Montogue

Project FM201

BIOFLUID MECHANICS

Vascular Mechanics, Blood Rheology, and Heart Valves

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Problems

→ Problem 1: Vascular Mechanics

Problem 1A

Describe the composition of the layers of the wall of a typical artery, labeled 1, 2 and 3 in the following figures, from the innermost to the outermost layer.

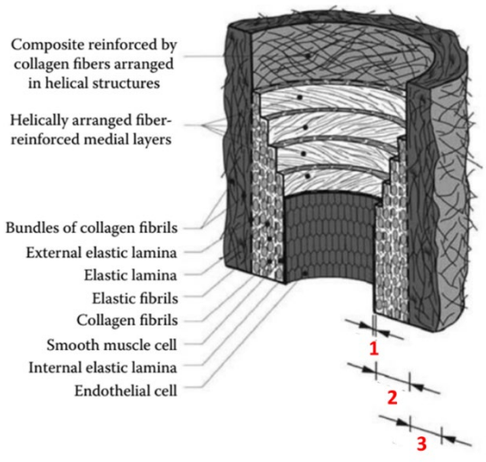


Figure 1 Illustration of the vessel wall composition of a typical artery.

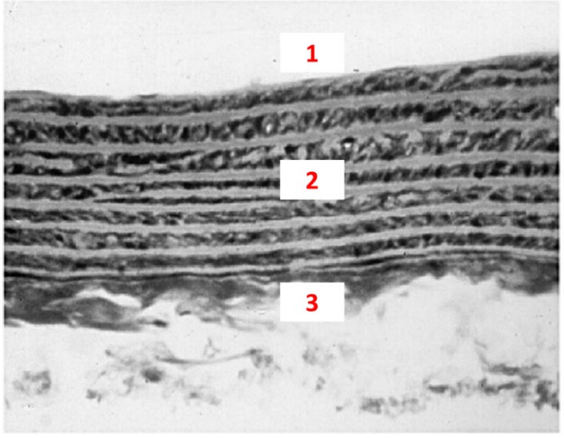


Figure 2 Scanning of the multi-layer structure of the artery wall (Masson trichrome staining).

Problem 1B

Blood vessels are constituted mainly of four structural components: (A) *elastic fibers*, which are mechanically rubber-like and have a key role in the stretch of blood vessels; these are mostly either *elastin*, a protein that allows the tissues to recoil after deformation, and *micro-fibrils*, which are created from glycoproteins; (B) *collagen fibers*, which are the key proteins of the connective tissue, and can be stretched by around 3 to 4%, thus being considered much stiffer than the elastic fibers; (C) *smooth muscle cells*, which are present in all blood vessels except the capillaries; they contract and relax the normal vessel wall in response to vasoactive stimuli; and (D) *endothelium*, which is a very thin layer that lines the interior surface of all vascular segments; indeed, they are the *only* components of the wall of many capillaries. The chart below contains the main vessel types and the relative quantity of each structural component in their wall composition. Assign the correct component, from A to D, to each color, from 1 to 4.

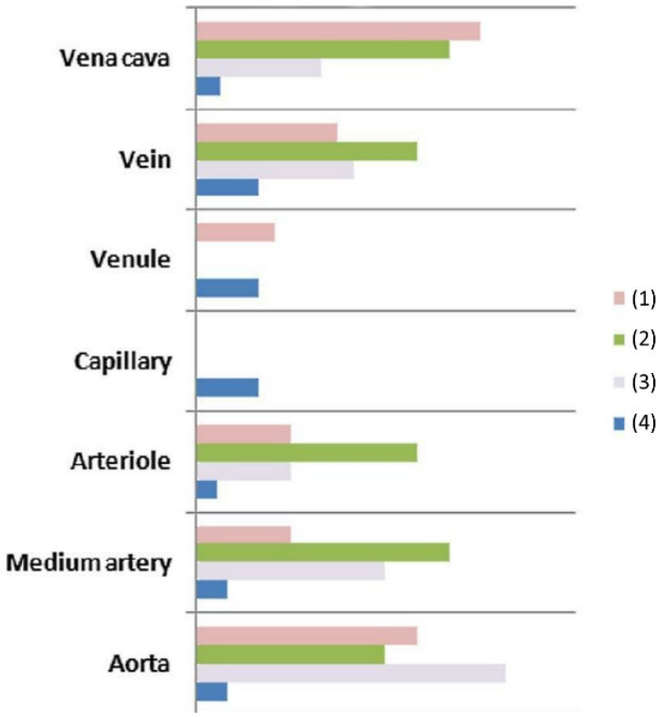


Figure 3 Relative quantity of each of the four vessel wall components in the blood vessels' walls.

Problem 1C

Comment on the following features of the mechanical behavior of vessel walls:

A) Heterogeneity;
B) Incompressibility.

Problem 1D

Artery wall tissue displays a series of special mechanical features, such as *stress relaxation*, *creep*, and *hysteresis*. Provide a brief definition of each of these terms and note how they apply to blood vessels. What is the term attributed to a system that displays these three features?

Problem 1E

Blood vessels are said to possess *residual stress*. What is residual stress? Illustrate this concept with a drawing and comment on its importance in constitutive modeling. Figure 4 shows an arterial ring used by Fung in his study of the concept of residual stress, published in 1984.

Figure 4 Arterial ring used by Fung in his 1984 study of residual stress.

→ Problem 2: Blood Rheology

Problem 2A

Explain how a capillary rheometer (Figure 5) and a cone-and-plate rheometer (Figure 6) can be used to measure the viscosity of a fluid, with reference to the figures below.

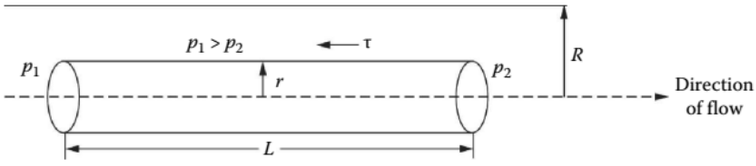


Figure 5 Capillary viscometer. Variables involved:
p_1 → Pressure at entrance of tube
p_2 → Pressure at exit of tube
Q → Flow rate in tube
L → Length of tube
R → Radius of tube

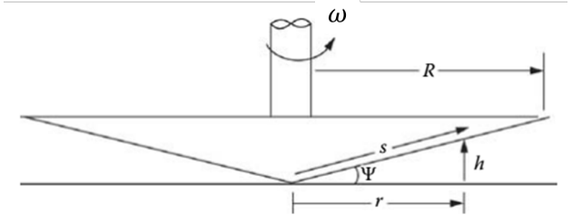


Figure 6 Cone-and-plate viscometer. Variables involved:
ω → Angular velocity around middle axis
Ψ → Angle between cone lateral surface and plate
R → Radius of cone
s → Distance from cone apex to a point in the lateral surface of the cone
h → height from plate to a point in the lateral surface of the cone

Problem 2B

Show that, for a Couette rheometer – i.e., a rotating cylinder rheometer – the viscosity of the fluid being measured can be established with the formula

$$\mu = \frac{4Th}{\pi D^3 L \omega}$$

in which T is the torque applied to the device, h is the thickness of the space between the two cylinders, D is the diameter of the cylinder being spun, ω is the angular velocity at which the cylinder is being spun, and L is the length of the cylinders. The device is illustrated in Figure 7.

