Correlation of blood flow in a packed bed of glass spheres
by Richard Dale Mountain

A thesis submitted to the Graduate Faculty in partial fulfillment of the requirements for the degree of
MASTER OF SCIENCE in Chemical Engineering
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Abstract:
The flow of blood in the human body is complicated by the complex non-Newtonian rheology of blood and the complex nature of the circulatory system. Recent attempts to quantitatively understand in vivo blood flow have raised many questions concerning the dynamics of blood flow both on a macroscopic level and a microscopic level. In an attempt to systematically approach some of the problems that need to be resolved the steady, laminar flow of human blood in a packed bed of glass spheres has been studied.

A capillary model to correlate the macroscopic flow of blood in a packed column was developed assuming that each pore could be viewed as a single straight tube. The Rabin-owitsch-Mooney relation describing non-Newton.ian flow in a straight pipe was modified and used to estimate an appropriate shear rate within the bed. The shear stress within the bed was estimated similarly and then shear stress and shear rate used to define a mean effective viscosity. This viscosity was then used to modify existing correlations describing Newtonian flow in a packed bed.

Blood flow was examined at modified Reynolds numbers ranging from 2.2x10-3 to 3.6x10-1 indicating laminar flow. Application of the capillary model yielded results that fit-a modified Kozeny-Carman equation with an average error of 1.87%.

Shear rate-viscosity data obtained from application of the capillary model were compared to actual viscometer data. It was found that experimental calculations yielded viscosities considerably lower than viscometer data at comparable shear rates. This discrepancy was minimized at shear rates sufficiently high to produce Newtonian behavior.

I It was concluded that the capillary model is an effective and powerful tool for correlating the macroscopic flow of blood in a packed bed since the method is independent of hematocrit and viscometer data. However, the method apparently fails to accurately predict and explain the microscopic flow of blood through the pores of the bed due to a breakdown of continuum mechanics.

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Signature Richard D. Mountain

Date July 26, 1973

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TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

The flow of blood in the human body is complicated by the complex non-Newtonian rheology of blood and the complex nature of the circulatory system. Recent attempts to quantitatively understand *in vivo* blood flow have raised many questions concerning the dynamics of blood flow both on a macroscopic level and a microscopic level. In an attempt to systematically approach some of the problems that need to be resolved the steady, laminar flow of human blood in a packed bed of glass spheres has been studied.

A capillary model to correlate the macroscopic flow of blood in a packed column was developed assuming that each pore could be viewed as a single straight tube. The Rabinowitsch-Mooney relation describing non-Newtonian flow in a straight pipe was modified and used to estimate an appropriate shear rate within the bed. The shear stress within the bed was estimated similarly and then shear stress and shear rate used to define a mean effective viscosity. This viscosity was then used to modify existing correlations describing Newtonian flow in a packed bed.

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It was concluded that the capillary model is an effective and powerful tool for correlating the macroscopic flow of blood in a packed bed since the method is independent of hematocrit and viscometer data. However, the method apparently fails to accurately predict and explain the microscopic flow of blood through the pores of the bed due to a breakdown of continuum mechanics.

INTRODUCTION

Recent advances in medicine and physiology, particularly the increased impetus to understand cardiovascular anomalies on a more scientific basis, have made it desirable to quantitatively understand the dynamics of blood as it flows through the human circulatory system. Indeed, maintenance of all aspects of homeostasis in the human body depends, to some extent, on the circulation. Thus, as medicine continues its radical transistion from art to science, it becomes increasingly important to be able to accurately predict how changes in microscopic and macroscopic properties will affect blood flow. However, an accurate correlation of blood flow in the human body is, in general, complicated by two factors: 1) The complex non-Newtonian rheology of human blood; and, 2) the variable and complex geometry of the circulatory system.

The complex rheology of human blood is due to its unique chemical and physical properties that enable it to fulfill its essential role as the medium of transport within the body. Essentially, blood consists of specialized cellular structures; erythrocytes, leukocytes, and thrombocytes, suspended in an extracellular liquid medium; the blood plasma.

