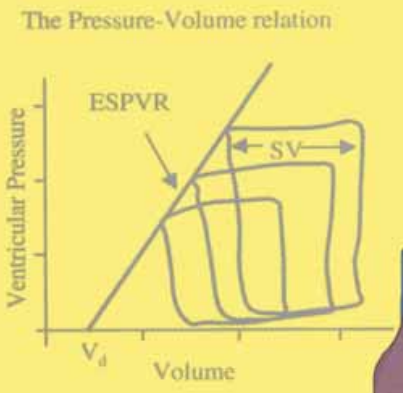
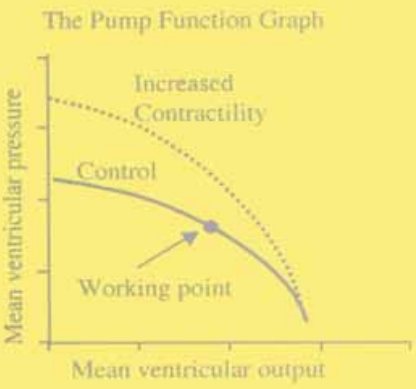
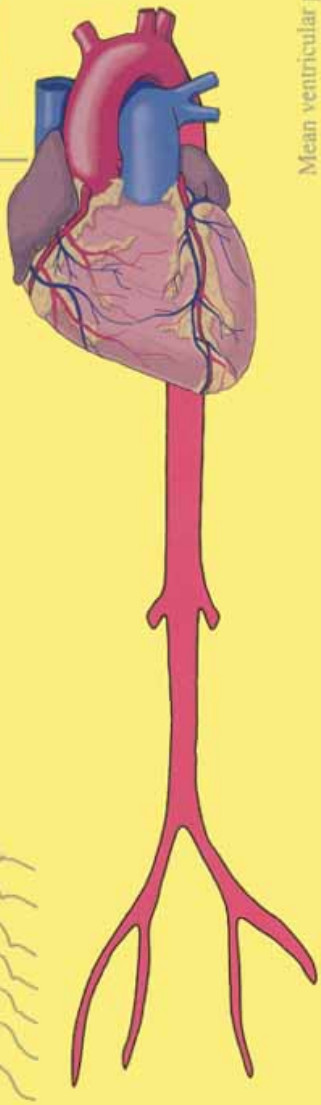
Snapshots of Hemodynamics

An Aid for Clinical Research and Graduate Education







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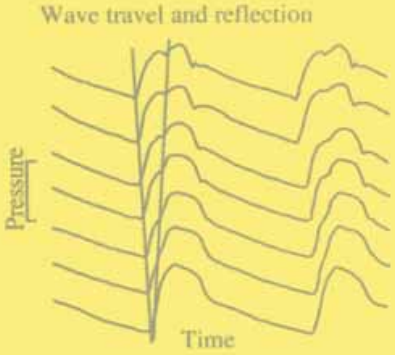

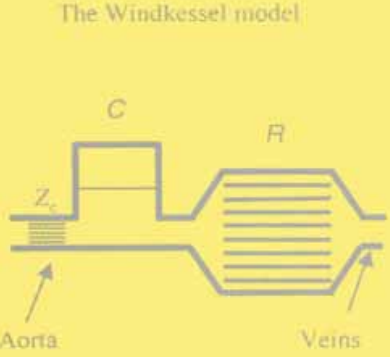

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Snapshots of Hemodynamics

An aid for clinical research and graduate education

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CONTENTS

PREFACE

This book is written to help clinical and basic researchers, as well as graduate students, in the understanding of hemodynamics. Recent developments in genetics and molecular biology on the one hand, and new non-invasive measurement techniques on the other hand, make it possible to measure and understand the hemodynamics of heart and vessels better than ever before. Hemodynamics makes it possible to characterize, in a quantitative way, the function of the heart and the arterial system, thereby producing information about what genetic and molecular processes are of importance for cardiovascular function.

We have made the layout of the book such that it gives a short overview of individual topics, in short chapters only giving the essentials, so that it is easy to use it as a quick reference guide. It is not necessary to read the book from cover to cover. Each chapter is written in such a way that one is able to grasp the basic and applied principles of the hemodynamic topic. If more details or broader perspectives are desired one can go to the other, related, chapters to which the text refers, or the textbooks listed in the 'Reference books' section (Appendix 5).