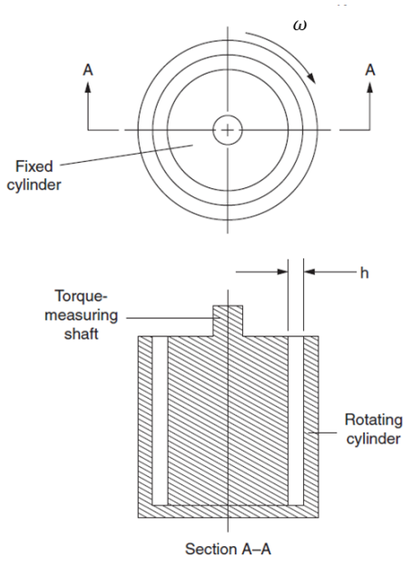


Figure 7 Couette viscometer.

Problem 2C

Discuss the effect of rate of shear on blood viscosity in large blood vessels subjected to low rates of shear. In these circumstances, is blood a *shear-thickening*, *Newtonian*, or *shear-thinning* fluid? Use Figure 8 as a reference for your answer.

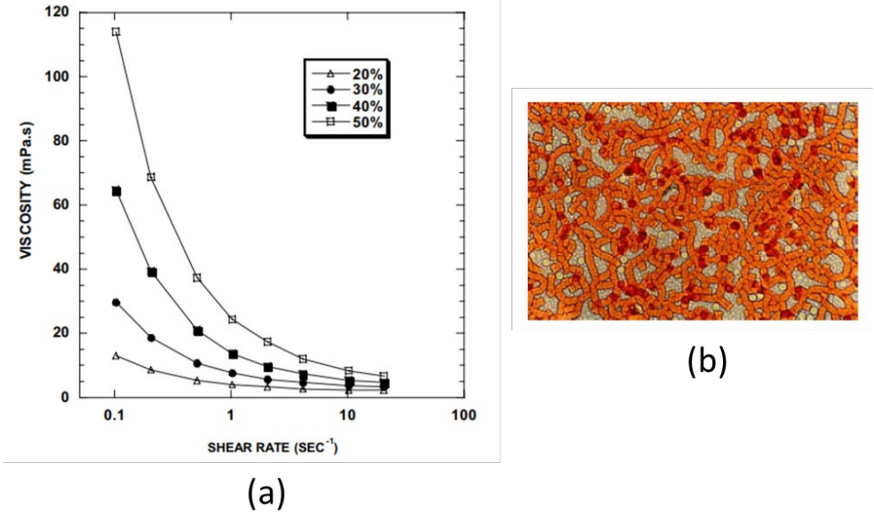


Figure 8 (a) Graph of blood viscosity (mPa·s) versus shear rate (sec^{-1}) with hematocrit as a parameter; (b) Three-dimensional structure of red blood cell aggregates in human blood from a healthy donor.

Problem 2D

Discuss the effect of hematocrit on blood viscosity. Using the graphs in Figure 9, discuss how hematocrit and the nature of red blood cells contributes to the non-Newtonian character of blood.

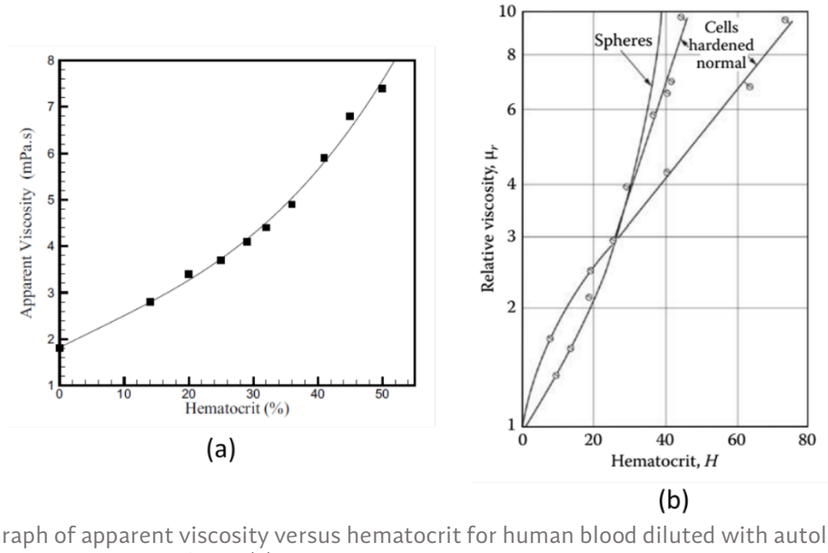


Figure 9 (a) Graph of apparent viscosity versus hematocrit for human blood diluted with autologous plasma at 21°C and shear rate $\dot{\gamma} = 128\ s^{-1}$; and (b) relative viscosity as a function of hematocrit for blood with normal red blood cells, blood with hardened RBCs, and blood with a suspension of rigid spheres.

Problem 2E

Discuss the effect of factors other than shear rate and hematocrit on blood viscosity. Use Figure 10.

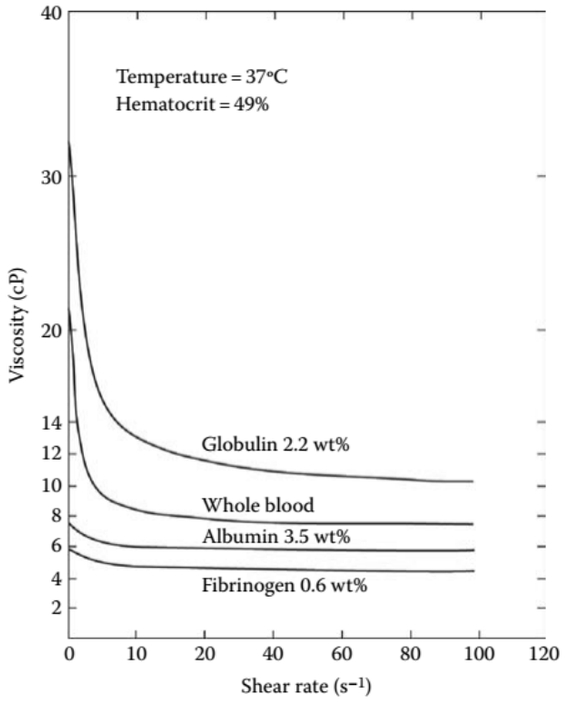


Figure 10 Effect of plasma proteins on the viscosity of whole blood.

Problem 2F

Discuss the existence of a yield stress for blood.