The erythrocyte (red blood cell) is a biconcave disc with a mean diameter of 8.5 microns and a maximum thickness of approximately 2.4 microns. The red cell membrane consists of proteins, lipids, and mucopolysaccharides that collectively confer certain antigenic properties and blood group specificity. Hemoglobin, the conjugated protein that functions in oxygen transport, is found within the red cell along with various electrolytes, enzymes, and metabolites. Erythrocytes constitute by far the majority of the formed elements and cause the non-Newtonian rheology of blood.

Leukocytes (white blood cells) and thrombocytes (platelets) function as a defense against infections and as a factor in blood clotting respectively. They constitute only a minute fraction of the formed elements and are thus considered not to significantly affect blood rheology.

Blood plasma is a complex solution containing approximately 90% water by weight. Its major solute is a group of heterogeneous proteins including albumin, antibodies, hormones, and clotting agents. Blood plasma also contains carbohydrates, lipids, and various electrolytes. Plasma, per se, is a Newtonian fluid.

The preceding description of blood has been intentionally brief and generalized; an attempt only to provide the

broad anatomical basis for viewing blood as a suspension of deformable particles (i.e., erythrocytes) that results in complex non-Newtonian rheology.

An accurate and complete quantitative description of blood rheology has evolved only within the past decade. It is due largely to the development of more accurate and complex laboratory instrumentation in the hands of experimenters sufficiently versed in fluid dynamics in general and rheology in particular to comprehend the limitations of the instruments and to accurately convert raw data into meaningful rheological parameters. Thus, it is useful to briefly outline currently accepted concepts of human blood rheology before defining and exploring the experimental problem presented in this paper. More detailed reviews of blood rheology have been given by Cokelet(1972), Merrill(1969), Wayland (1967), and Whitmore(1968).

Several investigators (Cokelet, 1963; Charm and Kurland, 1965; Merrill and Pelletier, 1967; Brooks, et al, 1970) have provided extensive experimental evidence showing that under certain conditions human blood exhibits non-Newtonian behavior; that is, the relationship between shear stress and shear rate is non-linear so the viscosity is, in general, dependent upon shear rate. Specifically, blood is non-

Newtonian at lower shear rates with a gradual transistion to Newtonian behavior at higher rates of shear. The point of transition depends to a large extent on hematocrit (defined as the per cent, by volume, of formed elements); the greater the hematocrit, the larger the rate of shear necessary to produce Newtonian behavior. This phenomenon can be qualitatively explained as follows: At low shear rates the red blood cells aggregate producing a fluid of greater viscosity; as the rate of shear increases the aggregation of cells decreases resulting in a decrease in viscosity. Eventually the shear rate is sufficient to prevent any aggregation of cells and Newtonian behavior is observed.

As well as shear rate and hematocrit, blood viscosity depends upon temperature and also more subtle factors such as concentration of plasma proteins and the physiological state of the erythrocyte. This latter factor is extremely difficult to control since even in the presence of a suitable anticoagulant erythrocytes removed from the body undergo gradual loss of adenosine triphosphate (ATP) with a subsequent change to a hardened, crenated form with radically different rheological behavior.

It should be noted that several investigators (Cokelet, 1963; Merrill, et al, 1965; Benis and LaCoste, 1968) have

provided convincing evidence indicating that blood has a yield stress, which is the minimum stress that must be overcome for flow to occur. The methods employed to demonstrate blood yield stress have been both direct application of torque-time measurements and indirect extrapolation of low shear rate data to zero flow.

The quantitative dependence of blood viscosity on shear rate and hematocrit will be readily apparent when actual viscometer data are presented in the experimental results. This qualitative discussion is given only to alert the reader to the complexities of blood rheology and the general factors which affect it.

