Flow of human blood through capillary tubes and red cell concentration
by Ann Elizabeth Berg

A thesis submitted to the Graduate Faculty in partial fulfillment of the requirements for the degree of
MASTER OF SCIENCE in Chemical Engineering
Montana State University

Abstract:
The flow of human "blood through capillary tubes ranging from 15.1 to 36.9 microns in diameter was studied.

It has been previously noted (2) that at small tube diameters, the red cell concentration [hematocrit) at the exit of a capillary tube may be less than the concentration at the entrance. It was hoped to find exactly where this decrease occurs, if at all. The red cell concentrations of the feed and discharge blood were measured, and were found to be almost equal. Thus there is no screening effect causing a reduction in red cell concentration with flow through small tubes.

Various feed concentrations were used, along with various flow rates. These did not change the red cell concentration of the discharge with respect to the feed.

High molecular weight Dextrans were added to change the properties of the blood. These did not change the results either; the discharge red cell concentration was virtually the same as the feed concentration.

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Signature Ann Berg

Date September 4, 1973

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ANN ELIZABETH BERG

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Approved:

Lloyd Berg
Head, Major Department

John R. Rokes
Chairman, Examining Committee

Henry L. Parsons
Graduate Dean

MONTANA STATE UNIVERSITY
Bozeman, Montana

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ABSTRACT

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BACKGROUND

Blood Characteristics

Understanding of the flow properties of blood has applications in many medical and pharmaceutical areas. By understanding both the macroscopic and microscopic behavior of blood, predictions may possibly be made about the flow in the circulatory system. Also, this information may be used in designing such medical equipment as heart-lung machines and artificial organs. Knowledge of the mechanisms of blood flow in glass capillary tubes is the first step in learning about flow in the small capillary networks of the body.

Blood is a suspension of cells in a solution called plasma. The plasma is an aqueous solution of organic and inorganic salts, other small organic molecules, such as urea and glucose, and proteins. The proteins, which make up about 7.0% of the plasma weight, are macromolecules of molecular weights ranging from 40,000 to over 1,000,000. These proteins consist of albumin, fibrinogen, and globulins. Albumin, with a molecular weight of 69,000, serves as a super transport molecule and helps regulate plasma volume. Fibrinogen is much larger, with a molecular weight of 170,000. It plays an important role in the clotting mechanism. Thrombin converts it to fibrin, which is the monomer used in building up a clot.

The cells consist of red blood cells (RBC's), white blood cells, and platelets. The red cells, also known as erythrocytes, make up about 97% of the cell volume. These cells have a biconcave disc shape,

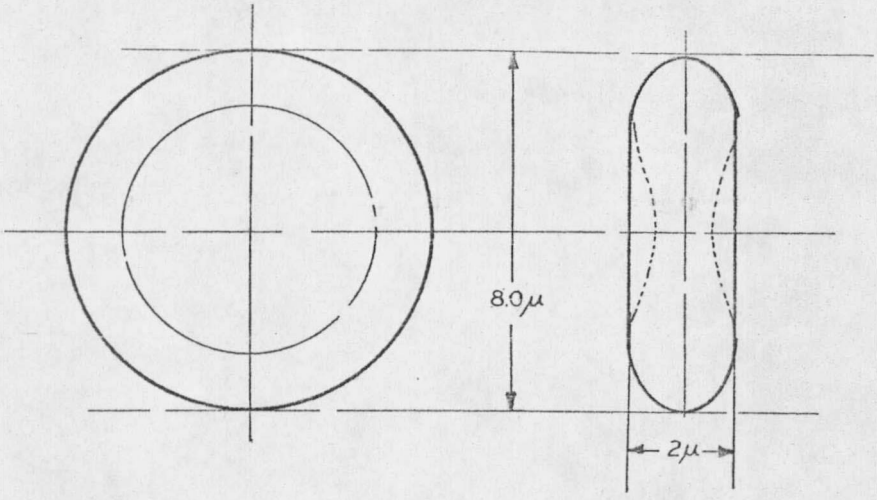

Fig. 1 Dimensions of a Red Blood Cell

averaging 8.0 microns in diameter and 2.0 microns in thickness. Various other values are also reported for the dimensions, however. A diagram of a red blood cell appears in Fig. 1.

The red cell is made up of a flexible membrane which is essentially unstretchable. The interior of this non-nucleated cell is a complex liquid, containing the hemoglobin. The membrane serves as a barrier to complex macromolecules, but allows small molecules to pass through rapidly. The membrane is the site of many chemical functions for the metabolism of the cell. The red cells serve to transport oxygen and carbon dioxide to and from the body.

The hematocrit is defined as the volume percent of the blood that is red blood cells. This is found by centrifuging a small volume of blood and comparing the relative volume of packed red cells to total volume. This gives accuracy to within 99%, as 1% of the packed cell

volume is trapped plasma.

The hematocrit can range from 37 to 54% in healthy humans. Changes in hematocrit for purposes of this study were made by centrifuging the sample and removing some of the plasma or red cell volume.

The white cells, also called leukocytes, are smaller in number and more varied in function than the red cells. There are five different kinds of white cells: basophils, eosinophils, segmented neutrophils, monocytes, and lymphocytes. Their sizes range from 8 to 22 microns in diameter. One of their main functions is fighting disease. These are nucleated cells and are more complicated in morphology than the red cells.

