SOME POTENTIAL BLOOD FLOW EXPERIMENTS FOR SPACE

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ABSTRACT

Blood is a colloidal suspension of cells, predominantly erythrocytes, (red cells) in an aqueous solution called plasma. Because the red cells are more dense than the plasma, and because they tend to aggregate, erythrocyte sedimentation can be significant when the shear stresses in flowing blood are small. This behavior, coupled with equipment restrictions, has prevented certain definitive fluid mechanical studies from being performed with blood in ground-based experiments. Among such experiments, which could be satisfactorily performed in a microgravity environment, are the following: (a) studies of blood flow in small tubes, to obtain pressure-flow rate relationships, to determine if increased red cell aggregation can be an aid to blood circulation, and to determine vessel entrance lengths, and (b) studies of blood flow through vessel junctions (bifurcations), to obtain information on cell distribution in downstream vessels of (arterial) bifurcations, and to test flow models of stratified convergent blood flows downstream from (venous) bifurcations.

INTRODUCTION

Blood is a rather typical colloidal suspension, consisting of dispersed phases, called cells, and a continuous aqueous phase, known as plasma. The red cells (erythrocytes) are the most numerous of the cells, numbering about 5×10^9 per cm^3 and normally occupying about 42% of the blood by volume (the hematocrit). In contrast, the other types of cells occupy only about 1% of the blood. Consequently, the red cells dominate the flow behavior of the blood (except in vessels whose diameter is comparable to the cellular characteristic dimension).

Each erythrocyte is a flexible particle with a biconcave discoid shape when not deformed by stresses or crowding by other cells. It has a volume of about 90 cubic microns, a major diameter of about 8 microns and a maximum thickness of about 2 microns. Its density is about 4% larger than that of plasma. Consequently, an individual red cell at the earth's surface has a very small sedimentation rate - about 0.1 micron/sec.

However, when the local shear stress is less than about 3 dyne/cm^3 in normal blood, the red cells aggregate. The primary aggregates are formed by the joining of erythrocytes face to face, to form stacks of disks, called rouleaux. In turn, these rouleaux aggregate into larger aggregates. The sizes of these rouleaux and secondary aggregates are a function primarily of shear stress, concentration of certain macromolecules (e.g., fibrinogen) and erythrocyte concentration. This aggregation results in two effects: (1) increased rate of red cell sedimentation, and (2) red cell syneresis.

On earth, because of this aggregation, the steady settling rate of erythrocytes in normal, quiescent blood is about 10 mm/hr, or 3 micron/sec. With increased aggregation, such as often found under pathological conditions, this sedimentation rate may increase by a factor of 10, or more. While sedimentation effects normally are not a factor in blood circulation in the body (except for slow flows in the veins), they are sufficient to interfere with or confound the analysis of some blood flow experiments. Syneresis on the other hand, not only confounds analysis of blood flows but also may have physiological significance, even in the small arteries and arterioles where the major resistance to blood flow generally occurs.

Syneresis is the attractive movement of red cells together, leaving an irregularly bounded, but well defined, layer of cell-free plasma next to solid boundaries, such as vessel walls and viscometer surfaces. In a concentric cylinder viscometer, for example, this results in a time-dependent response of the instrument as the plasma layer develops at the blood-instrument interfaces, and in the steady state results in a two-phase fluid flow with a torque less than what would be required if syneresis did not occur. This effect is seen for hematocrits between 10 and 70% with a maximum rate of plasma layer development for hematocrits of 30-35%. The effect of syneresis on blood flow in vessels is mentioned later.

EXPERIMENTS

In this section, discussion will center on specific studies, for the most part already performed in ground-based experiments, that could be performed profitably in a microgravity environment.

I. Single Tube Experiments

The simpliest blood flow experiments involve steady flow of blood from a feed reservoir through a straight, circular-cylindrical tube into a discharge reservoir. The quantities measured are tube dimensions, pressure drops versus blood flow rates, blood hematocrits in the feed reservoir, and, for tubes with inside diameters below 300 μm, hematocrits of the blood in the tube and of the blood flowing from the tube.

The preferred method of showing such pressure versus flow rate data is to plot the wall shear stress, τ_w, against the average velocity divided by the tube diameter, $\bar{U} = u/D$. It can be shown that for any fluid for which the shear stress is only a function of the shear rate, a plot of τ_w versus $\bar{U}$ will define a universe curve valid for steady flow in any size tube. A typical set of data for blood of hematocrit equal to 20.1% is shown in Figure 1.

