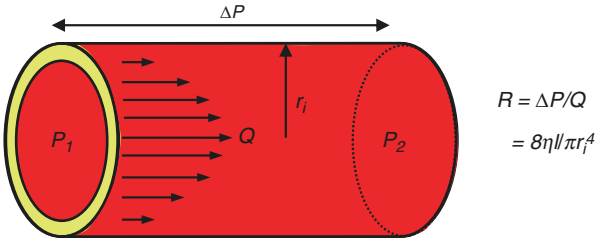
Chapter 6
Resistance



Resistance to blood flow is an important property of blood vessels. Resistance can be determined by the ratio of mean pressure difference over and mean flow through a blood vessel ($R = \Delta P/Q$, Ohm's law). For a single uniform vessel Poiseuille's law can predict its resistance, but in practice resistance is obtainable using Ohm's law. In other words, resistance although depending on the vascular geometry and blood viscosity, can be calculated directly from measurements of mean pressure difference, ΔP, and mean blood flow, Q. Detailed knowledge of the vascular geometry is not required. Ohm's law not only pertains to single blood vessels but may also be applied to combinations of vessels, whole organ beds, and the whole systemic or pulmonary circulation. Rules for addition of resistances are discussed below. Resistance should always be calculated from a mean pressure difference as indicated by ΔP. In the systemic circulation venous pressure is usually much lower than aortic pressure and ΔP is close to aortic pressure. However, this is not the case in the pulmonary circulation. The resistance in the systemic, and pulmonary circulation are mainly determined by the resistance of small arteries and arterioles, often called resistance arteries. This means that the mean pressure in all large, conduit arteries, is almost the same. The arterioles act as resistances to regulate flow to the local tissue.

N. Westerhof et al., *Snapshots of Hemodynamics*,
https://doi.org/10.1007/978-3-319-91932-4_6

6.1 Description

Poiseuille's law (Chap. 2) shows that resistance depends on the length and diameter of the vessel, and the viscosity of blood. However, even for a single blood vessel, it is difficult to derive the relation between pressure and flow on the basis of Poiseuille's law. The diameter of the vessel needs to be accurately known because of the fourth power law. Furthermore, the vessel should be uniform, and, especially for small vessels, the anomalous viscous properties of blood makes it impossible to use a single value for viscosity. Accurate calculation of resistance on the basis of Poiseuille's law is therefore virtually impossible. However, resistance can be calculated from the ratio of the *mean* pressure gradient and *mean* flow constituting a practical experimental approach. Thus, although Poiseuille's law makes it possible to arrive at several important conclusions regarding vascular function, in practice we use resistance as calculated using Ohm's law: the ratio of the mean pressure difference over the vessel or system and mean flow through it, $\Delta P/Q$ (Fig. 6.1).

To understand where resistance is located in the arterial tree we need to know some rules about resistances.

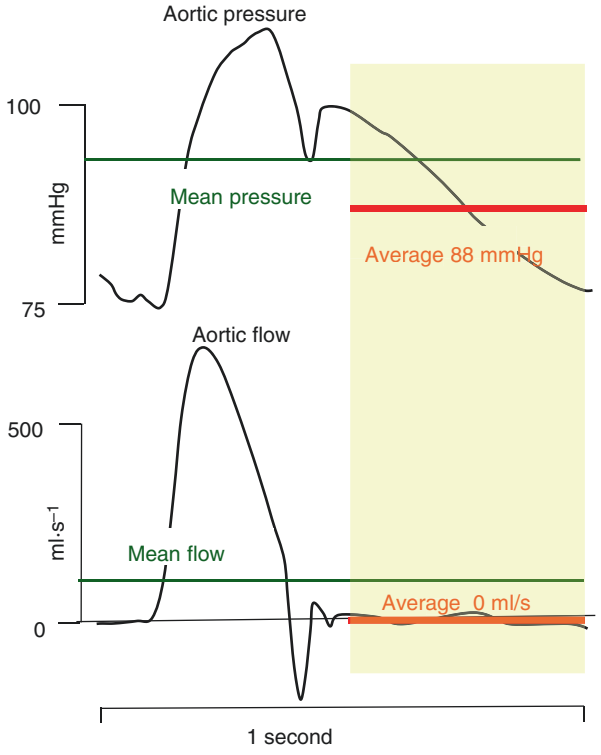


Fig. 6.1 Ohm's law quantifies the total arterial resistance by the ratio of mean pressure difference and mean flow. The instantaneous ratio of pressure and flow or the ratio of diastolic pressure and flow averaged over diastole only gives nonsensical results: divided by zero