The platelets (thrombocytes) are small non-nucleated cells about 2-3 microns in diameter. Their main function is in blood coagulation, and thus they are closely involved in the clotting mechanism, or hemostasis. Hemostasis is activated <u>in vivo</u> by a complex chain reaction, initiated often by the rough edges of a cut in a vessel wall. This is of interest in the present study, as the rough ends of glass capillaries may also induce the clotting mechanism.

In studying the flow of blood, as well as in blood banking for medicinal transfusion or in clinical testing of blood, clotting presents a serious problem. Various anti-coagulants are used, including an acidified-citrate-dextrose (ACD) solution in the storage bags, and

heparin, a mucopolysaccharide obtained from dogs and cattle, used in hematocrit tubes to prevent coagulation. These compounds interfere with the clotting mechanism, usually by binding some protein in the reaction pathway, or by chelating calcium ions, which are essential for the clotting process.

When centrifuging the samples, the red cells are found in the bottom of the tube with a thin white layer on the surface of the red cell pack containing the white cells and platelets. It can be removed for investigations involving only red cells and plasma. This decreases the possibilities of clotting, due to the lack of platelets.

In normal, non-flowing blood, the red cells can aggregate face-to-face into a cluster known as a rouleau. At sufficiently high shear rates these rouleaux break up and the red cells exist individually. The addition of high molecular weight Dextrans increases the formation of the rouleaux.

Many of blood's properties vary greatly from donor to donor. Hematocrit and protein content are among the characteristics that have large normal ranges. But for the enzyme specificity of the body's metabolic functions, temperature, pH and ionic strength are virtually the same level in all humans. Thus, when working with blood, one has to consider both the similarities and the differences encountered from sample to sample.

Blood Rheology

Rheology is the study of the flow properties of a fluid, dealing especially with viscoelastic and non-Newtonian fluids. Blood rheology is concerned with understanding the effects various changes in the blood will have on its measurable properties.

Shear stress for unidirectional flow between two parallel plates is the force required per unit area to move a top layer of liquid over a lower layer. This can be expressed as

$$\tau = \frac{F}{A} \qquad (\text{dynes/cm}^2)$$

The strain rate is the velocity gradient and is given by

$$\dot{\gamma} = \frac{\Delta x}{\Delta t \; \Delta y} \qquad (\text{sec}^{-1})$$

for a layer of liquid Δy cm. thick moving a maximum relative distance Δx. The viscosity coefficient is the shear stress divided by the strain rate

$$\eta = \frac{\tau}{\dot{\gamma}} \qquad (\text{dynes/cm}^2, \text{ or poise})$$

and is a measure of the force required to move one layer of fluid over another at a given shear rate.

If one measured the viscosity of a sample of water at different shear rates, he would come out with a constant viscosity. But with blood, the viscosity varies over the range of shear rates, being higher at low shear rates, and lower at high shear rates.. The values obtained

are termed apparent viscosity, as they are the values the blood would exhibit at all points only if the blood were Newtonian. For some purposes, a more significant number is the relative viscosity, which is the ratio of the apparent viscosity of the blood to that of the suspending medium, in this case the plasma.

Poiseiulle was one of the first to study the flow of blood. His famous pressure drop-flow rate relationship for steady flow through a tube was originally developed for blood flow; however, it only applies to Newtonian fluids such as water, alcohol, and mercury--the fluids he worked with.

$$Q = \pi \frac{\Delta P}{L} \frac{R^4}{8\eta}$$

where Q = flow rate, ΔP = pressure drop, R = tube diameter, L = axial length of the tube, and η = viscosity coefficent. This applies to blood only when the flow has moderate to high shear stresses.

Non-Newtonian flow occurs for blood in a tube less than 300 microns in diameter when the flows are physiologically significant. This was investigated by Fahraeus and Lindqvist in 1929 (7). They used a capillary viscometer to study the relationship between tube diameter and viscosity at such high shear rates that the blood acted as a Newtonian fluid. They found that the relative viscosity, that is, the viscosity found by taking the ratio of the apparent viscosity of blood to the

viscosity of water, decreases with tube diameter. This lowering of the viscosity is of great significance to the body, as it allows the heart to pump a given volume of blood through the circulatory system with a smaller pressure drop than if the blood had a constant viscosity. The pressure drop across the human circulatory system has been found to be about 120 mm Hg.

Another factor affecting the viscosity of blood is the hematocrit. The results of an investigation by Chien, et. al. (6) are shown in Fig. 2. The viscosity of suspensions of cells hardened with glutaraldehyde or acetaldehyde and of normal cells was measured as a function of hematocrit. These cells were all suspended in Ringer's solution. The hardened cells show little shear dependence, but the normal cells show dependence on both hematocrit and shear rate.

This decrease in viscosity with increasing shear rate is further illustrated in Fig. 3. The deformability of the normal cells causes them to slip past one another much more easily, thus lowering the viscosity. This is not the case for hardened cells. The marked difference in viscosity, especially at high shear rates, is easily seen.

Addition of Dextran-40 further decreases the relative viscosity at high shear rates. This is due to an increased plasma viscosity, which acts to deform the red cells even more. This is shown in Fig. 4, where various concentrations of Dextran-40 were added to the suspending media,