CHAPTER 1

Introduction to basic hemodynamic principles

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Hemodynamics is concerned with the mechanical and physiologic properties controlling blood pressure and flow through the body. A full discussion of hemodynamic principles is beyond the scope of this book. In this chapter, we present an overview of basic principles that are helpful in understanding hemodynamics.

1. Energy in the blood stream exists in three interchangeable forms: pressure arising from cardiac output and vascular resistance, "hydrostatic" pressure from gravitational forces, and kinetic energy of blood flow

Daniel Bernoulli was a physician and mathematician who lived in the eighteenth century. He had wide-ranging scientific interests and won the Grand Prize of the Paris Academy 10 times for advances in areas ranging from astronomy to physics. One of his insights was that the energy of an ideal fluid (a hypothetical concept referring to a fluid that is not subject to viscous or frictional energy losses) in a straight tube can exist in three interchangeable forms: perpendicular pressure (force exerted on the walls of the tube perpendicular to flow; a form of potential energy), kinetic energy of the flowing fluid, and pressure due to gravitational forces. Perpendicular pressure is transferred to the blood and vessel wall by cardiac pump function and vascular elasticity and is a function of cardiac output and vascular resistance.

$$\text{Total energy}(\text{TE}) = \text{potential energy} + \text{kinetic energy}$$

$$\text{TE} = (\text{perpendicular pressure} + \text{gravitational pressure}) + \text{kinetic energy}$$

$$\text{TE} = (P_{\text{Per}} + P_{\text{grav}}) + 1/2\rho V^2$$

where V is velocity and ρ is density of blood (approximately 1060 kg/m³)

$$\text{TE} = P_{\text{Per}} + (\rho \times h \times g) + 1/2\rho V^2$$

where g is gravitational constant and h is height of fluid above the point of interest.

Although blood is not an "ideal fluid" (in the Newtonian sense), Bernoulli's insight is helpful. Blood pressure is the summation of three components: lateral pressure, gravitational forces, and kinetic energy (also known as the impact pressure or the pressure required to cause flow to stop). Pressure is the force applied per unit area of a surface. In blood vessels or in the heart, the transmural pressure (i.e., pressure across the vessel wall or ventricular chamber wall) is equal to the intravascular pressure minus the pressure outside the vessel. The intravascular pressure is responsible for transmural pressure (i.e., vessel distention) and for longitudinal transport of blood through the vessels.

Gravitational forces are important in a standing person. Arterial pressure in the foot will exceed thoracic aortic pressure due to gravitational pull on a column of blood. Likewise, arterial pressure in the head will be less than thoracic aortic pressure. Similarly, gravitational forces are important in the venous system, since blood will pool in the legs when an individual is standing. Decreased ventricular filling pressure results in a lower cardiac output and explains why a person will feel lightheaded if rising abruptly from a sitting or supine position. In contrast, gravity has negligible effect on arterial or venous pressure when a person is lying flat. Gravitational pressure equals the height of a column of blood × the gravitational constant × the fluid density. To calculate hydrostatic pressure at the bedside (in mm Hg), measure the distance in millimeters between the points of interest, for example heart and foot, and divide by 13 (mercury is 13 times denser than water).

Kinetic energy is greatest in the ascending aorta where velocity is highest, but even there it contributes less than 5 mm Hg of equivalent pressure.

2. Blood flow is a function of pressure gradient and resistance

One of the properties of a fluid (or gas) is that it will flow from a region of higher pressure (e.g., the left ventricle) toward a region of lower pressure (e.g., the right atrium; Figure 1.1). In clinical practice, the patient is assumed to be supine (negating the gravitational component of pressure) and at rest. As already mentioned, kinetic energy is negligible compared to blood pressure at normal cardiac output and thus blood flow is estimated using the pressure gradient and resistance.