6.1.1 Addition of Resistances

Two resistances in series result in a total resistance equal to the sum of the resistances. This rule can be derived as follows. The total pressure drop over two resistances in series is the sum of the individual pressure drops, i.e., $\Delta P_{total} = \Delta P_I + \Delta P_{II}$ and flow is the same through both. Thus $\Delta P_{total} = Q \cdot R_I + Q \cdot R_{II} = Q \cdot (R_I + R_{II}) = Q \cdot R_{total}$. Thus, $R_{total} = R_I + R_{II}$, i.e., the total resistance is the sum and thus larger than each individual resistance.

Two resistances in parallel add up in a so-called 'inverse' fashion (Fig. 6.2). When in parallel, the pressure drop, ΔP, over both daughter vessels is the same, and the two flows add up to total flow, Q_{total}, thus

$$Q_m = Q_{total} = Q_{d,1} + Q_{d,2} = \Delta P / R_1 + \Delta P / R_2 = \Delta P / \left(1/R_1 + 1/R_2\right) = \Delta P / R_{sum}$$

and we find

$$1/R_{sum} = 1/R_1 + 1/R_2$$

For the two daughters and mother together, the resistance is then:

$$R_{total} = R_{mother} + R_{sum}$$

An easier calculation is through conductance (G), which is the inverse of resistance, G = 1/R. Ohm's law written in terms of conductance is $Q = \Delta P \cdot G$. Parallel conductances can be added directly: $G_{total} = G_1 + G_2$.

Thus, two equal resistances in parallel add to a total resistance of half the resistance of each. Ten equal arterioles in parallel result in an overall resistance equal to 1/10 of a single arteriole.

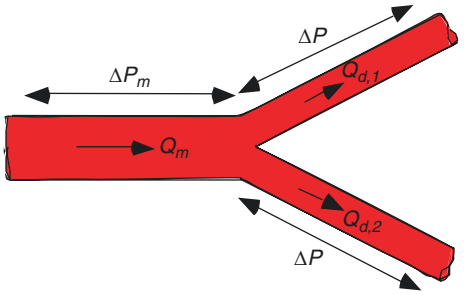


Fig. 6.2 A blood vessel, mother, divides into two smaller, daughter vessels. We determine the resistance of this network by proper addition of the two distal vessels in parallel and then add the resistance of the mother vessel. Note that we work from the distal end

6.1.2 Physical Reason Why the Systemic Resistance Is Mainly Located in the Arterioles

We first compare the resistance of the aorta with the resistance of an arteriole using Poiseuille's law. Comparing an aortic with radius of 15 mm and an (arbitrary) length of 50 cm with an arteriole with a radius of 7.5 micrometer and a length of 1 mm we can estimate the resistance ratio of the two. The radius ratio is 2000 and the length ratio is ~500, thus the resistance ratio is $(2000)^4/500$, i.e., $\sim 3 \cdot 10^{10}$. Thus, the resistance of a single arteriole is $3 \cdot 10^{10}$ larger than of a 50 cm long aorta.

However, there is only one aorta and about $3 \cdot 10^8$ arterioles, and since these arterioles all sprout (indirectly) from the single aorta we can consider them as in parallel. Thus, the total arteriolar resistance is about $3 \cdot 10^{10}/3 \cdot 10^8 \approx 100$ times as large as the resistance of the aorta.

