THE VISCOSITY OF ERYTHROCYTE SUSPENSIONS

A REVIEW OF THEORY

ROBERT H. HAYNES
From the Committee on Biophysics, University of Chicago, Chicago, and the Department of Biophysics, University of Western Ontario, London, Canada

ABSTRACT Blood and erythrocyte suspensions have non-linear pressure-flow curves and so do not possess a unique Newtonian coefficient of viscosity (or its reciprocal, the fluidity) except in the physically unrealizable limits of infinite flow rate and tube radius. However, three coefficients can be defined which are related mathematically to one another and which converge in these infinite limits. They are first, the apparent fluidity, which is proportional to the slope of the line joining any given point on the pressure-flow curve with the origin; second, the differential fluidity, which is proportional to the slope of the pressure-flow curve itself at any given point; and third, the generalized fluidity which is proportional to the ratio of the shear rate to the applied stress across any given cylindrical lamina (taken here at the tube wall) within the tube. These three coefficients, which are related mathematically to one another, have been calculated from measured pressure-flow curves for erythrocyte suspensions in glass tubes, and the differential viscosity has been used to develop a simple flow model in which the shear-dependent viscosity is assumed to arise from "structural changes" in the fluid as the flow rate increases. Although the physical basis of such structural changes is uncertain, it is likely that some sort of axial redistribution of the red cells is of greatest importance at normal, physiological hematocrit values.

Although the flow properties of a fluid in cylindrical tubes are completely specified by its pressure-flow curves, it is often convenient to describe its behavior in terms of a coefficient of viscosity or fluidity. For a Newtonian fluid, which obeys Poiseuille's law and has a linear pressure-flow curve (line) passing through the origin, there exists a unique coefficient of viscosity (for constant temperature) which is a constant inversely proportional to the slope of the pressure-flow line. However, in view of the non-linearity of the pressure-flow curves of blood or erythrocyte suspensions (1), it is not possible to define such a unique viscosity coefficient except in the physically unrealizable limits of infinite flow rate and tube diameter. In general, three coefficients can be defined, and they coincide in value only under the "asymptotic" conditions just mentioned. They are: first, the "apparent viscosity," which is the one most commonly quoted, and which is calculated by a direct application of Poiseuille's law to pressure-flow data (2, 3); second, the "differential viscosity," which is inversely proportional to the slope of the pressure-flow curve at a given point; and third, the "generalized viscosity," which is based on the fundamental definition of viscosity as the ratio of the applied stress to the rate of shear at a given point in the fluid (4). All these coefficients can be calculated explicitly from the empirical equation that has been used to represent the pressure-flow curves of erythrocyte suspensions (1).

The pressure-flow curves of erythrocyte suspensions in steady, non-turbulent flow, are non-linear near the origin (through which they appear to pass with a non-zero slope), but they become effectively linear with increasing pressure and flow (1). The general shape of these curves is indicated by curve A in Fig. 1; they can all be represented before the onset of gross turbulence, by an equation of the form,

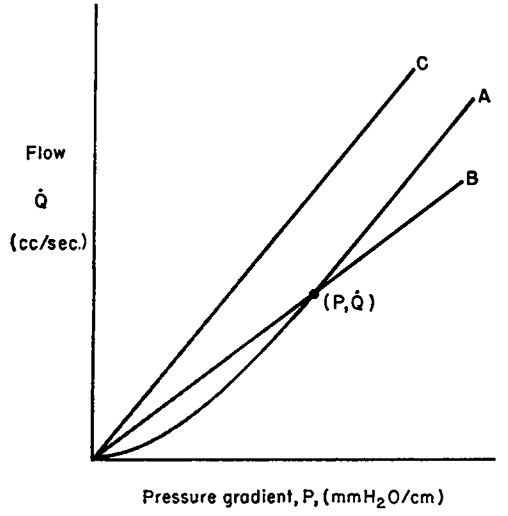

FIGURE 1 Diagram of a typical pressure-flow curve for blood or an erythrocyte suspension (*A*). The apparent fluidity of the suspension under the flow conditions defined by the point (P, $\dot{Q}$) is proportional to the slope of the line *B*. The differential fluidity at the point (P, $\dot{Q}$) is proportional to the slope of the pressure-flow curve itself at this point. Under asymptotic conditions, as the point (P, $\dot{Q}$) moves out to infinity along the curve *A*, the line *B* approaches the line *C* whose slope is equal to the final linear slope of *A* and is proportional to the asymptotic fluidity of the suspension.