The primary parameter used in clinical medicine to describe blood flow through the systemic circulation is cardiac output, which is the total volume of blood pumped by the ventricle per minute (generally expressed in L/min). Cardiac
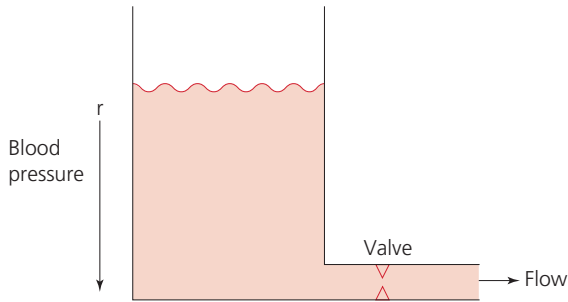
Figure 1.1 A simple hydraulic system demonstrating fluid flow from a high-pressure reservoir to a low-pressure reservoir. Note that the volume of flow can be affected by a focal resistance (i.e., the valve).

output is equal to the total volume of blood ejected into the aorta from the left ventricle (LV) per cardiac cycle (i.e., stroke volume) multiplied by the heart rate. This formula is important experimentally, but of limited used clinically because stroke volume is difficult to measure. Cardiac output is generally measured using the Fick equation or via thermodilution techniques, which are discussed in Chapter 6.

To compare cardiac output among individuals of different sizes, the cardiac index (cardiac output divided by body surface area) is used. Normalization of cardiac output for body surface area is important, as it enables proper interpretation of data independent of the patient's size (e.g., cardiac output will obviously differ widely between a 260-pound man and a 100-pound woman). Indexing to body surface area is also used for other measurements such as aortic valve area.

The relationship between blood flow, resistance, and pressure can be determined using a modification of Ohm's law for the flow of electrons in an electrical circuit:

$$\text{Flow}(Q) = \text{pressure gradient}(\Delta P) / \text{resistance}(R)$$

where ΔP is the difference in pressure between proximal and distal points in the system and R is the hydraulic resistance to blood flow between the proximal and distal points.

A useful clinical equation based on Ohm's law is:

$$\text{Mean arterial pressure}(\text{MAP}) - \text{central venous pressure}(\text{CVP})$$
$$= \text{cardiac output}(\text{CO}) \times \text{systemic vascular resistance}(\text{SVR})$$

Using this equation, we can calculate systemic vascular resistance knowing cardiac output, CVP, and arterial pressure. MAP is the average arterial pressure over time and is generally estimated using the following formula:

$$\text{MAP} = (1/3 \times \text{aortic systolic pressure}) + (2/3 \times \text{aortic diastolic pressure}).$$

This formula was developed for a heart rate of 60 beats per minute (bpm; at this heart rate, diastole is twice as long as systole) and becomes progressively more inaccurate as heart rate increases. In a patient in shock (i.e., low blood pressure and impaired tissue perfusion), measurement of CO and calculation of SVR can help identify the etiology (e.g., septic shock with high CO + low SVR or cardiogenic shock with low CO + high SVR).

3. Resistance to flow can be estimated using Poiseuille's law

Blood is not an "ideal fluid" and energy (and pressure) is lost as flowing blood encounters resistance to flow. Resistance to blood flow is a function of viscosity, vessel radius, and vessel length in a vessel without any focal obstruction (resistance to blood flow also occurs from focal obstruction such as seen with atherosclerotic disease of arteries). The relationship is known as Poiseuille's law (sometimes referred to as the Poiseuille–Hagen law) and is described by the following equation:

$$\text{Resistance} = 8 \times \text{viscosity} \times \text{length} / \pi \times \text{radius}^4$$

or, since flow = difference in pressure/resistance:

$$\text{Blood flow} = \pi \times \text{radius}^4 \times \text{difference in pressure} / 8 \times \text{viscosity} \times \text{length}$$

Since radius is raised to the fourth power, its importance in determining resistance is paramount. A 20% increase in radius leads to a doubling in flow if all other variables are constant. Or, as another example, resistance is 16 times greater in a coronary artery with a diameter of 2 mm (e.g., a distal obtuse marginal) than in a coronary artery with a diameter of 4 mm (e.g., the proximal left anterior descending).

Viscosity is also important in determining resistance (commonly abbreviated as η and with units of poise = dyne s/cm^2). It is difficult to measure directly and thus is commonly reported as relative to water. The viscosity of plasma is 1.7 × viscosity of water and viscosity of blood is 3–4 × viscosity of water, the difference being due to red blood cells and thus hematocrit.