At the outset it was also mentioned that analysis of blood flow in the human body is complicated considerably by the complexity of the circulatory system. That is, as the blood travels through the circulatory system it passes through vessels that vary considerably in size and geometry. For example, the blood may pass through a large, essentially straight vessel such as the aorta or a small, highly branched series of capillaries. Furthermore, the elastic nature of most blood vessels makes it impossible to generalize about size and geometry since both will vary locally with rate of flow.

One aspect of the circulation that has received much attention in recent years is the so-called microcirculation, a generic term referring to any and all of the small blood vessels including arterioles, capillaries, and venules. The quantitative study of the microcirculation is difficult since the diameter of these blood vessels is on the same order as the diameter of an erythrocyte. Hence, continuum fluid mechanics or theoretical equations of motion cannot be rigidly applied. This problem has been circumvented by either employing macroscopic empirical correlations or applying continuum mechanics anyway realizing the limitations of the approach. At any rate, the application of rheological data to blood flow in the microcirculation is limited and the work that has been done is conflicting and indicative of the complexity of the problem. Thus, a brief review of this work will point out the complex questions that have been raised and the incentive behind the research reported herein.

Workers in the laboratory of Bjorn Folkow at the University of Goteborg, Sweden, have reported (Djojosugito, et al, 1970) comparisons between blood viscosity <u>in vivo</u> ("apparent viscosity") and <u>in vitro</u> blood viscosity measured in a cone-plate viscometer. The <u>in vivo</u> viscometer was the

maximally dilated calf muscle vascular bed of the cat. The apparent *in vivo* viscosity was determined by comparing pressure flow relationships for blood and a Newtonian fluid assuming a linear pressure flow relationship for a constant vascular geometry. It was found that apparent *in vivo* viscosity was much lower than *in vitro* viscometer values at relatively high shear rates (230 sec^{-1}). This discrepancy was rationalized by assuming that the small vessels had favored local reductions in erythrocyte concentration as reported *in vitro* by Fahraeus and Lindqvist(1931).

On the other hand, workers at Columbia University's Laboratory of Hemorheology have reported (Benis, Usami, and Chien, 1972) a method of analysis that results in no apparent discrepancy between *in vivo* viscosity and *in vitro* viscometer data. Benis and co-workers studied steady blood flow in an isolated canine hindpaw and considered the situation to be similar to flow through a packed bed in which viscous and inertial pressure losses often occur simultaneously. Thus, the total pressure loss can be considered to be the sum of viscous and inertial pressure losses. That is,

$$\Delta P = \Delta P_v + \Delta P_i \qquad (1)$$

or

$$\Delta P = A\mu_a V + BV^2 \qquad (2)$$

where μ_a is the mean apparent viscosity of blood in the vascular bed and V is the volumetric flow rate. A and B are considered to be geometrical parameters that are a function of ΔP only. Utilization of Eq. (2) to determine apparent in vivo viscosity yielded results that agreed relatively well with in vitro viscometer data at comparable shear rates. Recall that the Swedish investigators had assumed a linear pressure flow relationship accounting only for the presence of viscous pressure losses whereas Benis and co-workers have included a term to account for possible inertial pressure losses.

The conflict existing between the Swedish investigators and the workers at Columbia has raised numerous questions that can only be resolved by a more systematic and objective approach. The model of Benis and co-workers suggests that much could possibly be learned by examining blood flow in a packed column wherein the flow is not complicated by changing vascular geometry. Thus, the research reported in these pages is hopefully a quantitative and objective consideration of blood flow in a packed bed of glass spheres.

Specifically, the research has been directed towards resolving two fundamentally important questions:

1) Can a workable model be developed to accurately correlate macroscopically the flow of blood in a packed bed?
2) Can the macroscopic model be extended to analysis of the microscopic behavior of blood within the bed?

It should be noted that the analysis of Newtonian flow in packed beds has been extensively studied and is of general importance in chemical engineering. However, non-Newtonian flow through packed beds is considerably more complicated and has received little attention.