$$\dot{Q} = MP - B(1 - e^{-kP}) \tag{1}$$

where $\dot{Q}$ is the volume rate of flow, P is the pressure gradient *per unit tube length,* M is the limiting asymptotic slope, B is the back extrapolation of the asymptote on the negative flow axis, and k is the parameter that characterizes the shear dependence. Curves showing the variation of M, B, and k with tube radius and hematocrit have already been reported (1). The basic physical variables that describe the dynamic state of the suspension are the pressure gradient and the corresponding flow rate, *i.e.* (P, Q). In the following mathematical formalism it is assumed that equation (1) can be continuously extrapolated to infinite pressures and flows, and an asymptotic viscosity defined in terms of the parameter M. Thus, the mathematical description has direct physical significance only before the onset of macroscopic turbulence in the fluid.

1. THE APPARENT VISCOSITY OR FLUIDITY

The pressure-flow curves of an ordinary Newtonian liquid such as water or glycerine, are linear and are given by Poiseuille's law,

$$\dot{Q} = \frac{\pi P R^4}{8\mu} \tag{2}$$

where R is the tube radius, P is the pressure gradient *per unit tube length*, and μ is the Newtonian coefficient of viscosity. The reciprocal of any viscosity coefficient is called the fluidity, and it is often more convenient to use this quantity rather than the corresponding viscosity. The fluidity will be denoted by ϕ, so that in general, $\phi = 1/\eta$. The symbol η will be used to denote a non-Newtonian viscosity, while the symbol μ will be used for a Newtonian viscosity. It is clear from equation 2 that the slope of the pressure-flow lines of a Newtonian fluid is proportional to the fluidity

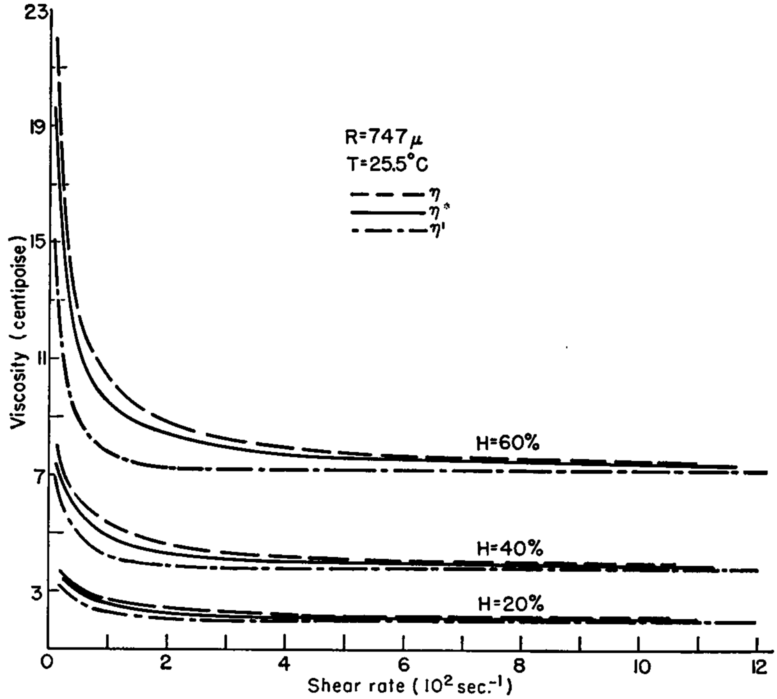

FIGURE 2 Curves of apparent (η), generalized (η^*), and differential (η') viscosity calculated from measurements of Haynes and Burton (1) for three erythrocyte suspensions (20, 40, and 60 per cent hematocrit values) in steady flow in a tube of radius 747 microns, and plotted as a function of the rate of shear at the tube wall.

and that the constant of proportionality is $\pi R^4/8$ (if the driving pressure is expressed per unit tube length).