It is important to note that Poiseuille's law only provides an approximation of resistance when used in blood vessels. The four important assumptions underlying the derivation of this equation are: (1) the viscosity of the fluid is unchanging over time or space; (2) the tube is rigid and cylindrical; (3) length of the tube greatly exceeds diameter; and (4) flow is steady, nonpulsatile, and nonturbulent. Many of these assumptions are violated when this equation is applied to blood flow in the body. Poiseuille's law is important, however, as it indicates the variables that are the determinants of resistance to flow.

In the mammalian circulation, resistance is greatest at the level of the arterioles. While the radius of a typical capillary (e.g., 2.5 microns) is smaller than the radius of the smallest arterioles (e.g., 4 microns), the number of capillaries greatly exceeds the number of arterioles, and thus the effective area is much larger. Also of importance is that arteriolar resistance can be regulated (capillaries have no smooth muscle and thus resistance cannot be regulated at that level; however, pericyte cells can constrict capillaries in certain specialized structures like the kidney's glomerulus). This enables rapid changes in vascular resistance to maintain blood pressure (e.g. in hypovolemic shock) and also enables regulation of blood flow to various organs (i.e., autoregulation). A general principle to remember is that reduction of arteriolar resistance in a tissue decreases SVR, resulting in increased cardiac output while simultaneously decreasing pressure proximal to the arterioles and increasing pressure distal to the arterioles.

4. Reynold's number can be used to determine whether flow is laminar or turbulent

Flow in blood vessels, as in any hydraulic system, is usually smooth and orderly because the fluid separates into an infinite number of concentric layers, with the highest velocity in the center and the lowest next to the vessel wall. When a fluid (such as blood) flows past a solid surface (such as the vascular wall), a thin layer develops adjacent to the surface where frictional forces retard the motion of the fluid (Figure 1.2). There is a gradient of frictional resistance (and thus velocity) between fluid in contact with the solid surface and fluid in the center of the stream. If the fluid elements travel along well-ordered, nonintersecting layers, this is termed laminar flow. The flow resistance in laminar flow is due entirely to viscous resistance of the fluid and the interactions between the fluid and the stationary wall. In laminar flow, the average velocity of a fluid is one half of the maximum velocity observed in the center of the stream.
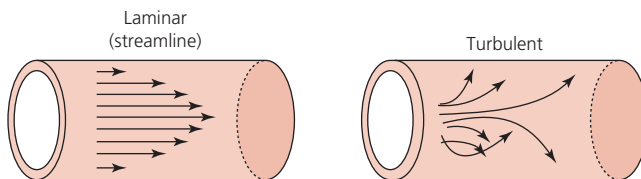
Figure 1.2 Schematic of laminar flow. Flow in straight, nonbranching tubes is usually smooth and orderly because the fluid separates into an infinite number of concentric layers with different velocities. When a fluid (such as blood) flows past a stationary surface (such as the vascular wall), a thin layer develops adjacent to the surface where frictional forces tend to retard the motion of the fluid. There is a gradient of frictional resistance (and thus velocity) between fluid in contact with the solid surface and fluid in the center of the stream. If the fluid particles travel along well-ordered, nonintersecting layers, this is termed laminar flow.
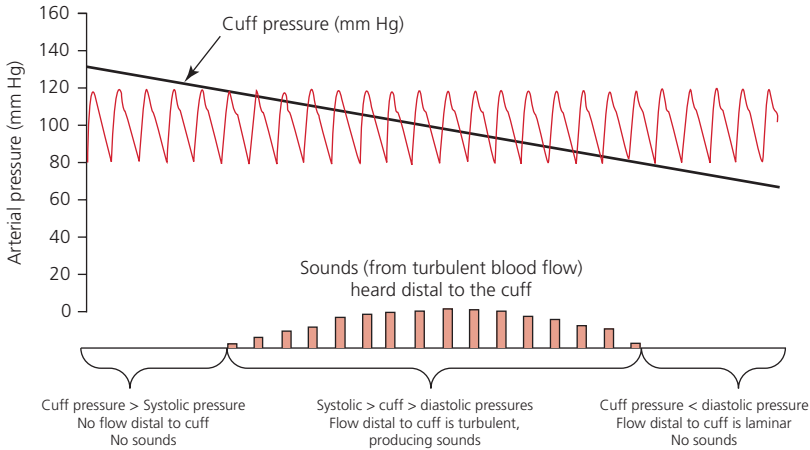
Figure 1.3 Schematic illustrating the use of transient transition from laminar to turbulent flow in measuring blood pressure.