→ Problem 3: Heart Valves

Problem 3A

To assess the seriousness of a heart valve stenosis, it would be helpful to know the area of the stenosed valve when open, or how much of the valve opening is being blocked by the stenosis. In 1951, Gorlin & Gorlin developed an equation to empirically predict valve area based on the pressure drop across the valve and the flow rate through the valve. Their equation is still used in cardiology today. Two observers (Harris & Robiolio, 1999) write that "*although the 'gold standard' for assessment of the severity of mitral stenosis has long been the Gorlin formula derived from data obtained from cardiac catheterization, advances in echocardiography have largely supplanted this procedure. Nonetheless, cardiac catheterization remains a mainstay in the management of mitral stenosis.*" To obtain the Gorlin equation, we note that the average flow rate per heartbeat, Q, is the ratio of cardiac output, CO, to the product of heart rate, HR, and ejection time per beat, T_E,

$$Q = \frac{CO}{HR \times T_E}$$

Combining the expression above with the Bernoulli equation and the equation of continuity, we can state that

$$A_V = \frac{CO}{T_E \times HR \times K \times \sqrt{\Delta p}}$$

in which A_V is the area of the stenotic valve, Δp is the mean pressure gradient over the ejection period in mmHg, and K is the so-called Gorlin coefficient, which encompasses the effects of two other constants, namely, C_V, which represents actual velocity through the valve, and C_C, which adjusts the cross-sectional valve area. Even though it is not strictly a constant, the value of K is usually fixed as 44.3 for aortic valves and 37.7 for mitral valves. Using centimeters, seconds, and millimeters of mercury, what are the units of the Gorlin coefficient to ensure

that the expression for A_V yields an area quantity in cm^2? Then, consider a patient with a cardiac output of 5 L/min; a systolic ejection period of 358 ms with a heart rate of 70 beats per minute; and a mean aortic gradient as measured by echocardiography of 81 mmHg. Find the aortic valve area as estimated by the Gorlin equation. What is the average flow rate across the aortic valve during ejection?

Problem 3B

Energy loss across a stenotic valve is influenced by more than the effective valve area predicted by the Gorlin equation. Garcia et al. (2000) have suggested an approach that uses an energy method to more accurately estimate the severity of an aortic stenosis. The authors suggest an index that they refer to as the *energy loss index*, E_L. Although it is a measure of energy loss, the energy loss index yields a value with units of pressure. The energy loss equation can be written as

$$E_L = \frac{\rho}{2}\left(V_{VC} + V_V \frac{A_V}{A_A}\right)^2$$

If we are to express the energy loss in terms of variables that are readily measurable through transthoracic echocardiography, E_L would be

$$E_L = \frac{\rho}{2}\left(V_{VC} + \frac{CO}{A_A}\right)^2$$

where ρ is the fluid density (≈1060 kg/m^3 for blood), V_{VC} is the blood velocity at the vena contracta (Figure 11), CO is the cardiac output, and A_A is the cross-sectional area of the aorta. The unitless energy loss coefficient associated with this energy loss is defined by the term

$$\text{Energy loss coefficient} = \frac{(EOA)\times A_A}{(A_A - EOA)}$$

An energy loss coefficient that is less than 0.5 cm^2/m^2 should probably be considered a critical value. A value less than 0.5 indicates a serious stenosis. Bear in mind that the *effective orifice area*, EOA, is the area at the vena contracta derived from the continuity equation; that is,

$$EOA = \frac{V_V \times A_V}{V_{VC}}$$

Suppose that the same patient from the previous problem has a cardiac output of 5 L/min. Also, the aortic area = 4.9 cm^2, blood density = 1060 kg/m^3, and velocity at vena contracta = 1.66 m/s. The mean aortic gradient as measured by echocardiography is 81 mmHg. Find the "energy loss" in mmHg and the energy loss coefficient.

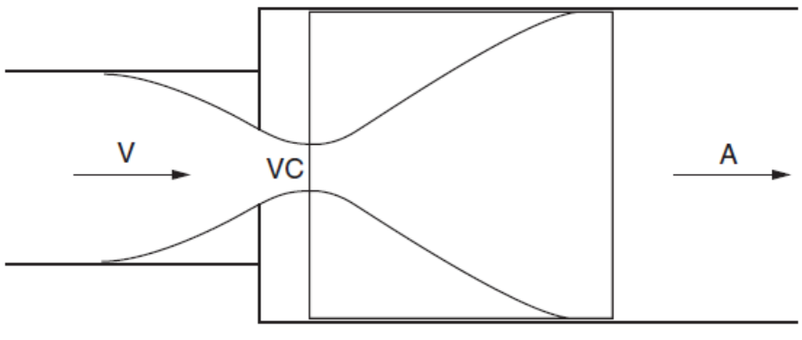


Figure 11 Schematic representation of flow through an aortic valve, where *V* is the left ventricle, *VC* represents the vena contracta, and *A* represents the aorta.

Problem 3C

Name some of the potential complications faced by individuals with prosthetic heart valves. One such possible complication can be noted from the echocardiographs of Figure 12.

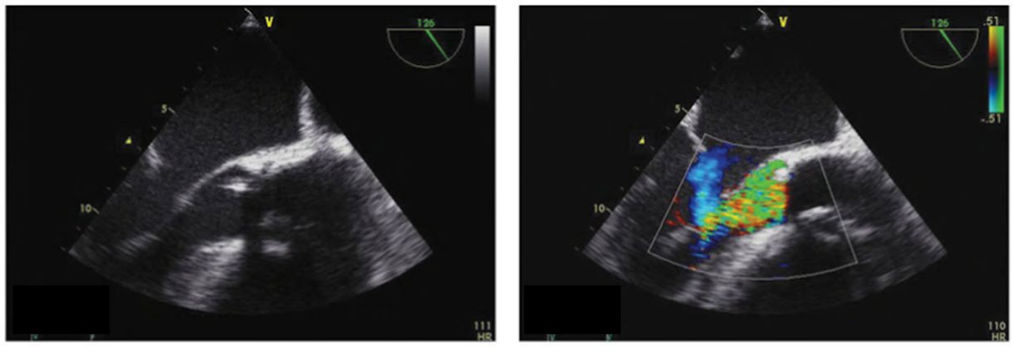


Figure 12 Transesophageal echocardiography showing degenerative calcification and rupture of a cusp (a) determining severe regurgitation, and (b) of a bioprosthesis in the aortic position.

→ Problem 4: Fahraeus and Fahraeus-Lindqvist Effects

Problem 4A

Explain the Fahraeus effect, and provide an equation that can be used in its mathematical description.

Problem 4B

Below, we have a plot of apparent viscosity of blood as a function of tube radius at a hematocrit of 40%. With reference to it, explain the Fahraeus-Lindqvist effect. How does this phenomenon help the body cope with potential resistance to blood flow?

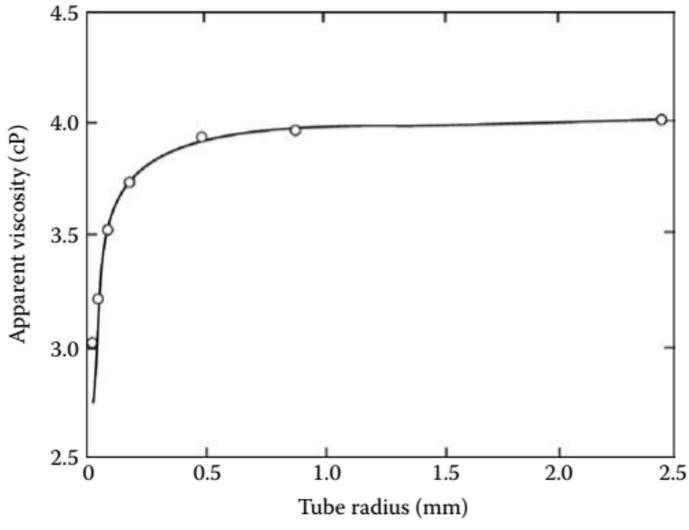


Figure 13 Variation of apparent viscosity of blood with tube radius for a fixed hematocrit of 40%.

