of 43 samples was analyzed. The data for each sample were obtained from the readings of torque in dynecentimeters, converted to shear stress in dynes per cm², and then plotted against the corresponding values of shear rate. The details of the mathematical development of the formula in which percentage of maximum torque relates to units of shear stress have been given elsewhere (4, 17). It can be shown with the present instrument that shear stress $= \frac{\max \text{ torque}}{2/3 \pi r^3} \times \text{scale reading in per cent, where } r$ represents the radius of the cone in centimeters. Therefore, each unit of scale reading (per cent of full scale) is multiplied by 0.206 to obtain the shear stress in dynes per

fore, each unit of scale reading (per cent of full scale) is multiplied by 0.206 to obtain the shear stress in dynes per cm². Apparent viscosity is expressed in units of centipoise (poise \times 100) as derived from the ratio of shear stress (dynes per cm²) to shear rate (sec⁻¹).

RESULTS

The plot of shear stress against shear rate produced a family of curves demonstrating the shear thinning properties (as shear rate increased) of whole blood in all instances (Figure 2A). From the shear stress: shear rate data, viscosity values in centipoise were obtained and plotted against the various values of shear rate in inverse seconds (Figure 2B). These lines reveal the viscosity: shear rate curves of shear thinning or pseudoplastic fluids in which viscosity is highest at the low shear rates, falling as shear rate increases. The Bureau of Standards calibration oil (H) has a constant viscosity of 4.69 centipoise at 37° C. Viscosity values of the 43 studies were plotted against per cent hematocrit at the lowest shear rate of 12 sec⁻¹ and at the highest shear rate of 120 sec^{-1} (Figure 3). The curve for 12 sec^{-1} shows that at hematocrit values below 25, the viscosity is 3 centipoise or less, whereas at hematocrit values near 70, viscosity approximates 20 centipoise. The plot is considerably less curved than the more familiar one of the reference text shown in Figure 1. At the higher shear rate of 120 sec⁻¹ the same blood is less viscous at any equivalent hematocrit value, hematocrit values below 25 revealing viscosities of 2 centipoise or less, whereas the higher hematocrit values near 70 show viscosities of approximately 12 centipoise. With this modest difference in shear rates (industrial fluids are frequently tested over a range of 100 to 100,000 sec^{-1}), there is a striking difference in the viscosity values for any given hematocrit. The curve at the higher shear rate moves down on the ordinate and to the right on the abscissa. The direction of this shift with increasing shear rate is substantiated when one compares the data obtained from capillary viscometers. Because of the dimensions of a small capillary and the pressure gradients or flow rates used in biological work, shear rates in these devices tend to be relatively high, as previously noted. The shear rate of a capillary tube can be estimated if certain assumptions are made. If it is assumed that blood is a Newtonian fluid, i.e., one with a constant viscosity, or one whose ratio of shear stress to shear rate remains at constant, it can be shown that the formula 4 \overline{V}/r represents the shear rate at the wall of the tube (18), \overline{V} representing the mean velocity in centimeters per sec-

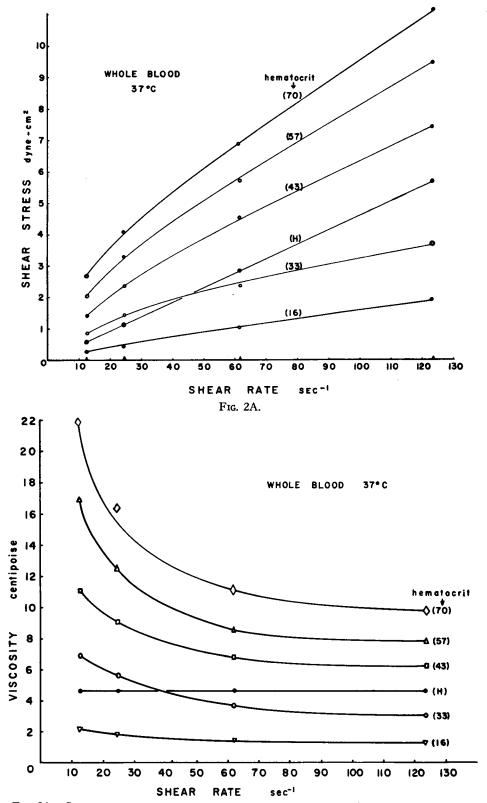


FIG. 2A. SHEAR STRESS-SHEAR RATE DIAGRAMS OF WHOLE BLOOD OF 5 DIFFERENT HEMATOCRIT VALUES. H is Bureau of Standards calibration oil. FIG. 2B. VISCOSITY-SHEAR RATE DIAGRAMS OF BLOOD SAMPLES DESCRIBED IN FIGURE 2A.