In contrast, turbulent flow occurs when fluid elements from adjacent layers become mixed. Turbulent flow is chaotic and less efficient because of energy losses (these losses are termed inertial resistance). In turbulent flow, the relationship between pressure difference and flow is no longer linear, since the amount of resistance in the tube increases with flow. Thus, larger pressure differences are required to maintain flow. Turbulence, and associated loss of energy along with the narrowed radius, are two of the primary causes of the drop in pressure that occurs distal to a severe stenosis.

Turbulence is important for several reasons, one of which is that it creates noise (e.g., in a pipe when flow velocity is high), which is the cause of some cardiac murmurs and the Korotkoff sounds (used when measuring blood pressure; Figure 1.3). Another is that turbulence alters the relationship between flow and perfusion pressure, as already mentioned. Because of increased energy losses associated with turbulence, the relationship between perfusion pressure and blood flow is no longer linear (as described by the Poiseuille relationship) but rather, greater pressure is required to maintain adequate flow (Figure 1.4).

The transition from laminar to turbulent flow can be predicted by calculating the Reynold's number, which is the ratio of inertial forces ($V\eta$) to viscous forces (ρ/L):

$$R = \text{diameter} \times \text{velocity} \times \text{density} / \text{viscosity}$$

where viscosity (η) of blood at 37 °C is 0.0035 Pa·s (pascal-seconds; 3.5 centipoise), density (ρ) of blood is approximately 1060 kg/m³, velocity (V) of blood is in m/s, and the diameter of the tube is in meters. Reynold's number is dimensionless.

In a given hydraulic system, a critical Reynold's number exists below which flow is laminar. At Reynold's numbers near this critical number, a transitional zone exists where flow is neither completely laminar nor turbulent. Higher Reynold's numbers are associated with turbulent flow. In a long, straight, nonbranching pipe
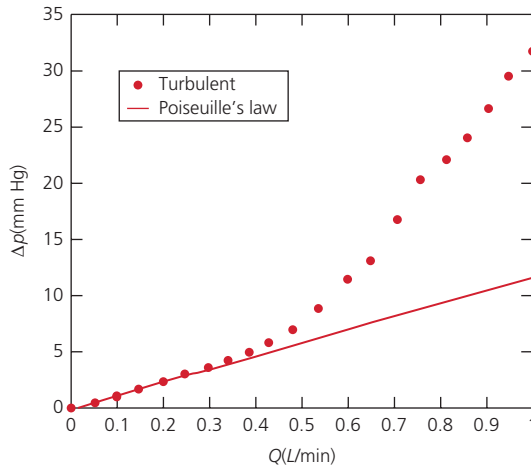
Figure 1.4 Transition from laminar to turbulent flow. Note that the pressure gradient required to increase flow increases markedly when flow transitions from laminar to turbulent.

with nonpulsatile flow, flow is generally laminar if $R < 2000$ and turbulent if $R > 2000$. It is important to note that the Reynold's number depends on the exact flow configuration and must be determined experimentally.

In the aorta, transition from laminar to turbulent flow generally occurs at a Reynold's number between 2000 and 2500. In atherosclerotic arteries and/or at branch points, the critical Reynold's number is much lower and there can be turbulence even at normal physiologic flow velocities. In severe stenoses, turbulence can be initiated at Reynold's numbers an order of magnitude less than in the theoretical, straight pipe.

The Reynold's equation is important for demonstrating variables important in determining whether flow is laminar or turbulent. As a simple approximation from this equation, we see that laminar flow is difficult to maintain in conditions of high velocity (e.g., stenotic artery) and large diameter. Vessel diameter is doubly important, for it is not only a direct variable in the equation but also influences velocity. Because of the continuity equation (see Principle 9 below), we know that velocity increases as diameter decreases. Thus, effects of blood vessel diameter on Reynold's number are magnified. Because both velocity and diameter decrease in the microcirculation, the flow there tends to be laminar.