Solutions

▸ Problem 1

P.1A ➡ *Solution*

The typical vessel wall consists of the *tunica intima*, which is the innermost layer, labeled 1 in the given figure; the *tunica media*, which is the middle layer, labeled 2; and the *tunica adventitia*, labeled 3 in the figure provided, the outermost layer. The intima is similar in most elastic and muscular arteries, typically consisting of a single layer of endothelial cells and an underlying thin (≈ 80 nm) basal lamina. Exceptions include the aorta and coronary arteries in which the intima may contain a subendothelial layer of connective tissue and axially oriented smooth muscle cells. Endothelial cells are usually flat and elongated in the direction of blood flow, often about 0.2 to 0.5 μm thick, 10 to 15 μm wide, and 25 to 50 μm long; exceptions occur near bifurcations wherein the blood flow is complex and the cells are often polygonal in shape. Endothelial cells may communicate directly with underlying smooth muscle cells via short, blunt processes that extend through the basal lamina and into the media. The basal lamina, sometimes referred to as the *basement membrane*, consists largely of net-like type IV collagen, the adhesion molecules laminin and fibronectin, and some proteoglycans.

The internal elastic lamina separates the intima and media, but is often considered to be part of the latter. It is a little thicker in muscular arteries and can be considered essentially a fenestrated "sheet" of elastin that allows H_2O, nutrients, and electrolytes across the wall as well as direct transmural cell-to-cell communication. The media contains smooth muscle cells that are embedded in an extracellular plexus of elastin and collagen (primarily types I, III, and V) as well as an aqueous ground substance matrix containing proteoglycans. Vascular smooth muscle cells are spindle-shaped; they are typically 100 μm long and about 5 μm in diameter, except near the nucleus where they are slightly thicker. Given this shape, they are often laid down such that the thicker portion of one cell is juxtaposed to the thin ends of the neighboring cells. Smooth muscle cells are covered by a thin (40 to 80 nm) basement-type membrane (likely type V collagen); hence, 12 to 50% of the volume of vascular smooth muscle is due to this investing connective tissue. Like endothelial cells, smooth muscle cells communicate, in part, via gap junctions. Their intracellular myofibrils are typically oriented along the long axis of the cell, and cell-to-cell force transmission is accomplished via thin (reticular) collagen fibers that connect the membranous sheaths on each cell. Although the orientation and distribution of the medial constituents vary with species and location along the vascular tree, vascular smooth muscle tends to be oriented helically, or nearly circumferentially in some vessels. This preferential orientation is expected, in part, because the primary roles of the contraction of vascular smooth muscle are to modify the distensibility of the large arteries or to regulate the luminal diameter in medium and small arteries.

Finally, the adventitia, or outermost layer of the wall, consists primarily of a dense network of type I collagen fibers with admixed elastin, nerves, fibroblasts, and the vasa vasorum. The adventitial collagen fibers tend to have an axial orientation in most arteries, and they are undulated slightly in the basal state. Although the adventitia comprises only ~10% and ~50% of the arterial wall in elastic and muscular arteries, respectively, it is thought to limit acute overdistension in all vessels. That is, the collagenous adventitia may serve primarily as a protective sheath, similar to the epicardium of the heart. Nonetheless, the presence of nerves within the adventitia also allows innervation of smooth muscle in the outer media via the diffusion of neurotransmitters, primarily norepinephrine (NE) and acetylcholine (ACh). The fibroblasts are responsible for regulating the connective tissue. The vasa vasorum is an intramural network of arterioles, capillaries, and venules that serves the outer portion of the wall in arteries that are too thick for sufficient transport of O_2, CO_2, nutrients, and metabolites from the intimal surface.

P.1B ➡ *Solution*

The correct associations are shown below.

(1)	Collagen fibers
(2)	Smooth muscle
(3)	Elastic fibers
(4)	Endothelial cells

P.1C ➡ *Solution*

As the artery is a layered structure, it is clearly heterogeneous. Experiments suggest that the intima does not contribute significantly to the load-carrying capability of the arterial wall, which is comprehensible given the fact that it is essentially constituted of no more than a basal lamina and one layer of endothelial cells. We can then surmise that the media and the adventitia are the most important components of the vessel wall in mechanical terms. Heterogeneity is increased in anomalous conditions such as the presence of atherosclerotic plaque, thrombi and necrotic tissue. Even today, however, many studies consider the artery to be a homogeneous material, which is somewhat of a lumped model approach, and may indeed allow for accurate results in models involving relatively large scales.

Because of the constituent regularity within each of the three layers that constitute the vessel wall, another common method is to assume that mechanical properties vary only from layer to layer, and are homogeneous for any one given layer. This separated layer approach is feasible on a large scale, but may be unacceptably inaccurate for smaller scale problems. A final alternative sometimes adopted by engineers is that there may be smooth gradients in wall constituents across the vessel wall. It is remarkable that most mechanical models involving vessel walls, including many performed after the advent of modern computers, were performed with vessel walls taken as homogeneous structures, particularly when the adventitia was sufficiently thin to be ignored altogether. The first models that dealt away with these gross simplifications were published in the 1980s, with von Maltzahn et al. noting, over the course of 3 years, that "*the media and adventitia are anisotropic; the media is stiffer, more nonlinear, and subjected to higher stresses than commonly assumed; and that both layers are stiffer in the axial direction than in the tangential (circumferential) direction.*" As of the early 2000s, von Maltzahn's work remained the most complete on the heterogeneity of the vessel wall, despite shortcomings such as not considering the existence of residual stresses. The first mechanical data on the separate response of the media and adventitia were reported by Vito & Demiray in 1982. Briefly, they performed uniaxial extension tests in the axial and circumferential directions on strips of media and adventitia excised from the canine aorta. Their data suggested (visually) that the adventitia was stiffer than the media, but both were nearly isotropic. A few years later, the same authors suggested that the media was cylindrically orthotropic.

In a finite elasticity framework, incompressibility means that the $\det(\boldsymbol{F}) \equiv 1$, $\boldsymbol{F}$ being a tensor that is representative of deformation for all conditions experienced by the material; that is, it is taken as a kinematic constraint; in a linearized elasticity framework, incompressibility means that the bulk modulus is much greater than the shear modulus. In addition to cells and connective tissue, the arterial wall contains significant amounts of intracellular and extracellular water – indeed, some 70 to 80% by wet weight. Based on histology, therefore, an artery can be classified as a "mixture-composite," that is, it contains a solid part that is primarily a layered composite of elastin, collagen, and smooth muscle, and a fluid part that is primarily extracellular water. Depending on the application, arteries can be treated as either a mixture or a homogenized fluid. Earlier studies performed by Lawton and Dobrin & Rovick had found that arteries deform approximately isochorically under various applied loads. Experimental measurement of wall compressibility of 0.06% at 270 cm of H_2O indicates that the vessel can indeed be considered incompressible when subjected to physiologic pressure and load. That is, although arteries are not truly incompressible, due in part to stress-induced movement of water in and out of the wall, they appear to experience near isochoric motions under many loading conditions of interest (e.g., isothermal, physiologic loads). Compressibility may be

important, however, to understanding some physiologic processes related to blood vessels, such as transport of interstitial fluid.