ond. A report of work in which a capillary tube was used (19) stated that the tube had a radius of 0.42 mm and that there was a mean flow rate of 0.1 ml per second. This capillary, therefore, had a shear rate of 1,722 sec⁻¹. The data from this work. which used a capillary tube, are plotted in conjunction with the viscosity and hematocrit values of 12 and 120 sec⁻¹ (Figure 4). The good comparison between the curve in Figure 1 and the curve in Figure 4 labeled "capillary" is due to the fact that most references from which these data are obtained use capillary-type viscometers. Two of the samples studied were obtained from patients with secondary polycythemia owing to chronic pulmonary insufficiency. The hematocrit of one was 66 per cent with an arterial oxygen saturation of 81.5 per cent. The other sample had a hematocrit of 68 per cent with an arterial oxygen saturation of 69 per cent. Since these two arterial samples were placed in an open cup, the Po2 was probably higher than the value which existed arterially in vivo. The Po2 was not monitored during viscometry nor was it measured in the other samples, all of which were venous in origin. All other samples of abnormally elevated hematocrit values were obtained from patients with well established diagnoses of polycythemia vera.

The flow properties of plasma were also studied.

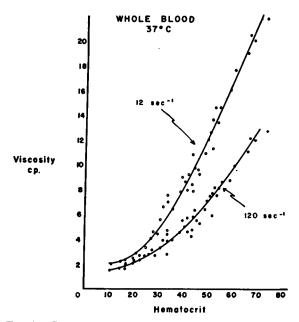


FIG. 3. COMPARISON OF VISCOSITY-HEMATOCRIT RELATION-SHIPS AT TWO DIFFERENT SHEAR RATES.

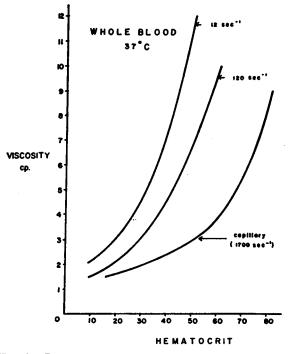


FIG. 4. COMPARISON OF VISCOSITY-HEMATOCRIT DIAGRAMS OF 3 SHEAR RATES.

Compared with the range of viscosity values for whole blood, viscosity values of plasma were small. Above a shear rate range of 60 sec⁻¹, the values were all approximately the same, 1.7 ± 0.1 centipoise. As Figure 3 shows, the viscosity curves approach the value of 1.7 as cell concentration approaches zero. The influence of anticoagulants and of other rheological properties of plasma has been discussed previously (20).

DISCUSSION

These studies indicate that the viscosity of whole blood is dependent not only upon the volume concentration of red cells, but also upon the mechanical forces operating within the fluid during flow. Well established principles of fluid mechanics define these internal flow forces in terms of shear stress and shear rate, the terms employed in this report. The many studies that describe the influence of percentage hematocrit upon blood viscosity are essentially similar in their conclusions as to the degree of effect red cell concentrations have upon viscosity values (19, 21, 22). In almost every instance these studies were conducted at relatively high ranges of driving pressure and in small capillary tubes. Since shear rate is a function of flow rate and tube radius, it can be shown that the shear rates in these studies were of the order of 1,000 sec⁻¹ or higher. The shear rate ranges of the report of Haynes are probably lower than this (23). This does not imply that such data do not have physiological significance, for it is likely that in the ascending aorta, in cases of high cardiac output, or at the orifices of stenotic valves in disease, shear rates in these higher ranges probably are present. The determination of what rates of shear are physiologically significant is complex. A crude approximation of the shear rate at the wall of the aorta in normal man at rest is probably around 100 sec⁻¹; this is based on the formula that for a Newtonian fluid the shear rate at the tube wall is obtained from the values of 4 \overline{V}/r , as stated above. An aortic blood flow velocity of 35 cm per second and a radius of 1.3 cm (24) would result in a shear rate of 108 sec⁻¹. This derivation does not take into account the influence of nonparallel walls, pulse waves in the fluid and in the vessel wall, and other related factors. The derivation or even estimation of shear rates in other parts of the microcirculation is hazardous, for acceptable definitions of flow rate in smaller arteries, arterioles, and venules have not been presented. Using photographic techniques, Lee has estimated that the blood flow in the "end arterioles" of the bulbar conjunctiva in man demonstrates a flow velocity of 0.11 mm per second (25). If one assumes that an end arteriole varies from 50 to 500 μ in diameter, then in a vessel 100 μ wide, by the formula 4 $\overline{\nabla}/r$ as above, blood in these arterioles would be subjected to a shear rate of about 10 sec⁻¹. The validity of these dimensions of flow rate values cannot be explored here, nor can the estimations of the shear rate in these smaller vessels be more than gross approximations until further quantification of the rates of flow in resting man is presented. For the present, we believe that the higher shear rates occur in the major vessels and the lower rates, perhaps less than 100 sec⁻¹, in the smaller arterioles and venules. Rheologically, the capillary is a separate problem, in that plug flow occurs in these smallest vessels so that the flow-dependent properties of the fluid rest with the plasma.