To bring the essentials even more directly across, every chapter starts with a 'box' containing a figure and caption, which give the basic aspects of the subject. It is often sufficient to study the contents of this box alone to obtain this basic information. Chapters end with a section 'Physiological and Clinical relevance' to place the information into perspective. The part in between, called 'Description', can be used to get more detailed information and find some references to more detailed work.

More comprehensive information on the subjects discussed can be found in textbooks on physiology and cardiology, as well as special books on hemodynamics. A number of these books are listed in the section 'Reference books' (Appendix 5). More literature also can easily be found on the internet. In the chapters the number of references therefore is limited to a few only.

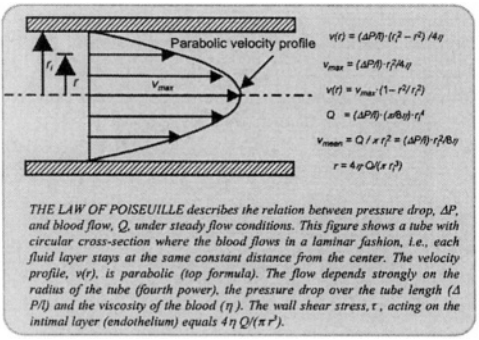
NW, NS, and MIMN

How to use the

Snapshots of Hemodynamics

Chapter 2 **Law of Poiseuille**

Chapter and title



THE LAW OF POISEUILLE describes the relation between pressure drop, ΔP, and blood flow, Q, under steady flow conditions. This figure shows a tube with circular cross-section where the blood flows in a laminar fashion, i.e., each fluid layer stays at the same constant distance from the center. The velocity profile, v(r), is parabolic (top formula). The flow depends strongly on the radius of the tube (fourth power), the pressure drop over the tube length (Δ P/l) and the viscosity of the blood (η). The wall shear stress, τ , acting on the intimal layer (endothelium) equals 4 η Q/(π r³).

The box contains a figure with a short text that illustrates the main message of the chapter.

Description

With laminar flow through a uniform tube of radius r_i the velocity profile over the cross-section is a parabola.

The 'Description" section gives the essential background and discusses the different aspects of the subject.

Physiological and clinical relevance

The more general form of Poiseuille's law given above, i.e., $Q = \Delta P/R$ allows us to derive resistance, *R,* from mean pressure and mean flow measurement.

The 'Physiological and clinical relevance' section places the subject in a broader physiological context and shows clinical applications.

References

1. The Murgo JP, Westerhof N, Giolma JP, Altobelli SA. Aortic input impedance in normal man: relationship to pressure wave forms. *Circulation* 1980;62:101-116.
2. Murgo JP, Westerhof N, Giolma JP, Altobelli

A limited number of references is given. Major reference books are given in Appendix 5.

ACKNOWLEDGEMENT

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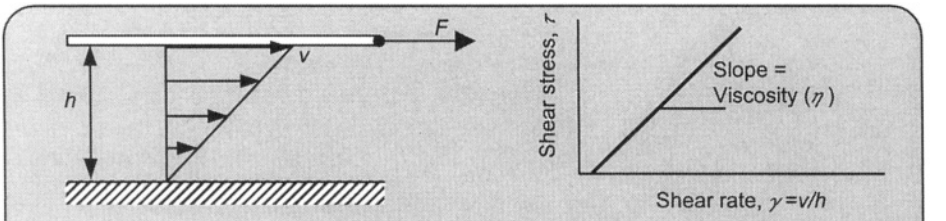
We thank Jan Paul Barends for all his help in aspects of layout and presentation.