THEORETICAL CONSIDERATIONS

Newtonian Flow Through Packed Beds

Newtonian flow through packed beds can be adequately correlated over the entire range of Reynolds numbers by an expression proposed by Ergun(1952),

$$\frac{\Delta P g_c D_p \epsilon^3}{L \rho U^2 (1-\epsilon)} = \frac{150}{(D_p U \rho)/\mu (1-\epsilon)} + 1.75 \qquad (3)$$

where

ΔP = pressure drop across bed, dynes/cm^2

g_c = constant, 1 (g-cm)/(dyne-sec^2)

D_p = effective particle diameter, cm

ϵ = void fraction, dimensionless

L = effective length of bed, cm

ρ = fluid density, g/cm^3

U = overall bulk average velocity, cm/sec

μ = fluid viscosity, poise=g/(cm-sec)

or in terms of modified friction factor and modified Reynolds number

$$f_m = 150/Re_m + 1.75 \qquad (4)$$

where

$$f_m = \frac{\Delta P g_c D_p \epsilon^3}{4\rho U^2 (1-\epsilon)} \tag{5}$$

and

$$Re_m = \frac{D_p U \rho}{\mu (1-\epsilon)} \tag{6}$$

Although Eq. (3) is essentially empirical in nature, it does have some theoretical basis by considering the packed column to be a composite of tortuous tubes of irregular cross-section; the overall equation is then obtained by applying results for single tubes to the composite. Nevertheless, empirical corrections must be considered to obtain an expression that accurately correlates experimental data. Such an analysis has been given by Bird, Stewart, and Lightfoot(1960).

It should be noted that the Ergun equation, Eq. (3), is simply the algebraic sum of two simplified expressions describing laminar and turbulent flow respectively. That is, laminar flow through a packed bed at $Re_m<1$ can be adequately described by the Kozeny-Carman equation

$$f_m = 150/Re_m \tag{7}$$

Eq. (7) states that the flow rate is proportional to the

pressure drop, which is Darcy's law. On the other hand, turbulent flow through a packed bed at $Re_m > 2000$ can be adequately correlated by the Burke-Plummer equation

$$f_m = 1.75 \tag{8}$$

The Ergun equation describing intermediate flow regimes ($1 < Re_m < 2000$) is then the sum of the Kozeny-Carman equation for laminar flow and the Burke-Plummer equation for turbulent flow. The general behavior of Newtonian flow through packed beds is depicted in Fig. 1, p. 13, by plotting f_m vs. Re_m on a log-log scale.

Non-Newtonian Flow and the Capillary Model

The correlation of non-Newtonian flow in packed beds is obviously quite complex since it will be characterized by local variations in shear rate and effective viscosity. The limited analysis of such flow reported in the literature thusfar has been confined to attempts to modify friction factor-Reynolds number expressions so that they adequately fit experimental observations. Sadowski and Bird(1965) have proposed a method for correlating the laminar flow of viscoelastic polymer solutions through packed beds by introducing another dimensionless group, the Ellis number, to describe the viscoelastic effects. Christopher and