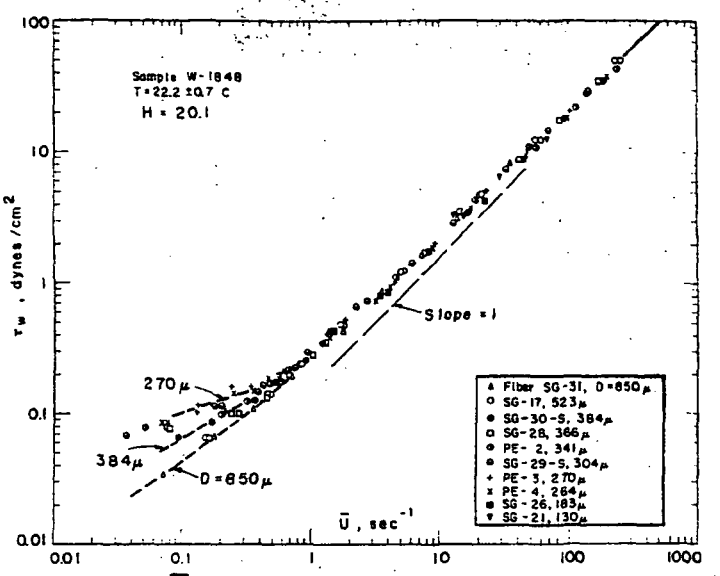

Figure 1. τ_w - $\bar{U}$ for blood in tubes of diameters from 130 to 850 μm. (Reproduced with permission from [1]).

These data were gathered by Benis for tubes whose inside diameters ranged from 130 μm to 850 μm. For $\bar{U} \geq 1$ sec^{-1}, all the data for a given blood fall on one curve, as expected, but for $\bar{U} < 1$ sec^{-1}, the data show a dependence on tube diameter. The tubes were horizontal. Original speculation as to the cause of this data dispersion centered on the possibility of erythrocyte adhesion to the tube walls at low flow rates.

However, Meiselman [2] found by microscopic observation that when $\bar{U} < 2$ sec^{-1}, the red cells flowed as aggregates and significant erythrocyte sedimentation occurred by the time blood flowed a few centimeters down the tubes. It therefore seems probable that the low $\bar{U}$ dispersion of data in Figure 1 is due to erythrocyte sedimentation. (Red cell sedimentation rate data, for blood in horizontal tubes 102-888 μm ID can be found in [2].)

It would be worthwhile to perform similar experiments in a microgravity environment so as to obtain τ_w - $\bar{U}$ data for low values of $\bar{U}$. But an even more important question could be answered by such experiments: When red cell aggregation increases (as it does in many pathological situations), does the resistance to blood flow, at a given flow rate, increase or decrease? On one hand, increasing aggregation increases viscosity and thereby flow resistance; on the other hand, the

increased aggregation (by syneresis) causes a larger marginal layer of plasma at the vessel wall, which would tend to decrease flow resistance. This question has not been answered, although it has both theoretical and clinical significance.

One study on this question, by Palmer and Jedrzezczyk [3], gives some information on this problem. Data obtained with flow of red cell suspensions through a vertical 400 μm ID tube are shown in Figure 2: a plot on the ordinate of the ratio of the pressure drop for the cell suspension to the suspending medium pressure drop (same flow rate) versus $8\bar{U}$.

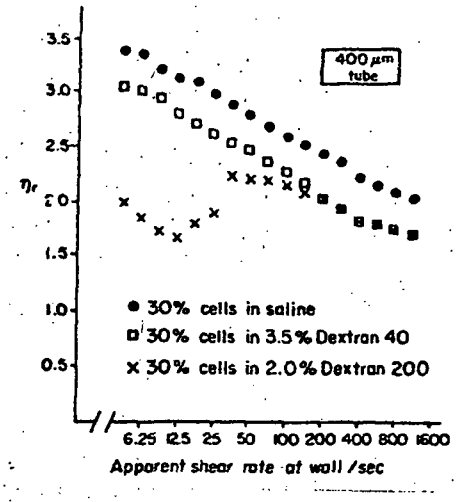

Figure 2: Relative flow resistance venous $8\bar{U}$ (Reproduced with permission from [3].)