Part A
Basics of Hemodynamics

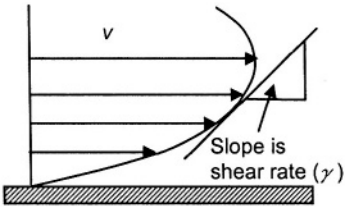
Chapter 1 VISCOSITY



HOW VISCOSITY IS DEFINED. A fluid is located between two parallel plates. The shear force, F, divided by the contact area between the liquid and the plate gives the shear stress, τ. The shear rate is the difference in velocity between the different fluid layers. It can here be calculated as the velocity of the top plate (the bottom plate does not move) divided by the distance between the plates, i.e., shear rate is γ = v/h. The ratio of shear stress and shear rate is the viscosity. If we change the plate velocity or change the distance between the plates, shear stress and shear rate will change. The slope of the relation between shear stress-shear rate gives the viscosity (η). If a straight line is obtained, as for plasma, we call the fluid Newtonian.

Description

Consider the experiment shown in the figure in the box. The top plate is moved with constant velocity, v, by the action of a shear force F, while the bottom plate is kept in place (velocity is zero). The result is that the different layers of blood move with different velocities. The difference in velocity in the different blood layers causes a shearing action between them.



VELOCITY and shear rate for a general profile.

The rate of shear, γ, is the relative displacement of one fluid layer with respect to the next. In general, the shear rate is the slope of the velocity profile, as shown in the figure on the right. In our particular example the velocity profile is linear, going from zero at the bottom to v at the top plate. Therefore, the slope of the velocity profile, and thus the rate of shear, is equal to v/h, h being the distance between the plates. The units of shear rate are 1/s. The force needed to obtain a certain velocity, is proportional to the contact area, A, between fluid and plates. It is therefore convenient, instead of force, to use the term shear stress, defined as the force per area $\tau = F/A$, with units Pa or N/m^2.

We may think of the following experiment: we pull the top plate at different velocities v and we measure the shear force F. Then we plot the shear stress, τ, against the shear rate, γ. The resulting relation is given in the figure in the box and the slope is the viscosity:

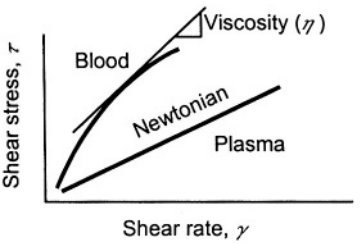
$$\eta = \textit{shear stress/shear rate} = \tau/\gamma$$

The units of viscosity are $Pa{\cdot}s = Ns/m^2$, or Poise $(dynes{\cdot}s/cm^2)$, with 1 Pa·s =10 Poise. Fluids with a straight relationship between shear stress and shear rate are called Newtonian fluids, i.e., viscosity does not depend on shear stress or shear rate. Viscosity is sometimes called dynamic viscosity in

contrast to the kinematic viscosity, which is defined as viscosity divided by density ρ, thus η/ρ.

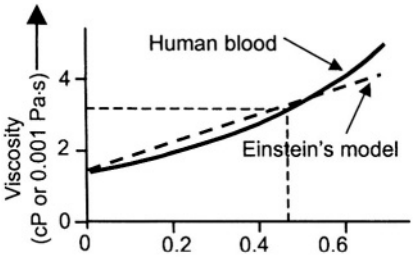
Viscosity of blood

Blood consists of plasma and particles, with 99% of the particle volume taken by the red blood cells, RBC's, or erythrocytes. Thus the red blood cells mainly determine the difference between plasma and blood viscosity. The viscosity of blood therefore depends on the viscosity of the plasma, in combination with the hematocrit (volume % of red blood cells, Ht) and red cell deformability. Higher hematocrit and less deformable cells imply higher viscosity. The relation between hematocrit and viscosity is complex and many formulas exist. One of the simplest is the one by Einstein:



VISCOSITY of plasma and blood.

$$\eta = \eta_{plasma} \cdot (1 + 2.5\ Ht)$$



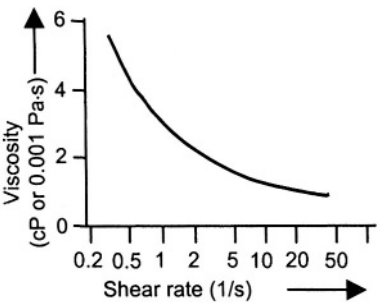
VISCOSITY as function of hematocrit.