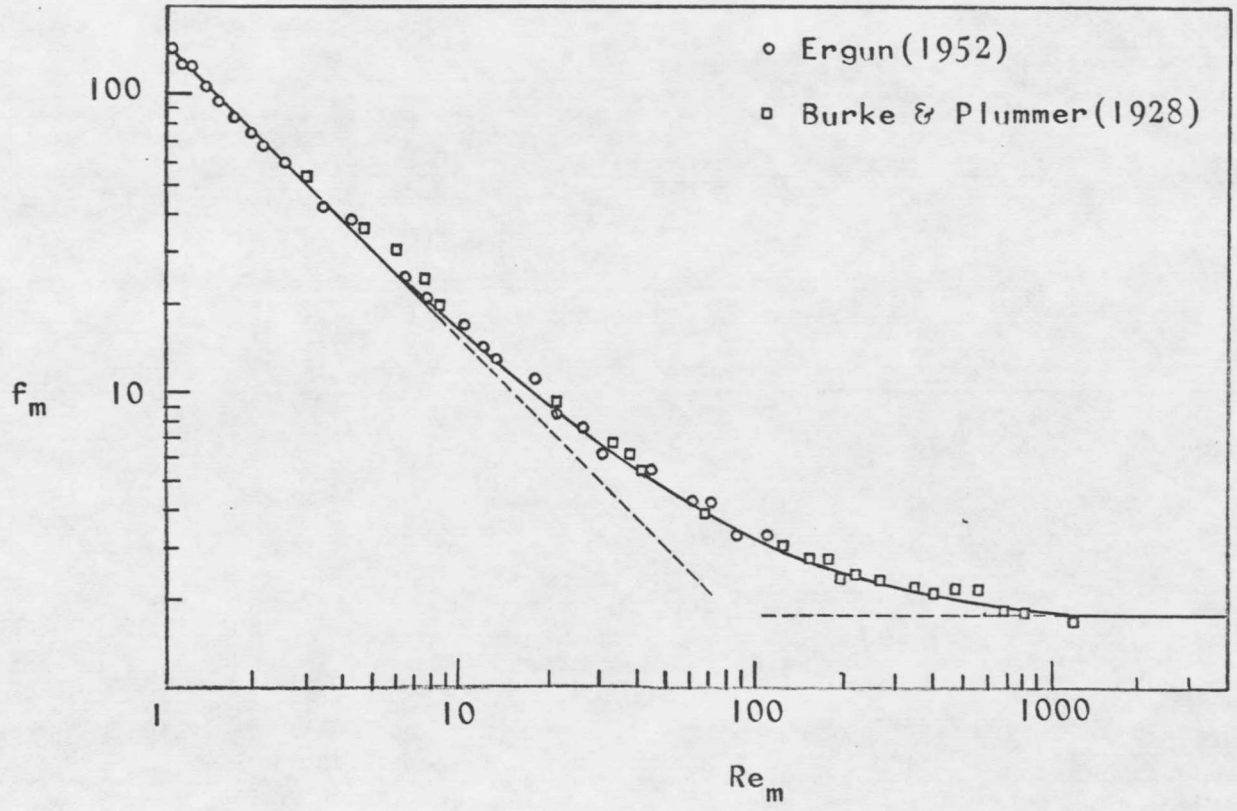

Figure 1. General behavior of Newtonian flow through packed beds. (Redrawn from Bird, Stewart, and Lightfoot, 1960).

Middleman(1965) have developed a modified Kozeny-Carman equation to describe the laminar flow of a power-law fluid through a packed bed. Gregory and Griskey(1967) have applied a similar approach to the flow of molten polymers.

Since blood does not apparently exhibit thixotropic or rheopectic effects, it can be considered rheologically a time-independent fluid. Thus, the primary problem in correlating blood flow in a packed bed is defining and quantifying shear stress, shear rate, and corresponding viscosity. These rheological parameters will, in general, vary locally throughout the bed even at a steady rate of bulk flow. Hence, any workable model of blood flow in a packed bed must necessarily resort to the use of average, yet physically realistic, values of these parameters.

Keeping the aforementioned limitations in mind, a workable model of blood flow in packed beds will now be developed. It is assumed that the packed bed can be viewed as a series of single tubes arranged in a tortuous, irregular manner. Equations describing non-Newtonian flow in a single pipe can then be used to estimate shear stress, shear rate, and corresponding effective viscosity as the blood flows through a single pore within the bed. The effective viscosity can then be used in a friction factor-Reynolds number

relationship. Such an approach can appropriately be termed a "capillary model" and is similar in principle to the approach of Bird, Stewart, and Lightfoot(1960) mentioned previously in conjunction with Newtonian flow.