Two suspensions are of interest: cells in 3.5 Dextran 40 solution (where cell aggregation does not occur) and cells in 2% Dextran 200 solution (very strong aggregation); the suspending media have the same viscosities. At high flow rates ($\bar{U} > 200\ sec^{-1}$) all cells are dispersed and the two suspensions show identical flow resistances; for $\bar{U} < 200\ sec^{-1}$, the aggregating suspension shows a lower flow resistance than the suspension of dispersed cells. Two comments need to be made about these experiments: (1) the red cell sedimentation velocity in the direction of flow is estimated to be significant compared to the fluid

flow velocity, and (2) this level of cell aggregation is probably at the high end of the range of pathological conditions. It would be worthwhile to repeat and extend this type of experimentation in a microgravity environment.

An additional question which needs investigation and which could be most easily studied in a microgravity environment is that of the extent of the entrance length in blood flow in vessels. Even in the absence of cell aggregation, radial redistribution of cells on entering a small vessel causes entrance lengths to be much longer than predicted on the basis of the behavior of continuum fluids, e.g., about 5000 μm in a 25 μm parallel plate channel [4]. Entrance lengths for blood flow, when stresses are low enough to permit red cell aggregation, can best be determined in the absence of sedimentation effects.

II. Bifurcation Experiments

Hollow replicas of vascular bifurcations can be made in clear, rigid plastic blocks [5]. With these flow channels, one can then study blood flow through arterial and venous bifurcations.

In arterial bifurcations (blood flows into the junction through one vessel and leaves in two other vessels) in the microcirculation (vessel diameters less than about 100 μm), erythrocytes are not distributed between the downstream vessels in proportion to the blood flow rates. Since the Reynolds number is small (1-0.01), this is not due to inertial effects, but rather due to the nonuniform distribution of red cells across the feed vessel lumen and to cell-wall interactions. The physical laws governing red cell distribution at such bifurcations are not known. Investigation of this problem, for low flow rates where red cell aggregation occurs, could be best performed under microgravity conditions.

With the Reynolds number for microcirculatory blood flow so small, there is essentially no mixing between two convergent flows downstream from a venous bifurcation, even over an axial distance of a thousand vessel diameters. If the two convergent streams of blood have markedly different hematocrits, stratified flow persists downstream from the bifurcation. Bifurcations occur so frequently along a small vein,

that several layers could exist in the stratified flow. Some combinations of layers are unstable on earth, due to gravity; a few such flows could be studied in a low gravity field to establish the validity of theoretical models of such flows.

COMMENT

A natural question asks why such experiments should be performed under conditions which minimize sedimentation effects. After all, real circulatory systems operate in a one-g field. The answer is that usually sedimentation effects are not found in the body, except perhaps in slow venous flows. This is because an elementary volume of blood, as it flows, is continuously having its orientation in the gravitational field varied and the conditions under which it flows are continuously changing. The sedimentation effects, found in in vitro experiments, are therefore of our own making; this comes about for two reasons. First, the demands of experimental precision require us to make the flow channels long (e.g., long cylindrical tubes so that the pressure drops for physiologically relevant flow rates can be precisely measured with currently available instruments) with resultant blood residence times in the flow channels of the order of minutes, allowing significant cell sedimentation. Second, when performing experiments on systems composed of very small vessels (5-100 μm ID), fluids must be brought into (and away from) the flow system through tubes which may be several inches long and in which the flow is very slow, again leading to complications due to sedimentation. These problems can be circumvented in a microgravity field.

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REFERENCES

1. Merrill, E. W., A. M. Benis, E. R. Gilliland T. K. Sherwood and E. W. Salzman: J. Appl. Physiol., 20(5), 954-967 (1965).

2. Meiselman, H. J.: Ph.D. thesis, Dept. of Chem. Eng. Mass. Inst. Tech., Oct. 1965.

3. Palmer, A. A. and H. J. Jedrzejczyk: Biorheology, 12(5), 257-264 (1975).

4. Palmer, A. A. and W. H. Betts: Biorheology, 12(5), 283-292 (1975).

5. Meiselman, H. J. and G. R. Cokelet: Microvasc. Res. 9, 182-189 (1975).