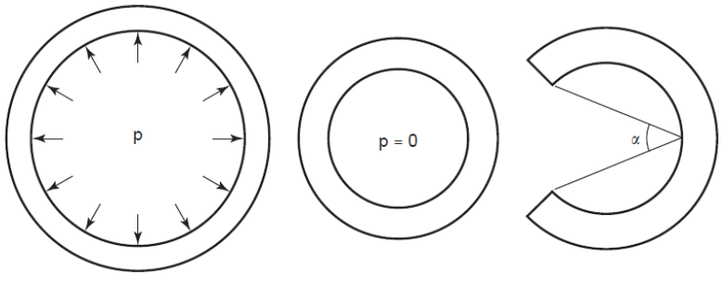
P.1D ➡ *Solution*

When a body is suddenly strained and then the strain is maintained constant afterward, the corresponding stresses induced in the body decrease with time. This phenomenon is called *stress relaxation*. If the body is suddenly stressed and then, with the stress is maintained constant afterward, the body continues to deform, a phenomenon called *creep* is defined. If the body is subjected to cyclic loading, the stress-strain relationship in the loading process may be somewhat different from that in the unloading process, in which case the material is said to have *hysteresis*. The features of stress relaxation, creep, and hysteresis are found in many materials. Collectively, they are features of *viscoelasticity*.

As the name implies, a viscoelastic material has properties both of an elastic solid and a viscous fluid. When an instantaneous load is applied to vascular tissue, the corresponding deformations do not occur instantaneously; rather, one observes an initial deformation followed by a slowing time dependent deformation, or creep, to an equilibrium value. Similarly, when the load is removed, an instantaneous recovery or relaxation occurs followed by time-dependent recovery. It is thought that the smooth muscle is the primary source of the viscoelastic properties of artery walls, although collagen, despite its great stiffness, also exhibits viscoelasticity in in vitro experiments. In contrast, elastin has a purely elastic response to stress, and it is this component of vessel walls that prevents creep or stress relaxation from continuing indefinitely. It is important to note that viscoelasticity is only relevant when the stress or strain varies with time. For example, if a segment of artery is subjected to a cyclically varying strain of given frequency and amplitude, the stress required for a given strain is greater during extension than during recoil, that is, the mechanical behavior involves hysteresis. For most applications, however, arteries are assumed to be purely elastic, and only the loading part of the stress-strain curve is applied (this concept, in turn, is known as *pseudoelasticity*).

P.1E ➡ *Solution*

The arteries possess *residual stresses*, which can be visualized by performing a radial cut on a short, unloaded ring segment such as the one shown below. Under normal conditions, the artery section is subjected to a continuously changing radial pressure, which keeps the vessel stretched in this direction (leftmost drawing). If the pressure were no longer applied, the vessel would contract and attain a constant circular shape (middle drawing). Finally, if we performed a radial cut in the ring, the artery would spring open, indicating the presence of residual stress (rightmost drawing). The ensuing opening occurs as a result of the cut ring minimizing its stored strain-energy. The opening angle α indicates the amount of residual stress. The residual stress results in compressive stresses near the wall of the artery and tensile stresses near the outer wall. In the loaded configuration, however, the stress through the wall is more uniform. That is, the stress at the inner wall would be much higher than the stress at the outer wall, which demonstrates that arteries adapt their configuration to account for stress concentrations.



A constitutive model ideally defines strain with respect to the truly relaxed, “natural” state, the original stress-free configuration to which the material will return following any reversible process. This can only be done, if at all, with knowledge of residual stress. Fung and other investigators have commented that the existence of a single natural configuration for soft tissues is unlikely. At best, therefore, the engineer can only obtain a single reference

configuration for which the properties are well-known in order to carry out a mechanical analysis. Nevertheless, the discovery of residual stress in excised, unloaded arteries was of paramount importance in the identification of reference configurations.

▸ Problem 2

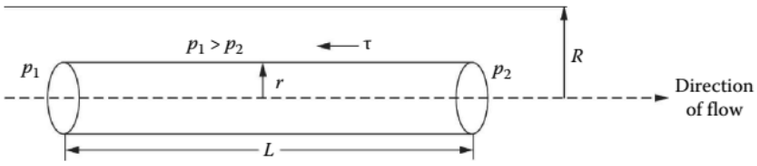
P.2A ➡ *Solution*

Capillary viscometry is based on the Poiseuille flow relationship for steady flow in a long, cylindrical tube. The tube has a capillary-size cross-section to ensure that flow in it is fully developed. The expression in question relates flow rate and pressure drop by means of Poiseuille's law,

$$Q = \frac{\pi R^4 \Delta p}{8 \mu L}$$

Referring to the figure below, the net force pushing fluid to the right is

$$F_p = p_1 \pi r^2 - p_2 \pi r^2 = (p_1 - p_2) \pi r^2$$



while the shear force that retards the motion acts on the circumferential surface of the fluid element and is given by

$$F_\tau = \tau \times 2 \pi r L$$

In fully-developed, steady flow, these two forces balance each other and we obtain

$$F_p = F_\tau \rightarrow (p_1 - p_2) \pi r^2 = \tau \times 2 \pi r L$$

$$\therefore \tau = \frac{(p_1 - p_2) \pi r^2}{2 \pi r L} = \frac{(p_1 - p_2) r}{2 L}$$

From this expression for the magnitude of shear stress, the magnitude of shear stress at the wall (i.e., where $r = R$) becomes

$$|\tau| = \frac{|\Delta p| R}{2 L} \quad \text{(I)}$$

In addition, the constitutive law for a Newtonian fluid is given in cylindrical coordinates as

$$\tau = -\mu \frac{du}{dr}$$

where u is the velocity of the fluid. Combining the two previous expressions, we can determine the shear rate at the wall,

$$|\tau| = \left| \mu \frac{du}{dr} \right|$$

$$\therefore \frac{|\Delta p| R}{2 L} = \mu |\dot{\gamma}_w|$$

$$\therefore |\dot{\gamma}_w| = \frac{|\Delta p| R}{2 \mu L}$$

Then, using Poiseuille's law, we can provide an expression for wall shear rate based on the flow rate and the wall radius,

$$|\dot{\gamma}_w| = \frac{4Q}{\pi R^3} \quad \text{(II)}$$

Finally, having obtained the wall shear stress with equation (I), and the wall shear rate with equation (II), the engineer can establish the viscosity coefficient as their ratio, $\mu = \tau/|\dot{\gamma}_w|$. Notice that equation (I) requires knowledge of the pressure drop, while equation (II) requires the flow rate. In addition to the assumptions mentioned heretofore, we have used a linear relationship between shear stress and shear rate, $\tau = \mu\dot{\gamma}$, which is inherent to a Newtonian fluid. It is to be noted, furthermore, that in most types of capillary viscometers part of the amount of energy imparted to the system is used to induce kinetic energy to the fluid, and a small amount of energy is also expended in overcoming the viscous forces at the converging and diverging streamlines at the entrance and exit of the capillary. Consequently, kinetic energy and "Couette" corrections need to be applied to the measurements for more accurate results. In viscometers with externally applied pressure, the effective pressure gradient includes the externally applied pressure gradient as well as the hydrostatic head of the fluid in the viscometer. Thus, hydrostatic corrections are also needed to account for the constantly decreasing hydrostatic head. Use of this correction is crucial for the Poiseuille relation to hold (i.e., for a velocity profile in which the rate of shear is a function of radial position, r).