The apparent fluidity of a non-Newtonian fluid is obtained directly from Poiseuille's law by substituting a given pair of values of pressure and flow, into equation 2, *i.e.*,

$$\phi = 1/\eta = \frac{8}{\pi R^4}\cdot\frac{\dot{Q}}{P} \tag{3}$$

Thus, the apparent fluidity of a non-Newtonian fluid is proportional to the slope of the line joining a given point on the pressure-flow curve with the origin, but, except at zero and infinite pressures, it bears no obvious relation to the slope of the pressure-flow curve itself (see Fig. 1). Substituting for $\dot{Q}$ from equation 1, the apparent fluidity of erythrocyte suspensions can be written,

$$\phi = \frac{8M}{\pi R^4} - \frac{8B}{\pi P R^4}(1 - e^{-kP}) \tag{4}$$

For large pressure gradients, the second term above vanishes, and the apparent asymptotic fluidity, ϕ_∞, is given by the first term only. It is clear from equation 4 and Fig. 1 that the apparent fluidity increases toward the asymptotic value as the point $(P, \dot{Q})$ moves out along the pressure-flow curve, which corresponds to an increase in all the following variables: pressure gradient or applied stress, volume rate of flow or mean velocity of flow, and mean rate of shear. Thus, the apparent viscosity of erythrocyte suspensions is a monotonically decreasing function of any of these variables. In Fig. 2, the apparent viscosity (dashed curves) is plotted against the shear rate at the tube wall for erythrocyte suspensions of three hematocrit values (20, 40, and 60 per cent) in steady flow at 25.5°C in a tube of radius 747 microns; the curves were calculated from previously reported pressure-flow measurements (1).

2. THE DIFFERENTIAL VISCOSITY OR FLUIDITY

The differential viscosity or fluidity is a useful quantity in hemodynamics, because, unlike the apparent viscosity, it characterizes the actual slope of the pressure-flow curve, as well as a material property of the fluid. The differential fluidity is defined to be proportional to the slope of the pressure-flow curve, with the constant of proportionality $8/\pi R^4$, so that it also reduces to the ordinary coefficient of fluidity in the case of a Newtonian liquid. Thus, we write,

$$\phi' = 1/\eta' = \frac{8}{\pi R^4}\cdot\frac{d\dot{Q}}{dP} \tag{5}$$

For suspensions described by equation 1 we have therefore,

$$\phi' = \frac{8M}{\pi R^4} - \frac{8kB}{\pi R^4}e^{-kP} \tag{6}$$

By comparing equations 4 and 6, it can be seen that the apparent and differential fluidities are equal at both zero and infinite pressure gradients. Again in Fig. 2, the differential viscosity (lower dashed and dotted curves) is plotted for the erythrocyte suspensions described above. The differential viscosity curves are of the same general shape as the apparent viscosity curves, but give a somewhat more precise picture of the dynamic behavior of the suspension, since their flatness at moderate shear rates reflects directly the corresponding effective linearity of the pressure-flow curves.

3. THE GENERALIZED VISCOSITY OR FLUIDITY

For a Newtonian fluid, the general equilibrium condition in steady flow between the applied stress and the viscous drag can be shown from simple physical considerations to be,

$$-\frac{Pr}{2} = \mu \frac{dv}{dr} \tag{7}$$

where r is the radial distance from the tube axis and dv/dr is the velocity gradient (or rate of shear). This equation defines the coefficient of viscosity as the ratio of the applied stress to the velocity gradient or rate of shear across any thin cylindrical lamina in the fluid. In a non-Newtonian fluid, the coefficient of viscosity depends on the velocity gradient across the lamina, and so in equation 7, the viscosity must be written as a function of the velocity gradient. If we write θ for $Pr/2$, and g for $-dv/dr$, the equilibrium condition for a non-Newtonian fluid can be written in the form,