5. Force developed by the ventricles is a function of preload or stretch—the Frank–Starling law

The three most important factors in the regulation of ventricular function (and thus cardiac output) are preload, afterload, and contractility. Preload for the ventricles is defined as amount of passive tension or stretch exerted on the ventricular walls (i.e., intraventricular pressure) just prior to the initiation of systole. This "load" applied to the ventricular wall determines end-diastolic sarcomere length and thus the force of
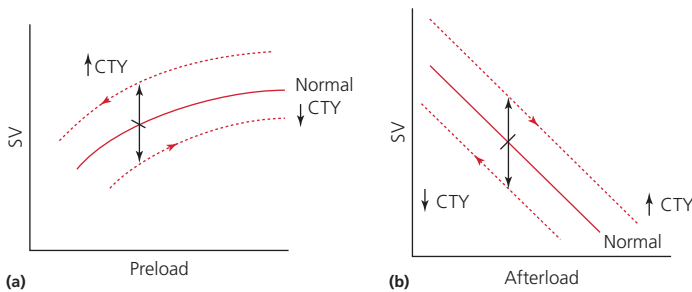
Figure 1.5 Frank–Starling principle. In panel (a), note that stroke volume (SV) increases as preload increases on any given line of contractility (CTY). Panel (b) demonstrates that stroke volume increases as afterload decreases.

contraction. The Frank–Starling law states that the passive length to which the myocardial cells are stretched at the end of diastole is a determinant of the active tension they develop when stimulated to contract. The Frank–Starling law is an intrinsic property of myocytes; that is, it is not dependent on nerve signals or hormones. The general principle is that increased preload causes increased force of contraction, which increases stroke volume and thus cardiac output (Figure 1.5). The Frank–Starling law (or mechanism) helps the heart match cardiac output to venous return.

The Frank–Starling law was derived from independent work by two investigators. In the 1890s, Otto Frank measured pressure developed by the isolated beating frog ventricle against an occluded aorta under varying preloading conditions. He found that as end-diastolic volume increased, ventricular systolic pressure and the maximum rate of pressure development (dP/dT_{max}) increased. Approximately 20 years later, Ernst Starling found similar results using a heart–lung preparation in an anesthetized dog in which he controlled heart rate, venous pressure, venous return, arterial pressure, and arterial resistance.

For any given heart, there is not just a single Frank–Starling curve. Rather, there is a family of curves, each of which is determined by the afterload and inotropic state (i.e., contractility) of the heart. While changes in venous return cause a ventricle to move along a single Frank–Starling curve, changes in contractility and afterload cause the heart to shift to a different Frank–Starling curve.

6. Wall tension is a function of pressure and radius divided by wall thickness—the Laplace relationship

Laplace's law describes the relationship between the transmural pressure difference and the tension, radius, and thickness of the vessel wall or ventricular chamber (Figure 1.6). A good approximation of wall tension in a vessel or chamber according to Laplace is:

Wall tension = pressure × radius / wall thickness
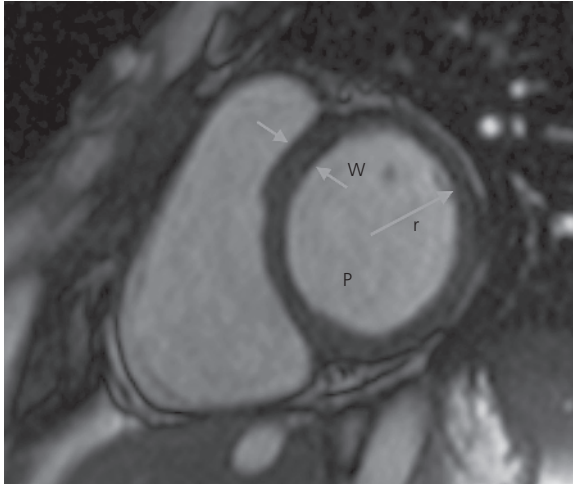
Figure 1.6 Magnetic resonance imaging (MRI) of a right ventricle and a left ventricle. The left ventricle is labeled to demonstrate Laplace's law: $t = (P \times r)/W$, where P is pressure; r is radius; W is wall thickness; and t is wall tension.