Next, consider the functioning of a cone-and-plate viscometer. For this device, the fluid sample is contained between a cone of large apical angle and a plate normal to its axis. If the angle between the cone and the plate, Ψ, is small, the rate of shear is essentially constant and can be determined as follows. Variable ω is the angular velocity at which the cone is rotated. The linear velocity of the fluid at any radial distance r is then

$$V = \omega r$$

The rate of shear will be given by the ratio of the linear velocity and the gap between the cone and plate h at that radius. From the figure we were given, it is easy to see that $\tan\Psi = h/r$. The shear rate $\dot{\gamma} = \omega r/r\tan\Psi \approx \omega/\Psi$ provided that the cone angle Ψ is small. Thus, the shearing stress is independent of the radius in this configuration, and the entire fluid sample is being subjected to a constant rate of shear. The total torque T is determined by integration,

$$T = \int_A r\tau_r dA$$

where the area element $dA = 2\pi r dS$. However, the figure enables us to write $r = s\cos\Psi$, so that $ds = dr/\cos\Psi$ or simply $ds = dr$ if Ψ is small. The integral then becomes

$$T = \tau_r \int_0^R 2\pi r^2 dr = \tau_r \times \frac{2\pi R^3}{3}$$

$$\therefore \tau_r = \frac{3T}{2\pi R^3}$$

For a Newtonian fluid, $\tau_r = \mu\dot{\gamma}$, with the result that

$$\tau_r = \frac{3T}{2\pi R^3} = \mu \times \frac{\omega}{\Psi} \rightarrow \mu = \frac{3\Psi T}{2\pi\,\omega R^3}$$

That is, the viscosity of the fluid can be obtained with knowledge of the torque T, the angular velocity ω, and the geometry of the device.

P.2B ➡ *Solution*

In the coaxial cylinder rheometer, the fluid for which the viscosity is to be established is placed in the space between two cylinders. The inner cylinder, also referred to as the "bob," remains stationary while the outer cylinder, named the "cup," is rotated at a constant speed V (although both cylinders may be spun in some configurations). The shear stress in the fluid is equal to the force F applied to the outer cylinder divided by the surface area A of the internal cylinder,

$$\tau = \frac{F}{A}$$

The shear rate $\dot{\gamma}$ for the fluid in the gap between the cylinders may be calculated as the ratio of the velocity of the cylinder, V, to the gap width h; that is,

$$\dot{\gamma} = \frac{V}{h}$$

We know that the product of shear rate and viscosity yields the shear stress,

$$\tau = \mu\dot{\gamma} \rightarrow \mu = \frac{\tau}{\dot{\gamma}}$$

so that

$$\tau = \mu\dot{\gamma}$$

$$\therefore \mu = \frac{\tau}{\dot{\gamma}} = \frac{\left(\frac{F}{A}\right)}{\left(\frac{V}{h}\right)} = \frac{Fh}{VA}$$

Suppose that D is the diameter of the inner rheometer cylinder, and L is its length. The fluid velocity at the inner surface is

$$V = \omega\frac{D}{2}$$

Also, the torque T acting on the system is the product of force F and $D/2$,

$$T = F\frac{D}{2} \rightarrow F = \frac{2T}{D}$$

Substituting the expressions we have for the velocity V and the force F in the equation that provides the coefficient of viscosity, it follows that

$$\tau = \mu\dot{\gamma}$$

$$\therefore \mu = \frac{Fh}{VA} = \frac{\left(\frac{2T}{D}\right)h}{\left(\omega\frac{D}{2}\right)A} = \frac{\frac{2Th}{D}}{\frac{\omega AD}{2}} = \frac{2Th}{D} \times \frac{2}{\omega AD} = \frac{4Th}{\omega AD^2}$$

Finally, substituting $A = \pi DL$, we obtain

$$\mu = \frac{4Th}{\omega \times \pi DL \times D^2} \rightarrow \boxed{\mu = \frac{4Th}{\pi D^3 L\omega}}$$

Thus, with knowledge of the torque imparted on the system and of the angular velocity of one of the cylinders, along with some geometric parameters, one could easily determine the viscosity of the fluid. Note that this expression is quite similar to the relationship we derived earlier for μ in the cone-and-plate viscometer, which is to be expected given the similar functioning of these devices. Bear in mind that these are simplifications of the real problem and are not used in rheometry practice.

P.2C ➡ *Solution*

In the lower range of rates of shear, the viscosity of blood decreases with increasing $\dot{\gamma}$, as shown in Figure 8. One of the reasons for this behavior is that, at low shear rates, the red blood cells tend to agglutinate in rod-shaped stacks of individual cells (rouleaux). These structures align themselves in an end-to-side and side-to-side fashion and form a secondary structure consisting of branched three-dimensional aggregates, a solid-like formation that resists flow and contributes significantly to the large viscosity of blood at low $\dot{\gamma}$. The amount of cells agglutinated in a rouleaux decreases as the shear rate is augmented; indeed, some investigators have shown that, as $\dot{\gamma}$ increased from 5.8 to 46 s^{-1}, each doubling of shear rate resulted in a decrease in average rouleaux size of approximately 50%. It is believed that, in the majority of the circulation, under healthy conditions, the shear rates are too high to allow for the appearance of

rouleaux. Since the viscosity of blood in large blood vessels at low rates of shear is inversely proportional to $\dot{\gamma}$, blood is said to be a *shear-thinning* fluid. As $\dot{\gamma}$ becomes greater than 200 s^{-1}, the viscosity becomes approximately constant, at least in the case of large arteries, and the fluid can then be considered Newtonian (Figure 8a). When the shear rate is about 1000 s^{-1}, which is typical for many blood vessels in vivo, the non-Newtonian behavior is insignificant and the apparent viscosity approaches an asymptotic value, which is in the range of 3 – 4 $mNs \cdot m^{-2}$.