Therefore, the pressure drop over the aorta is about 1% of the total pressure drop over the systemic arterial system, which is about 100 mmHg. Indeed, the mean pressure in the dorsalis pedis artery is, in the supine human, only a few mmHg lower than mean pressure the ascending aorta.

6.1.3 Resistance of Capillaries and Veins

Capillaries have diameters that are of the same order as the smallest arterioles but their number is larger (4–5 capillaries per arteriole) and therefore their resistance is about 4–5 times smaller. The glycocalyx, the carbohydrate structures on the luminal surface of the microvascular endothelial cells, not only protects against edema, but also reduces the effective capillary diameter and thus increases capillary resistance [1]. At present an unresolved controversy is the mechanism of the low resistance of capillaries when the red cells (RBCs) have a diameter larger than the capillary. The red blood cells deform to squeeze through even though the pressure gradient is very small. An important role is thus played by the deformability of the RBCs [2], reduced RBC deformability as in Sickle Cell Anemia increases the resistance to capillary flow. The interaction of the capillary endothelial glycocalyx with the RBCs has been likened to skiing on compressible porous media which would reduce resistance to flow [3]. A possibly different mechanism is that the red blood cell endothelium interface consists of a layer of water that is not liquid [4]. Still capillaries contribute little to total systemic resistance.

In the systemic vascular system venules and veins have larger diameters than their accompanying arteries and often appear as two veins to one artery. Therefore, total venous resistance in the systemic circulation is about 1/20 of total resistance. It is still not entirely clear whether resistance and its regulation should be based on diameters or anatomical location [5].

However, in the pulmonary vascular system the veins appear to contribute to overall resistance (Chap. 28) [6].

6.1.4 Calculation of Vascular Resistance

The total resistance of the systemic circulation can be calculated as follows. When mean aortic pressure is taken to be about 105 mmHg and central venous pressure is about 5 mmHg the pressure difference is 100 mmHg. With a Cardiac Output of 6 l/min, thus 100 ml/s, the total resistance is 100/100 = 1 mmHg·s·ml^{-1}. The units are mmHg·s·ml^{-1} and called peripheral resistance units, PRU. Often physical resistance units are used in the clinic and resistance is then expressed in dyn·s·cm^{-5} or Pa·s·m^{-3}. As can be seen from Appendix 7 the following holds: $7.5 \cdot 10^{-9}$ mmHg·s·ml^{-1} = 10^{-5} dyn·s·cm^{-5} = 1 Pa·s·m^{-3} or a resistance of 1 mmHg·s·ml^{-1} = $1.3 \cdot 10^{3}$ dyn·s·cm^{-5} = $1.3 \cdot 10^{8}$ Pa·s·m^{-3}.

For the systemic circulation subtraction of venous pressure is often omitted without introducing large errors. However, in the pulmonary circulation with mean pulmonary artery pressure of about 20 mmHg and a pulmonary venous pressure of 5 mmHg, use of the pressure difference is mandatory, and pulmonary resistance is (20 – 5)/100 = 0.15 PRU, which is about 15% of the resistance of the systemic circulation.

6.1.5 The Zero Flow Intercept Pressure, Starling Resistor and the Waterfall Model

Pressure-flow relations often show and intercept with the pressure axis: the zero-flow pressure intercept. This intercept depends on vasoactive state: with vasodilation the intercept is lower. It has been suggested that the intercept depends on microvascular compliance [7]. Sipkema et al. [8], using a thin-walled latex microtube, showed that the intercept pressure relates to the plateau of its pressure-volume relation. Thus, implicating vessel compliance as the explanation. Others have suggested that the rheological properties of blood play a role [9], but changing the perfusion fluid from blood to a crystalloid medium did not change the intercept pressure [10]. Sagawa et al. showed that the intercept pressure depends on smooth muscle tone [11]. Surface tension between blood and vessel wall [12] and the role of the glycocalyx have been suggested to play a role.