Although many of the reports on studies of

blood viscosity in capillary tube systems refer to the dimensions of shear stress and shear rate, none has measured one while holding the other constant. The measurement or derivation of shear rate below 100 to 200 sec⁻¹ for non-Newtonian fluids in capillary tubes requires precise, microscopic measurements of flow rate and tube dimensions. It seems more practical and is mathematically less complex to use those devices capable of quantitating shear stress and shear rate values directly. Derived values of viscosity can then be applied to the conditions of flow within the vascular system where shear rate can be specified.

On the basis of modern concepts of fluid engineering, a cellular suspension such as blood would be predicted to show a shear rate dependence of the shear thinning variety. It has been shown that suspensions with 30 per cent or more of suspended matter will characteristically demonstrate this type of flow behavior (26). At least four mechanisms can be invoked to explain or predict the shear rate dependence of blood: 1) the alignment of the asymmetrical protein molecules at increasing rates of shear; 2) the disassociation of associated proteins in aggregated clusters; 3) the disassociation of a protein red cell network; and 4) the orientation of the suspended red cells at increasing rates of shear (27-30). In both 1 and 4, alignment produces a situation in which there is less interference between molecules or cells. Disassociation of clusters or networks may or may not produce the decrease of viscosity, but unquestionably 1 and 4 would produce a decrease with increasing shear rate. These matters have been explored in detail elsewhere (15, 31). This report is not designed to review or extend these considerations except in respect to a fifth mechanism used in the biological literature to explain changes in blood viscosity as a function of tube or vessel diameter. The phenomenon by which viscosity falls as tube diameter is decreased was described by Fåhraeus and Lindqvist (10). This well known observation has been ascribed to the accumulation of cells near the central axis of the stream, thus allowing a fluid very low in or free of cells to flow along the wall. The reduced resistance to flow resulting therefrom is considered to account for the viscosity changes in the small Although widely accepted, the precise tubes.

definition of how, or final proof that axial streaming occurs and accounts for the viscosity change is not yet at hand. Bayliss (31), in a review of this matter, comments on the reservations necessary even in the interpretation of cinephotomicrography where a cell-free layer would appear to be well established (32), and Haynes (33) also notes that few quantitative studies have been made of this effect. Very high-speed photography (3,000 frames per second and more) by Bloch (34) of blood flow in the mesenteric vessels of small animals also leads to some reservations as to the validity of an axial streaming theory. His films, which we have observed with care, do not demonstrate a persistent cell-free layer at the wall, but rather an erratic cellular concentration across the entire vessel segment, with plasma gaps appearing without specific orientation or location. The pros and cons of this matter are beyond the scope of this paper, although the viscosity variations in small tubes may be related in part to the mechanical (shear thinning) properties of the fluid. For a Newtonian fluid, shear rate varies directly as a function of flow velocity and inversely as a function of vessel radius or diameter. If these functions of shear rate are applicable to blood, then a decreasing vessel size should lead to an increasing shear rate and a decreasing blood viscosity. Such an application of the properties of blood that are dependent on shear rate must be considered in the context of the many other variables of the flow dynamics operating within the vascular system.

It does seem appropriate, however, with present knowledge, to take cognizance of the fact that the viscosity of blood is not a constant value under the dynamic flow conditions and considering the physical characteristics of the human circulatory system. The fluid mechanical forces that determine the dependence of viscosity upon flow velocity and vessel radius are measurable. To this extent the use of viscosity values and the interpretation of hemodynamic phenomena will be more meaningful if the rheological parameters of shear rate are known or specified.

SUMMARY

The viscosity of samples of freshly drawn whole blood of many different hematocrit values was analyzed in a cone-plate viscometer over a shear rate range of 12 to 120 sec⁻¹. The viscosity of blood was shown to be dependent upon the percentage hematocrit and the velocity distribution, or shear rate, during flow. It was demonstrated that for a given hematocrit value, blood viscosity is elevated at low rates of shear and decreases as shear rate is increased. Since there is a broad range of shear rate values throughout the vascular system, the viscosity of blood may be any one of many values in different parts of the system.

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