The steady, laminar flow of a non-Newtonian fluid in a straight pipe can be described by the Rabinowitsch-Mooney relation (see Rabinowitsch, 1929; Mooney, 1931)

$$\gamma_w = \frac{3}{4}\frac{8U}{D} + \frac{1}{4}\tau_w \frac{d(8U/D)}{d\tau_w} \tag{9}$$

and

$$\tau_w = \frac{D(\Delta P)}{4L} \tag{10}$$

where

γ_w = shear rate at the wall, sec^{-1}

τ_w = shear stress at the wall, $dynes/cm^2$

U = overall bulk average velocity, cm/sec

D = diameter of pipe, cm

L = axial distance, cm

ΔP = axial pressure drop for two points a distance L apart, $dynes/cm^2$

The derivation of Equations (9) and (10) is given in the Appendix. Equations (9) and (10) are very powerful tools

for analysis of flow in pipes since they are independent of fluid properties. The only restriction in addition to steady, laminar flow is that the shear rate be a function only of shear stress. This restriction is probably not rigorously met for blood flow in extremely small tubes such as the vessels of the microcirculation since blood then cannot strictly be viewed as a homogeneous continuum.

Now, Equations (9) and (10) can be applied at a point in a packed bed as fluid moves through a single pore. That is,

$$\gamma_o = \frac{3}{4}\frac{8u}{D_o} + \frac{1}{4}\tau_o\frac{d(8u/D_o)}{d\tau_o} \qquad (11)$$

and

$$\tau_o = \frac{D_o}{4}\frac{dP}{dx} \qquad (12)$$

where

γ_o = shear rate at wall of pore, sec^{-1}

τ_o = shear stress at wall of pore, $dynes/cm^2$

u = local interstitial velocity, cm/sec

D_o = effective pore diameter, cm

$\frac{dP}{dx}$ = differential pressure gradient at pore, $dynes/cm^2/cm$

However, the local interstitial velocity, u, can be related to the overall bulk average velocity, U, by

$$u = U/\epsilon \tag{13}$$

Also

$$U = V/A_b \tag{14}$$

where V is the overall volumetric flow rate and A_b is the cross-sectional area of the bed. Thus,

$$u = \frac{V}{\epsilon A_b} \tag{15}$$

Furthermore, the differential pressure gradient at the pore can be considered constant along the axis of the bed so

$$\frac{dP}{dx} = \frac{\Delta P}{L} \tag{16}$$

where ΔP is the axial pressure drop across the effective length of the bed, L.

Now, substituting Equations (15) and (16) into Equations (11) and (12) gives

$$\gamma_o = \frac{3}{4}\frac{8V}{\epsilon A_b D_o} + \frac{1}{4}\tau_o \frac{d(8V/\epsilon A_b D_o)}{d\tau_o} \tag{17}$$

and

$$\tau_o = \frac{D_o}{4} \frac{\Delta P}{L} \tag{18}$$

Thus, the local shear rate and shear stress at the wall of a single pore within the bed have been related to the overall variables of flow. The only parameter in Equations (17) and (18) that does not lend itself to direct observation is the effective pore diameter, D_o. The resolution of this problem will be presented shortly.

Equations (17) and (18) can then be used to estimate the mean apparent viscosity for the fluid flowing through the bed. That is,

$$\mu_a = \frac{\tau_o g_c}{\gamma_o} \tag{19}$$

In reality, Eq. (19) gives the local viscosity at the wall of a single pore. However, it is felt that such a value should be reasonable to use in attempting to correlate pressure drop flow rate data. Thus, the mean apparent viscosity, μ_a, for blood flowing through a packed bed would, in general, vary with overall rate of flow but would be considered constant for a given rate of flow.