Einstein's relation for the viscosity of fluids containing particles applies only to very low particle concentrations. Nevertheless, it gives some indication. The viscosity of plasma is about 0.015 Poise (1.5 centipoise, cP) and the viscosity of whole blood at a physiological hematocrit of 40 - 45% is about 3.2 cP, or $3.2\ 10^{-3}$ Pa·s.

Blood viscosity depends not only on plasma viscosity and hematocrit, but also on the size, shape and flexibility of the red blood cells. For instance, the hematocrit of camel blood is about half of that of human blood, but the camel's red blood cells are more rigid, and the overall effect is a similar blood viscosity.

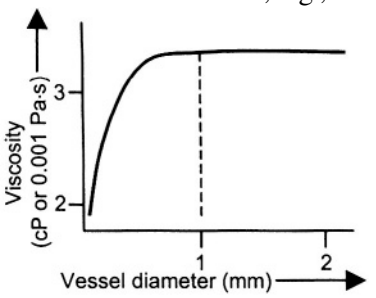
Anomalous viscosity or non-Newtonian behavior of blood

The viscosity of blood depends on its velocity. More exactly formulated, when shear rate increases viscosity decreases. At high shear rates the doughnut-shaped RBC's orient themselves in the direction of flow and viscosity is lower. For extremely low shear rates formation of RBC aggregates may occur, thereby increasing viscosity to very high values. It has even been suggested that a certain minimum shear stress is required before the blood will start to flow, the so-called yield stress. In large and medium size arteries shear rates are higher than $100\ s^{-1}$, so viscosity is practically constant.



VISCOSITY as function of shear rate for hematocrit of 48.

The physiological range of wall shear stress is 10 to 20 dynes/cm^2, or 1 to 2 Pa, with 1Pa = 0.0075 mmHg. Several equations exist that relate shear stress and shear rate of blood, e.g., Casson fluid, and Herschel-Bulkley fluid [1,2].



VISCOSITY as function of vessel size.

Viscosity also depends on the size of blood vessel. In small blood vessels and at high velocities, blood viscosity apparently decreases with decreasing vessel size. This is known as the Fahraeus-Lindqvist effect, and it begins to play a role in vessels smaller than 1 mm in diameter. Red blood cells show axial accumulation, while the concentration of platelets appears highest at the wall. The non-Newtonian character of blood only plays a role in the microcirculation.

Viscosity depends on temperature. A decrease of 1°C in temperature yields a 2% increase in viscosity. Thus in a cold foot blood viscosity is much higher than in the brain.

How to measure viscosity

Blood viscosity is measured using viscometers. Viscometers consist essentially of two rotating surfaces, as a model of the two plates shown in the box figure. Blood is usually prevented from air contact and temperature is controlled. When comparing data on viscosity one should always keep in mind the measurement technique, as results are often device dependent.

Physiological and clinical relevance

The anomalous character of blood viscosity results from the red blood cells, and the effects are mainly found in the microcirculation at low shear and small diameters. The effects are of little importance for the hemodynamics of large arteries. Thus, in hemodynamics, it may be assumed that viscosity is independent of vessel size and shear rate.

Determination of blood viscosity *in vivo* is almost impossible. In principle, the pressure drop over a blood vessel and the flow through it, together with vessel size, can be used to derive viscosity on the basis of Poiseuille's law. However, the vessel diameter in Poiseuille's law (Chapter 2) appears as the fourth power, so that a small error in the vessel diameter leads to a considerable error in the calculated viscosity. Also, the mean pressure drop over a segment of artery is typically a fraction of 1 mmHg. Moreover, hematocrit is not the same in all vessels due to plasma skimming effects. And finally, Poiseuille's law may only be applied when there are no effects of inlet length (see Chapter 2).

The main purpose of the circulation is to supply tissues with oxygen. Oxygen supply is the product of flow and oxygen content. The hematocrit determines the (maximum) oxygen carrying capacity of blood and its viscosity, and therefore the resistance to blood flow. These counteracting effects on oxygen transport result in an optimal hematocrit of about 45 in the human at sea level, with a small difference between males and females. It appears that in mammals, blood viscosity is similar, but the hematocrit is not

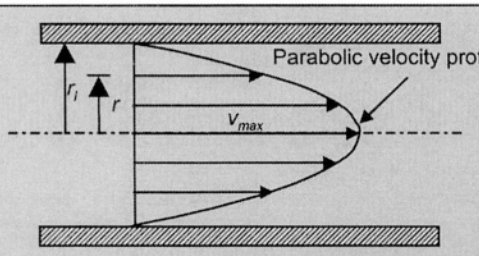
because of the different size, shape and flexibility of the red blood cells as mentioned above.