The calculation of resistance assumes the vascular system to be linear and resistance to be pressure independent. In reality the vessels are compliant implying that with increased pressure vessel diameters are larger (nonlinear pressure-flow relation) and resistance smaller. Linehan et al. developed a model to quantify the effect of hematocrit, Hct, and vessel distensibility, $\alpha = \Delta D/D_o \Delta P$, on pressure-flow relations [13].

$$P_a = \left\{ \left[\left(1 + \alpha P_v\right)^5 + 5\alpha \cdot Q \cdot R_o\left(Hct\right) \right]^{1/5} - 1 \right\} / \alpha$$

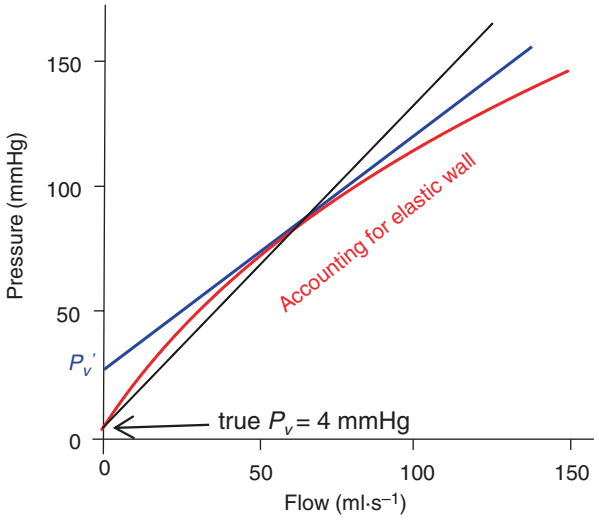


Fig. 6.3 A pressure-flow relation (red) fitted by the equation discussed in the text using human parameters, α = 0.025 mmHg^{-1}, (wall thickness radius ratio of 0.1; Young modulus 400 kPa), R_o(Hct) = 2 mmHg·s·ml^{-1} and venous pressure P_v = 4 mmHg. It may be seen that a piecewise approximation with a straight line (blue) gives an apparent intercept, P_v' higher than true venous pressure, P_v. The apparent intercept depends on Hematocrit (not shown here). A linear approximation using $(P_a - P_v)/Q$ (black line) deviates from the flow-dependent true resistance

with P_a arterial and P_v venous pressure. At a known Hct the parameters α, R_o(Hct), the reference resistance, can be determined from a pressure-flow relation [13]. Figure 6.3 shows an example of a pressure-flow relation of the systemic arterial tree, as predicted by the above formula. The local slope is flow dependent and overestimates the 'zero-flow pressure intercept'.

The intercept pressure has led to the so-called Waterfall (Fig. 6.4) as arterial model. The 'Starling resistor', a compliant tube with adjustable external pressure (Fig. 6.5), was used as vascular model in heart studies. The Starling resistor is actually more a mechanical pressure control system than a resistor.

6.2 Physiological and Clinical Relevance

The small arteries and arterioles (Peripheral Resistance) mainly determine total systemic resistance. Resistance can be regulated by the arterioles, because they are muscular arteries and it follows from Poiseuille's law that rather small changes in diameter (and cross-sectional area) result in large resistance changes. A 10% change in diameter corresponds to a change in resistance by 1.1^4, or about 50%.

The resistance of the aorta and conduit arteries is so low that the mean pressure hardly decreases from heart to the small peripheral arteries, the pressure drop being

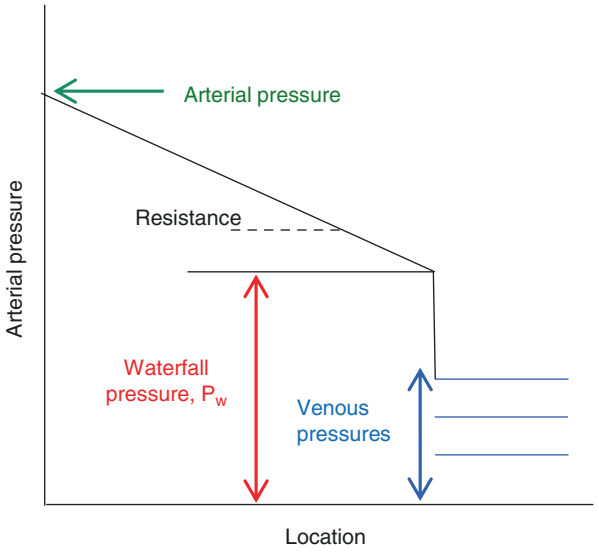


Fig. 6.4 The Waterfall model. The slope, 'resistance', and Arterial minus Waterfall pressure, $P_a - P_w$ determine flow. Venous pressures less than waterfall pressure P_w do not affect flow