Using the concept of mean apparent viscosity it should be possible to correlate blood flow in a packed bed. That

is,

$$Re_m = \frac{D_p U \rho}{\mu_a (1-\epsilon)} \tag{20}$$

Hence, laminar blood flow should be described by a modified Kozeny-Carman equation

$$\frac{\Delta P g_c D_p \epsilon^3}{L \rho U^2 (1-\epsilon)} = \frac{150}{(D_p U \rho)/\mu_a (1-\epsilon)} \tag{21}$$

Turbulent blood flow should be described by the Burke-Plummer equation as for Newtonian flow since the fluid viscosity does not enter into the correlation. Blood flow in intermediate regions could then be described by a modification of the Ergun equation

$$\frac{\Delta P g_c D_p \epsilon^3}{L \rho U^2 (1-\epsilon)} = \frac{150}{(D_p U \rho)/\mu_a (1-\epsilon)} + 1.75 \tag{22}$$

Thus, the only modification that need be made for non-Newtonian blood flow is the determination of the appropriate mean apparent viscosity which is now a variable as are pressure drop and flow rate.

It should be noted the Eq. (22) can be rearranged to give

$$\Delta P = \frac{150L(1-\epsilon)^2}{g_c D_p^2}\mu_a U + \frac{1.75L\rho(1-\epsilon)}{g_c D_p \epsilon^3} U^2 \qquad (23)$$

Thus, it can readily be seen that the correlation proposed by Benis and co-workers to describe blood flow in the microcirculation, Eq. (2), is essentially the same as Eq. (23) which is proposed to adequately describe blood flow in a packed bed.

The effective pore diameter, D_o, can be determined by examining Newtonian flow through a packed bed. That is, for Newtonian flow

$$\frac{d(8V/\epsilon A_b D_o)}{d\tau_o} = \frac{8V/\epsilon A_b D_o}{\tau_o} \qquad (24)$$

so Eq. (17) becomes

$$\gamma_o = \frac{8V}{\epsilon A_b D_o} \qquad (25)$$

Thus, for Newtonian flow

$$\mu = \frac{\tau_o g_c}{\gamma_o} = \frac{D_o^2 \Delta P g_c \epsilon A_b}{32VL} \qquad (26)$$

so

$$D_o = \left(\frac{32\mu VL}{\Delta P g_c \epsilon A_b}\right)^{\frac{1}{2}} \qquad (27)$$

D_o should, of course, be constant for a given bed.

It is now useful to summarize the steps involved in the application of the capillary model to analysis of blood flow in a packed bed.

1) Obtain pressure drop flow rate data for a Newtonian fluid.
2) Determine D_o using Eq. (27).
3) Obtain pressure drop flow rate data for blood flow.
4) Determine shear rate and shear stress within the bed using Equations (17) and (18).
5) Determine mean apparent viscosity for each flow rate using Eq. (19).
6) Calculate modified friction factor and modified Reynolds number using Equations (5) and (20).
7) Plot friction factor vs. Reynolds number on a log-log scale to see if the appropriate relationship is satisfied.

EXPERIMENTAL APPARATUS AND PROCEDURE

Experimental Apparatus

A general schematic diagram of the experimental apparatus used is shown in Fig. 2, p. 23. Steady flow was initiated with a syringe pump (Harvard Apparatus Co., Model 902) utilizing 30 and 50 cm^3 gas-tight syringes (Hamilton Co., #1030 and #1050). The pressure drop across the column was monitored by a differential strain-gauge transducer (Statham Instruments, Inc., Model PL280TC) which converted the pressure drop to a corresponding electrical output that was then read on a universal transducer readout (Statham Instruments, Inc., Model SC1001). Standard luer-lok fittings were used in conjunction with polyethylene tubing (Becton, Dickinson and Co.) to connect the syringe to the column as well as to connect the pressure taps to the transducer.

A more detailed diagram of the column used is shown in Fig. 3, p. 24. The column was cast of clear lucite polymer with an inside bore diameter of 1.27 cm corresponding to a cross-sectional area of 1.267 cm^2. The pressure taps were 15.24 cm apart which, of course, was then the effective length of the column. Both ends of the column were threaded to fit a solid stainless steel end cap with luer-lok fitting (Millipore Corp., Model XX30 025 00). In addition, a teflon gasket, a porous stainless steel support plate, and a mesh