The pressure inside a blood vessel or ventricle exerts a distending force (tension) on the walls that is proportional to the magnitude of the pressure and radius. Thus, wall tension in the aorta is high. In chronic hypertension, aortic wall thickness increases as an adaptation to normalize wall tension. Similarly, LV hypertrophy develops in response to chronic elevations in ventricular pressure and/or dilatation, again as an adaptation.

There are several important implications of this relationship. One is that larger arteries must have stronger walls, since an artery of twice the radius must be able to withstand twice the wall tension at a given blood pressure. Similarly, the increased wall tension is thought to contribute to the development of aneurysms (and possibly to predict aneurysm rupture) in larger arteries. Another implication is that as the radius of the LV increases (e.g., in dilated cardiomyopathy), increased active wall tension must be developed during systole by the myocytes in order to create the same ventricular pressures for ejection. Thus, a dilated ventricle uses more adenosine triphosphate (ATP) and oxygen to generate the same stroke volume.

7. The normal venous system is a low pressure, large volume reservoir of blood which enables rapid increases in cardiac output

Approximately 60–80% of blood in the normal individual is in the venous system (with 8–10% being within the heart, 15–20% in arteries, and 5% in capillaries). There is a large capacitance in the normal venous system, and large veins are not
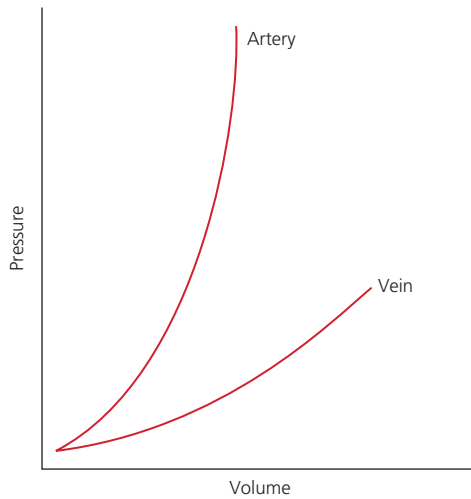
Figure 1.7 Pressure–volume relationship for arteries and veins.

fully filled but instead partially collapsed (elliptical). Thus, the venous system can absorb a large amount of volume with minimal increase in pressure. Once veins become fully distended, however, the pressure–volume relationship changes significantly (Figure 1.7). Veins have limited elasticity once they are fully distended, and at this point pressure increases rapidly with increased volume.

Since the cardiovascular system is a closed loop, venous return and cardiac output are closely coupled, and increased venous return to the heart is one of the primary mechanisms by which cardiac output is increased rapidly. For example, venous return (and cardiac output) can be rapidly augmented by increased sympathetic tone, which causes the smooth muscle in veins to contract. Similarly, skeletal muscular contractions during exercise reduce venous capacitance in the muscle beds by rhythmically compressing the veins and can markedly increase venous return.

8. The pressure and velocity of a fluid in a closed system are related

As we saw in Principle 1, Bernoulli derived the formula (now known as the Bernoulli equation) that relates the pressure, velocity, and height (i.e., gravitational forces) in the steady motion of an ideal fluid (i.e., a fluid with constant viscosity and in which there are no frictional losses during flow). The usual form is $\text{TE} = P_{\text{Per}} + (\rho \times h \times g) + 1/2\ \rho V^2$, where TE is the total energy, V is the blood velocity, P_{Per} the perpendicular pressure, ρ the blood density, g the gravitational constant, and h the height above an arbitrary reference level. It is based on the law of conservation of energy and states that the sum of potential and kinetic energy is the same at every point throughout a rigid tube.

The Bernoulli equation provides the theoretical foundation for the use of pulse wave and continuous wave Doppler to estimate pressures. While the actual derivation is more complex, for practical use in Doppler echocardiography the Bernoulli equation is simplified to $P_1 - P_2 = 4V^2$, where P is pressure and V is velocity (labeled the modified Bernoulli equation). Because of the relationship between velocity and pressure, Doppler-determined blood velocity can be used to estimate pressures within the heart and vasculature (e.g., estimating pulmonary artery pressures at the time of echocardiography by measuring the velocity of tricuspid regurgitation).