P.2D ➡ *Solution*

As can be seen in Figure 9a, blood viscosity increases dramatically as the hematocrit increases. The strong nonlinear increase in viscosity with hematocrit at low shear rates is thought to be due to an increase in rouleaux density, length, and cell-cell interaction with increasing RBC concentration. Fluid mechanics studies have shown that liquid droplets in a sheared suspension deform. There is experimental evidence, obtained with dilute suspensions of red cells, that indicates that they too deform when in a sheared flow. Thus, it seems likely that it is this deformation and rotation of the red cells which contribute to the non-Newtonian behavior of blood. Strong support for this argument comes from a study with experimentally hardened red cells; a suspension in such modified cells, even at a hematocrit of 40%, is approximately Newtonian, much like a suspension of rigid spheres. The fact that blood with the same level of suspended red blood cells does not display such behavior suggests that the mechanical properties of red blood cells play an important role in the hemodynamics of blood vessels. As seen in Figure 9b, at relatively large values of hematocrit (i.e., greater than about 30%), the viscosity of a suspension of rigid spheres becomes larger than that of a suspension of hardened cells, and much more so than a suspension of normal cells. The flexibility of erythrocytes has an attenuating effect on the relative viscosity of the fluid, particularly at high values of hematocrit, and makes the suspension less resistant to flow. It is a striking fact that the viscosity of a suspension of rigid spheres tends to infinity as the volume concentration (equivalent to hematocrit) approaches 60% - that is, it cannot be sheared – whereas a suspension of normal red cells, on the other hand, will flow even at a hematocrit as high as 98%.

P.2E ➡ *Solution*

Walburn & Schneck attempted to obtain a power law expression for viscosity based on a number of parameters and verified that, if we were to consider a three-parameter model for this quantity, the most important variables would be shear rate, hematocrit, and TPMA, or total protein minus albumin, in decreasing order of importance. Accordingly, blood proteins other than albumin might be yet another important factor in the determination of blood viscosity. The graph we were given suggests that globulin has the dominant effect on increasing the viscosity of blood, particularly at low shear rates, whereas albumin moderates the rise in viscosity. The effect of fibrinogen is insignificant. A fourth supposedly influential factor would be temperature, which is kept in a narrow range to maintain homeostasis and thus should affect blood viscosity substantially if it were changed even slightly. Indeed, blood viscosity does vary significantly with this variable; it has been found, for example, that when the temperature of blood with Ht = 40% is decreased from body temperature (37°C) to room temperature (22°C), the viscosity at a shear rate of 212 s^{-1} increases from 3.8 mPa·s to 6.3 mPa·s, an increase of nearly 66%. On the other hand, Merrill et al. have found that the ratio of whole blood viscosity to the viscosity of water remains approximately constant for temperatures ranging from 10 to 40°C and shear rates varying from 1 to 100 s^{-1}. Consequently, blood viscosity is often reported relative to the viscosity of water at the same temperature. A fifth component that may affect the viscosity of blood substantially is plasma, the extracellular matrix of blood cells. Properties of this fluid are sufficiently similar to water – a density of 1.035 g/cm^3, a viscosity ranging from 1.1 cP to 1.6 cP – for us to assume that its contribution to the viscosity of blood is identical, or slightly greater, than the viscosity of water itself. Also, plasma can be considered a Newtonian fluid, despite the existence of mammalian studies that have suggested otherwise. Early reports of non-Newtonian behavior in plasma were attributed to the formation of a surface film at the plasma/air interface in the rheometer.

P.2F ➡ *Solution*

When blood is subjected to very low rates of shear, rouleaux are known to form in blood and a tangled network of aggregated red cells can be observed. If such blood is subjected to a shear stress below a critical value, the aggregated cell structure is believed to deform, without the blood flowing; that is, the fluid exhibits a *yield stress*. There is certain experimental evidence supporting the existence of a yield stress for blood, and careful measurements have suggested a yield stress of 1.5 – 5.0 mN/m^2. Predictably, this decreases with hematocrit, and there is a critical hematocrit below which no yield stress is found, which usually ranges between 5 and 8%. It is presumed that there are then too few red cells per unit volume of blood to permit complete bridging of the sample by a structure of aggregated red cells. The yield stress of blood is increased if the concentration of fibrinogen or gamma globulin in the blood is high, which is expected because of the tendency for these asymptotic protein molecules to promote rouleaux formation. In closing, it can be noted that, despite the existence of such a yield stress for blood, its value is far too small to be of physiological importance in most cases.

▸ Problem 3

P.3A ➡ *Solution*

Before anything else, we need to investigate the dimensions of A_V for it to be given in cm^2. Substituting $[CO] = [\text{cm}]^3/[\text{min}]$, $[T_E] = [\text{s}]/[\text{beat}]$, $[HR] = [\text{beat}]/[\text{min}]$, and $[\Delta p] = [\text{mmHg}]$, it follows that

$$[\text{cm}]^2 = \frac{[\text{cm}]^3/[\text{min}]}{\frac{[\text{s}]}{[\text{beat}]}\times\frac{[\text{beat}]}{[\text{min}]}\times[K]\times\sqrt{[\text{mmHg}]}}$$

$$\therefore 1 = \frac{[\text{cm}]}{[\text{s}]\times[K]\times\sqrt{[\text{mmHg}]}}$$

$$\therefore [K] = \frac{[\text{cm}]}{[\text{s}]\sqrt{[\text{mmHg}]}}$$

That is to say, the Gorlin coefficient has units of cm divided by seconds times the square root of millimeters of mercury. Let us consider the hypothetical patient for the present problem. The cardiac output is 5 L/min = 5000 cm^3/min, the ejection time per beat is 358 ms = 0.358 s, the heart rate is 70 beats per minute, and the pressure gradient is 81 mmHg. Also, K = 44.3 cm/s$\sqrt{\text{mmHg}}$. Then, substituting the pertaining variables, A_V is computed as

$$A_V = \frac{5}{0.358\times 70\times 44.3\times\sqrt{81}} = 0.50\ \text{cm}^2$$

The average flow rate across the valve is 5000 mL/25 s = 200 mL/s.

P.3B ➡ *Solution*

Given the blood density ρ = 1060 kg/m^3, the flow velocity at the vena contracta V_{VC} = 1.66 m/s, the cardiac output CO = 5000/60 = 83.33 cm^3/s, and the aortic area A_A = 4.9 cm^2, we can determine the energy loss as

$$E_L = \frac{1060}{2}\left[1.66+\frac{5000/60}{4.9}\left(\times\frac{1}{100}\right)\right]^2\times\left(\frac{1}{133.3}\right) = 13\ \text{mmHg}$$

where the terms in parentheses are unit conversion factors. We proceed to compute the effective orifice area, EOA, as

$$EOA = \frac{V_V A_V}{V_{VC}} = \frac{CO}{V_{VC}} = \frac{5000/60}{1.66(\times 100)} = 0.50\ \text{cm}^2$$

where, as before, 100 is introduced in the denominator as a unit conversion factor. Finally, to obtain the energy loss coefficient, all we have to do is substitute the values of EOA and A_A into the formula we were given, namely,

$$\text{Energy loss coefficient} = \frac{(EOA)\times A_A}{A_A - EOA} = \frac{0.50\times 4.9}{4.9-0.50} = 0.56$$

P.3C ➡ *Solution*

After valve replacement, heart valve patients never recover completely, and are prone to a number of deleterious, and sometimes fatal, events. Incidence of potential valve-related complications, such as thromboembolic events, ranges between 2 and 4% per patient-year, and risk of death is about 1% per year of life with the prosthesis. Heart valve patients should be examined annually by a cardiologist. Some clinicians request annual echocardiograms, but examination every 3 to 5 years is probably adequate, with an increase in the frequency of examination for tissue valves starting 10 years after implantation.