$$\theta = \eta^*(g)\cdot g \tag{8}$$

where η^* (g) is the generalized viscosity, and is thereby defined in analogy with the fundamental definition of viscosity for a Newtonian fluid. Alternatively, we can write g as a function of θ by formally inverting equation 8, *viz.*,

$$g = F(\theta) \tag{9}$$

where F is at present undetermined. An explicit representation of F at the tube wall can be obtained as follows. We note first that the volume efflux from a cylindrical tube is given by,

$$\dot{Q} = 2\pi \int_0^R r\, v(r)\, dr \tag{10}$$

which, upon integration by parts and assuming no slippage at the tube wall, can be written,

$$\dot{Q} = \pi \int_0^R r^2 g\, dr \tag{11}$$

Changing variables from r to θ, this becomes,

$$\dot{Q} = \frac{8\pi}{P^3} \int_0^{PR/2} \theta^2 F(\theta)\, d\theta \tag{12}$$

Since an integral is a function only of its limits, and θ is a running variable, we can differentiate through equation 12 with respect to P, and solve for F. We therefore get the following expression for the rate of shear (velocity gradient) at the tube wall,

$$g = F(PR/2) = \frac{1}{\pi R^3}\left[3\dot{Q} + P\frac{d\dot{Q}}{dP}\right] \tag{13}$$

And so, from equation 8, the generalized fluidity at the tube wall can be written,

$$\phi^* = 1/\eta^* = \frac{2F(PR/2)}{PR} = \frac{6}{\pi R^4}\cdot\frac{\dot{Q}}{P} + \frac{2}{\pi R^4}\cdot\frac{d\dot{Q}}{dP} \tag{14}$$

For erythrocyte suspensions described by equation 1, this becomes,

$$\phi^* = \frac{8M}{\pi R^4} - \frac{6B}{\pi P R^4}\left[1 - (1 - kP/3)e^{-kP}\right] \tag{15}$$

which gives the ratio of the rate of shear to the applied stress at the tube wall in terms of the parameters of the pressure-flow relation. In comparing this with equations 4 and 6, it can be seen that all three coefficients are equal at both limits $P \to 0, \infty$. The generalized viscosity at the tube wall (middle solid curves) is also plotted in Fig. 2 *versus* the rate of shear at the tube wall.

Having now defined the apparent, differential, and generalized coefficients of viscosity, it is easy to deduce a simple relation among them. Recalling the definitions given in equations 3 and 5, it is clear from equation 14 that we can write,

$$4\phi^* = 3\phi + \phi' \tag{16}$$

or, in terms of viscosities,

$$\frac{1}{\eta'} + \frac{3}{\eta} = \frac{4}{\eta^*} \tag{17}$$

This relation depends ultimately on the general equilibrium condition (equation 8) for steady flow, and therefore serves to emphasize the fact that the viscous properties of non-Newtonian fluid cannot be completely specified by an one single coefficient of viscosity. However, at the zero and infinite limits of shear stress, all three coefficients are equal and equations 16 and 17 reduce to an identity.

FLOW MODEL FOR ERYTHROCYTE SUSPENSIONS

Fluids whose pressure-flow curves are similar to those shown in Fig. 1 (curve A) may be said to possess a "structural viscosity." This means that the decline in viscosity with increasing shear or flow rates is assumed to arise from some corresponding change in the internal structure of the fluid. In the case of blood or erythrocyte suspensions with hematocrit values below 50 per cent, the structural change that gives rise to the shear-dependent viscosity is probably some sort of axial redistribution of the red cells. This idea of a structural change with increasing shear can be used as the basis of a simple phenomenological model of flow which predicts a pressure-flow relation identical with that given in equation 1.