Derivation of the modified Bernoulli equation

Ignoring gravitational forces, the Bernoulli equation predicts that the relationship between pressures at two points (P1 and P2) within a system with a flowing fluid would be:

$P_1 + 1/2\rho V^2 = P_2$

Or, stated another way, the difference in pressure between the two points would be:

$P_2 - P_1 = 1/2\rho V^2$

Inserting units and blood density ($\rho = 1050$ kg/m³):

$\Delta P(\text{kg}/\text{ms}^2) = 1/2(1050\text{kg}/\text{m}^3)V^2\left(\text{m}^2/\text{s}^2\right)$

Since 1 mm Hg = 133.3 Pa = 133.3 kg/m²

$\Delta P \times 133.3 = 1/2(1050)V^2$

and thus we arrive at the formula we recognize:

$\Delta P(\text{mmHg}) = 3.938V^2$

commonly abbreviated to:

$\Delta P(\text{mmHg}) = 4V^2$

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9. The velocity of blood increases and pressure decreases as the cross-sectional area of the blood vessel decreases

An important hemodynamic concept is the continuity equation, which is derived from the law of conservation of mass. This equation is based on the principle that flow at any given point in series in a closed hydraulic system will be equal to flow at any other point. Thus, since flow is constant, velocity is inversely proportional to the cross-sectional area (Figure 1.8):

$Q = A_1V_1 = A_2V_2 = A_3V_3$

where A is area and V is velocity at any given point within the system. An implication of this equation is that velocity increases as the cross-sectional area decreases (e.g., at the site of an arterial stenosis). Similarly, blood velocity decreases as it
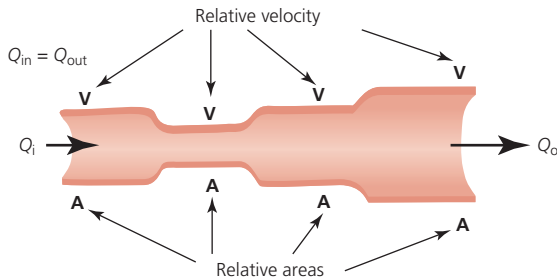
Figure 1.8 Relationship between blood velocity and cross-sectional area of blood vessels. Because of the law of conservation of mass, flow within any given major division of the circulatory system in a closed hydraulic system will be equal to flow within any other major division. Thus, velocity in a major division is inversely proportional to the aggregate vessel cross-sectional area in that division.

flows from the aorta into the capillary system (which, for the purpose of this discussion, can be thought of as "one very large vessel" in series with the aorta and vena cava), but then increases again as it coalesces from venules to veins to the vena cava. An average velocity of blood at any given point within the major divisions of the circulation (i.e., aorta, arteries, arterioles, capillaries, venules, veins, vena cava) can be estimated, knowing the volume of blood and the aggregate cross-sectional area of the blood vessels in a given division.

The continuity equation is used in the echocardiography laboratory to estimate aortic valve area. The cross-sectional area of the LV outflow tract is measured along with blood velocity at that point (using pulse wave Doppler) and then volumetric blood flow in the outflow tract is calculated. Using the continuity equation, the cross-sectional area of the valve can be calculated by dividing volumetric blood flow by the measured velocity at the valve.

10. Resistance increases when blood vessels are connected in series and decreases when blood vessels are connected in parallel

Poiseuille's equation estimates resistance to flow in a single vessel. The human cardiovascular system, however, includes complex circuitry with distinct blood vessels in series (connected one after another) and in parallel (arising from the dichotomous divisions of larger vessels into smaller branches). Blood ejected from the heart moves from aorta → large arteries → small arteries → arterioles → capillaries → venous system → heart. While the aorta is a single vessel, the rest of the circulatory system involves multiple vessels connected in parallel (e.g., the carotid arteries, renal arteries, and other major branches from the aorta form a parallel circuit).
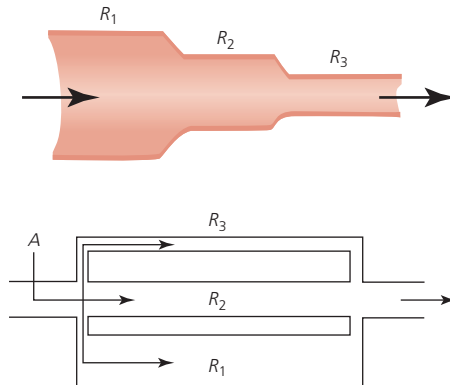
Figure 1.9 Circuits (or blood vessels) in series and in parallel.