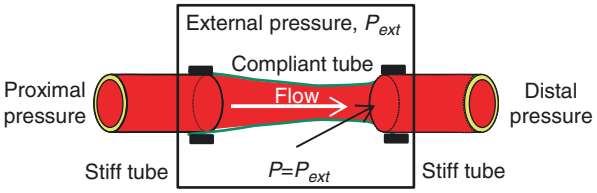


Fig. 6.5 The Starling resistor. The external pressure in the chamber, by partially decreasing the diameter of the compliant tube, results a tube pressure equal to external pressure. The term resistor is not correct. The Starling Resistor was used to study cardiac output as a function of ventricular filling under constant pressure load (Chaps. 14 and 15)

only a few mmHg. This means that in the supine human, *mean* blood pressure is practically the same in all conduit arteries, and therefore *mean* blood pressure may be determined in any conduit artery. This also implies that conduit arteries can be seen as a supply reservoir with (the local) peripheral resistances adjusting themselves such that the demand of flow to the (local) tissue is met.

When perfusion flow is high, e.g., during exercise, the large artery resistance could cause a sizable pressure drop. However, with increased flow the conduit arteries dilate through 'Flow Mediated Dilation', FMD, to decrease their resistance. An FMD of 7% gives a resistance decrease of more than 30%.

Vascular smooth muscle tone is regulated by the nervous and hormonal systems and through autoregulation (see also Chap. 19). Autoregulation is based on metabolic, myogenic, and endothelial mechanisms, as response to NO. With increased pressure arteriolar resistance increases thereby keeping capillary pressure constant to maintain tissue fluid equilibrium, the Starling equilibrium (see Appendix 4). The

lateral area or exchange area is the area involved in the exchange of oxygen, substrates and metabolites between tissue and blood. This area is largest in the capillaries and can be calculated as $2\pi rl$, with l capillary length. The total exchange area of all capillaries together is about 6000 m^2.

The total cross-sectional area is the largest in capillaries, and velocity of blood is lowest allowing ample time for exchange with the tissues [14]. It is incorrect to apply Poiseuille's law using total cross-sectional area. The cross-sectional area (radius) of individual vessels should be used to calculate resistance and then resistances must be added in series and in parallel according to the anatomy.

6.2.1 Low Resistance of an Arterio-Venous Fistula

Several arterio-venous fistulas may exist, such as an open ductus arteriosus, and the fistula between the radial artery and vein made for dialysis. As an example, the latter an arterio-venous shunt causes a low resistance in parallel with the resistance of the lower arm. However, the shunt does not always cause ischemia in the hand for the following reason (steal syndrome). The mean blood pressure in the aorta is 100 mmHg and is in the radial artery normally about 3 mmHg lower, and thus 97 mmHg. The venous pressure is about 5 mmHg and in the vena cava pressure is 2 mmHg. The low resistance of the conduit arteries and veins will, with a large shunt flow, decrease arterial pressure by about 10 mmHg and increase the venous pressure by the same amount. The perfusion pressure for the hand is then 87–15 = 72 mmHg, which is high enough to avoid ischemia. The fistula will, however, lower the total systemic peripheral resistance and increase Cardiac Output thereby affecting cardiac function.

Qualitatively stated: the conduit arterial system and venous system can be viewed as pressure reservoirs with resistance arteries as a resistor. Another way of stating this is that conduit arteries and veins are pressure sources, i.e., pressure is hardly affected by flow. The venous reservoir is much larger than the arterial reservoir and plays a major role in ventricular filling.

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