We assume that the red cell distribution across the tube at any given steady flow rate constitutes a rather labile internal "structure" which changes with the flow or pressure gradient in such a way that the fluidity increases from a value ϕ_0 at zero pressure and approaches the limiting value ϕ_∞ as the pressure gradient is increased. Also, in view of the foregoing discussion of viscosity coefficients, it is not unreasonable to assume that at intermediate pressures, this internal structure can be characterized by the differential fluidity at any given intermediate value. Thus, let $\Phi = \phi_\infty - \phi'$ be the parameter which defines the internal structure of the fluid at any given flow rate or pressure gradient. One of the simplest assumptions that one can make regarding the change in structure with increasing pressure gradient is that the fractional change in Φ is proportional to the change in pressure, that is,

$$\frac{d\Phi}{\Phi} = -k\, dP \qquad (18)$$

This equation can be solved to give,

$$\Phi = \Phi_0 e^{-kP} \qquad (19)$$

Since $\phi' = \phi_0$ when $P = 0$, we can rewrite this in the form

$$\phi' = \phi_\infty - (\phi_\infty - \phi_0)e^{-kP} \qquad (20)$$

Recalling the definition of ϕ' and applying the boundary condition $P = 0$, $\dot{Q} = 0$, equation 20 can be integrated directly to give a pressure-flow relation identical with equation 1 in which $M = \pi R^4 \phi_\infty / 8$ and $B = \pi R^4 (\phi_\infty - \phi_0)/8k$.

DISCUSSION

Although such a mathematical model provides some further insight into the flow properties of erythrocyte and other physically similar suspensions, the physical basis of the assumed structural change is unfortunately still rather vague. The gross rheological behavior, as reflected in the general shape of the pressure-flow and viscosity curves is similar for all hematocrit values from 10 to 80 per cent. However, it is apparent that any structural changes in the suspension should be highly dependent on the hematocrit; thus, it is difficult to draw any unambiguous conclusions about the mechanism of these structural changes from the shape of the pressure-flow or viscosity curves alone.

A variety of mechanisms for structural change which could qualitatively account for the shape of the viscosity curves have been suggested (5): for example, such phenomena as rouleaux breakdown, slippage at the tube wall, seepage of the suspending liquid past cell clusters or rouleaux, and hydrodynamic orientation or axial redistribution of red cells might all contribute to the observed behavior, although the relative importance of each mechanism would presumably depend on the hematocrit. However, for erythrocyte suspensions with hematocrits up to about 50 or 60 per cent, an axial redistribution of the red cells is perhaps the most likely mechanism of "structural" change with increasing shear.

Although the existence of an axial accumulation of red cells is supported by some direct experimental evidence (6–8), the theoretical situation is by no means clear. However, two approaches to this problem might be noted. The first is based on Jeffrey's hypothesis (9) that a particle in suspension will move in such a way that the energy dissipation is a minimum. Saffman (10) has investigated the effect of the inertia of the liquid on such a particle, and found that it gives rise to a transverse force which would tend to make the particle migrate toward the tube axis; this is in accord with Jeffrey's hypothesis, since the energy dissipation due to the suspended particle is a minimum in the region of minimum shear. Unfortunately, these inertial effects are much too small to account for the degree of axial drift observed by Taylor (6). The second approach is based on the assumption that the cells rotate in the velocity gradient and are thereby subject to a transverse Magnus force; the details of this hypothesis have not been worked out for blood, although such a mechanism has been suggested for similar problems by Starkey (11) and Tollert (12). The recent model experiments of Segré and Silberberg (8) appear to have revealed an astonishing and quite unexpected feature of the axial redistribution of suspended particles: they found that small spheres of polymethyl methacrylate suspended in a liquid of equal density not only tend to move away from the tube wall in steady flow, but also away from the tube axis, so that the particles actually concentrate in an annular region concentric with the tube axis! The physical basis of the drift *away* from the tube axis is completely unknown, but it may also occur in blood, since Taylor (6) observed a decrease in optical density near the axis as well as at the tube wall; however, this axial density minimum was originally attributed to orientation of the red cells rather than to any centrifugal drift.

Thus, it would appear that although the shear-dependent viscosity of erythrocyte suspensions, as illustrated in Fig. 2, can be interpreted as arising from a change in the internal structure of the fluid with increasing shear, and although this structural change is probably caused by a redistribution of the red cells across the tube in the form of axial accumulation, the precise mechanical details of the process are still not well understood.

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