For blood vessels connected in series, the total resistance of the system is equal to the sum of resistance in each vessel (Figure 1.9):

$$R_{total} = R_1 + R_2 + R_3$$

Thus, for blood vessels connected in series, the resistance of the system is always greater than resistance in any one vessel. Thus, for three vessels in series, each with resistance R, the total resistance of the system is $3R$.

For blood vessels connected in parallel, resistance is equal to the sum of the reciprocal of the resistance in each vessel:

$$1 / R_{total} = 1 / R_1 + 1 / R_2 + 1 / R_3$$

Thus, for blood vessels connected in parallel, resistance of the system is always less than resistance in any vessel. For three vessels in parallel, each with resistance R, the total resistance of the system is R/3.

An important principle is that more than 60% of the resistance to flow occurs within the arterioles. The diameter of the arterial system progressively decreases from aorta→arteriole. Energy losses (pressure drop) are minimized in the larger arteries, despite decreases in diameter, by having many arteries in parallel. The large pressure loss in arterioles is due to a dramatic decrease in diameter (Figure 1.10) without a correspondingly large enough increase in the number of arterioles in parallel. It goes without saying that the energy loss in arterioles serves many important functions, such as lowering pressure and velocity in capillaries to allow optimal transit time for red blood cells for diffusion of oxygen (O_2) and carbon dioxide (CO_2).

Since the greatest resistance occurs within the arterioles, systemic vascular resistance is very sensitive to changes in arteriolar diameter from constriction and dilation. Assuming constant cardiac output (keep in mind that cardiac output is a dynamic process and may increase or decrease by mechanisms other than changes
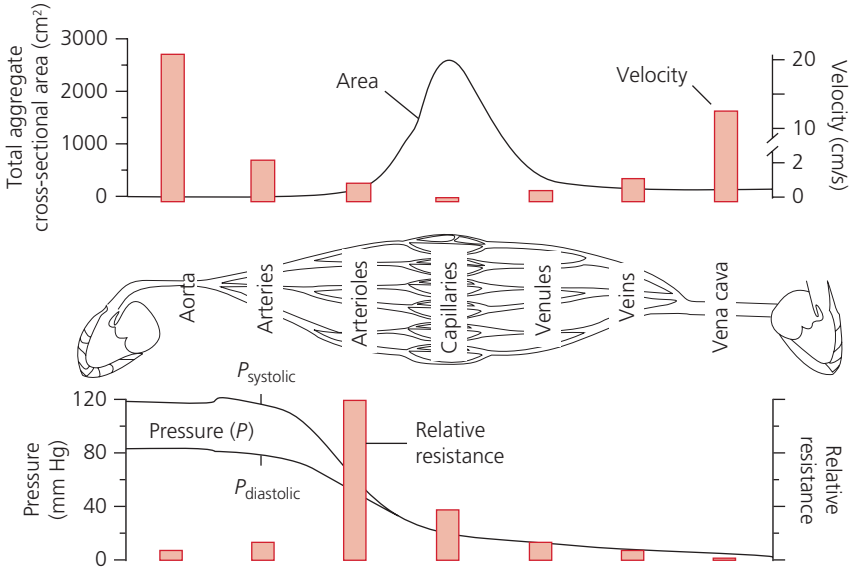
Figure 1.10 Pressure, velocity, and flow in various parts of the circulation.

in vascular resistance), agents that dilate arterioles in a tissue bed will decrease blood pressure (i.e., pressure proximal to the arterioles), but also increase pressures in the capillary bed. Similarly, vasoconstrictors increase blood pressure but reduce pressure within capillaries. In real life, cardiac output does not remain constant. The use of vasopressors to maintain blood pressure will increase vascular resistance but at a potential cost of decreased cardiac output (e.g., in the patient with cardiogenic shock) and/or organ failure due to increased vascular resistance (e.g., worsening renal function in patients on vasopressors).