Thromboembolic complications – namely, thrombolic stenosis, which is the partial blockage of part of the prosthesis, and thromboembolism - are a major cause of morbidity and mortality in patients with a prosthetic heart valve, with an estimated clinical event rate between 0.6% and 2.3% per patient year. Thrombosis of mechanical valves can also increase regurgitation.

Stenosis of bioprosthetic valves is often a consequence of progressive valve calcification, with a variable time from valve implantation to calcification depending on the specific valve type and on patient characteristics. An increased rate of tissue valve calcification is seen with younger age, pregnancy, mitral valve position, chronic renal failure, and hypercalcemia. Patients with prosthetic valve stenosis have symptoms, physical examination, and echocardiographic findings similar to those with native valve stenosis.

A small degree of prosthetic valve regurgitation is normal with characteristic patterns of regurgitation for each valve type. Pathologic mechanical prosthetic valve regurgitation most often is paravalvular or may be related to leaflet calcification and degeneration. Specifically, tissue valves are prone to rupture of thin areas adjacent to a calcific nodule and in the setting of endocarditis. After closure of the valve, paraprosthetic blood regurgitation of various degrees of severity occurs through this communication. It seldom surpasses 10 percent of systolic volume. Paraprosthetic regurgitation is always pathological and has to be distinguished from transvalvular regurgitation, which is in a minimal quantity present in all prostheses.

Another common dangerous event in blood flow across valves is hemolysis, the destruction of blood cells. Heart valves typically give rise to regions of locally accelerated blood flow, inducing abnormally high fluid forces and shear stresses that may destroy red blood cells. Fortunately, this is often compensated by the body's capacity to bolster the production of erythrocytes when needed, although anemia may result if the rate of cell destruction surpasses that of cell production.

The most serious complication of prosthetic heart valves is prosthetic valve endocarditis, which is the infection of the implanted heart valve either in early or late postoperative course. The characteristic lesion of valve prosthesis endocarditis is similar to vegetations in native valves. Small vegetations are immobile and attached to valve components, but the larger ones become sessile and move following the blood flow through the valve. It has been reported that vegetations longer than 10 mm are associated with an increased risk of embolization, and large vegetations can occasionally cause prosthesis obstruction. Vegetation size is a useful indicator to plan the urgency of surgical intervention. Incidence of prosthetic endocarditis is reported in the literature to be most often between 0.2 and 0.8% for each year of life with an implanted valve.

▸ Problem 4

P.4A ➡ *Solution*

Fahraeus studied the flow of blood from large feeding tubes into long, narrow glass tubes (i.e., capillary tubes) of diameters between 0.05 and 1.5 mm. He found that in capillary tubes with diameters below 0.3 mm the ratio of the tube hematocrit to that in the feeding tube decreased with decreasing diameter. If we measure the hematocrit of whole blood in a reservoir and flowing out through a tube attached to the reservoir, hematocrit will be found to be lower in the tube. Fahraeus conjectured that as the red blood cells migrate toward the center of the capillary tube, their average velocity increases. For the mass flow rate of RBC in the larger feeding tube to be the equal to that in the capillary tube,

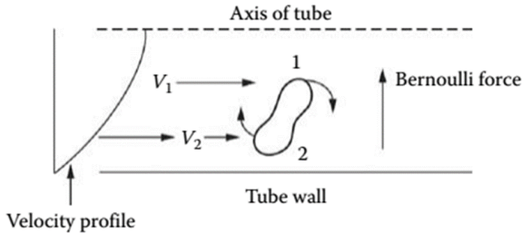
the density of RBCs must be lower in the capillary tube. This reduced hematocrit is a consequence of the cell-free layer, for the suspended red cells move down the central portion of the tube at a relatively fast velocity, whereas plasma also flows in the slower moving region near the wall. This effect will occur regardless of the velocity profile. The mean time for red cells to traverse a given length of tube becomes less than that for the plasma; if the dynamic hematocrit were the same as the static value at the entrance, then we would end up with an increased concentration of red cells at the end of the tube. In fact, the dynamic hematocrit measured in any fairly narrow tube is always less than the static hematocrit, so that while the transit time per cell is reduced relative to the plasma, the total number of cells passing through the tube is maintained at the appropriate level. This phenomenon is known as the *Fahraeus effect*, but is sometimes referred to simply as *dynamic hematocrit*. Note that this is a separate effect from any change in the tube hematocrit due to entrance or "screening" effects as blood flows from the feeding tube into the capillary tube.

Mathematically, the hematocrit within a microsize vessel (H_t) is lower than the hematocrit in the blood entering and the blood discharge hematocrit (H_d), i.e., $H_t < H_d$. This is attributed to the pronounced axial migration of the erythrocytes. One expression used to provide H_t as a function of H_d and vessel diameter D, given in μm, was proposed by Pries et al. in 1990,

$$\frac{H_t}{H_d} = H_d + (1 - H_d)\left(1 + 1.7e^{-0.415D} - 0.6e^{-0.011D}\right)$$

P.4B ➡ *Solution*

As noted in the graph, the apparent viscosity for blood has a very low value in very small diameter tubes (i.e., tubes with diameters ranging from 0.04 and 0.5 mm). The viscosity increases with the increase in tube diameter and approaches an asymptotic value at tube diameters larger than about 0.5 mm. This phenomenon of a decrease in the apparent viscosity in small diameter tubes is referred to as the *Fahraeus-Lindqvist effect*. To obtain a reasoning for this phenomenon, consider the following illustration.



Above we have a red blood cell moving close to the lower tube wall of a vessel. As the blood flows through a tube, the blood cells tend to rotate as shown. Due to the spinning of the red blood cells, they tend to move toward the center of the tube, and, consequently, a cell-free layer, known as the plasma-skimming layer, exists near the wall. In tubes with small diameters, the cross-sectional area of the cell-free zone is comparable with the central core. Hence, the net effect of the cell-free zone with a lower viscosity (that of plasma alone) is to reduce the apparent viscosity of flow through the tube. The smaller the vessel, the larger the fraction of volume occupied by the cell-free layer, and the lower the hematocrit. As the tube diameter increases, the effect of the cell-free zone reduces and hence the viscosity approaches an asymptotic value. Note that Fahraeus and Lindqvist, as well as Barbee and Cokelet and others who have investigated this phenomenon since the 1930s, provided their conduits with flow rates large enough for blood viscosity not to vary with this parameter.

It is evident that the potential resistance to blood flow through a vascular network is enormous. One of the ways the body copes with such a resistance is by means of the radial migration of red blood cells, that is, the Fahraeus-Lindqvist effect itself. In the case of the arteriolar bifurcations, the cells tend to occupy the central flow axis in a parabolic profile, resulting in lower hematocrit values at the luminal wall. On reaching a branching system, the blood cells follow the larger daughter vessel due to the shear stresses and the pressure drop caused by the faster flow through it, thereby ensuring that the progressively smaller diameter branches have lower hematocrit values, and eventually helps reduce hematocrit to near-zero values. In summary, the body

copes with resistance to blood flow by maintaining an adequate traffic of blood cells across the circulation, which is guaranteed, among other mechanisms, by the aforementioned FL effect.

Finally, it should be noted that, for microvessels close to the size of a capillary, the Fahraeus-Lindqvist is reversed and a large *increase* in viscosity is observed.

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