Low hematocrit, as in anemia, decreases oxygen content and viscosity of blood. The former lowers oxygen supply and the latter increases blood flow thus increasing supply. Inversely, polycythemia increases oxygen content but lowers blood flow. At high altitude, where oxygen tension is lower and thus oxygen saturation in the blood is lower, a larger hematocrit is advantageous. In endurance sports higher hematocrit is more efficacious during increased oxygen demand. This is the reason EPO is sometimes used by the athletes.

References

1. Merrill EW. Rheology of blood. *Physiol Rev* 1969;49:863-888.
2. Scott Blair GW, Spanner DC. *An introduction to biorheology.* 1974, Amsterdam, Elsevier Sc Publ.

Chapter 2 LAW OF POISEUILLE



$$v(r) = (\Delta P/l)\cdot(r_i^2 - r^2)/4\eta$$

$$v_{max} = (\Delta P/l)\cdot r_i^2/4\eta$$

$$v(r) = v_{max}\cdot(1 - r^2/r_i^2)$$

$$Q = (\Delta P/l)\cdot(\pi/8\eta)\cdot r_i^4$$

$$v_{mean} = Q/\pi r_i^2 = (\Delta P/l)\cdot r_i^2/8\eta$$

$$\tau = 4\eta Q/(\pi r_i^3)$$

THE LAW OF POISEUILLE describes the relation between pressure drop, ΔP, and blood flow, Q, under steady flow conditions. This figure shows a tube with circular cross-section where the blood flows in a laminar fashion, i.e., each fluid layer stays at the same constant distance from the center. The velocity profile, v(r), is parabolic (top formula). The flow depends strongly on the radius of the tube (fourth power), the pressure drop over the tube length (ΔP/l) and the viscosity of the blood (η). The wall shear stress, τ, acting on the intimal layer (endothelium) equals $4\eta\, Q/(\pi r_i^3)$.

Description

With laminar and steady flow through a uniform tube of radius r_i the velocity profile over the cross-section is a parabola. The formula that describes the velocity (v) as a function of the radius, r is:

$$v_r = \frac{\Delta P \cdot (r_i^2 - r^2)}{4 \cdot \eta \cdot l}$$

ΔP is the pressure drop over the tube of length (l), and η is blood viscosity. At the axis ($r = 0$), velocity is maximal, v_{max}, while at the wall ($r = r_i$) the velocity is zero. Mean velocity is:

$$v_{mean} = \frac{\Delta P \cdot r_i^2}{8 \cdot \eta \cdot l}$$

and is found at $r \approx 0.7\, r_i$.

Blood flow (Q) is mean velocity times the cross-sectional area of the tube, πr_i^2, giving:

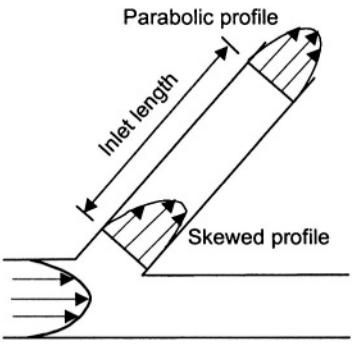
$$Q = \frac{\Delta P \cdot \pi \cdot r_i^4}{8 \cdot \eta \cdot l}$$

This is Poiseuille's law relating the pressure difference, ΔP, and the steady flow, Q, through a uniform (constant radius) and stiff blood vessel. Hagen, in 1860, theoretically derived the law and therefore it is sometimes called the law of Hagen-Poiseuille. The law can be derived from very basic physics (Newton's law) or the general Navier-Stokes equations.

The major assumptions for Poiseuille's law to hold are:

- The tube is stiff, straight, and uniform

- Blood is Newtonian, i.e., viscosity is constant
- The flow is laminar and steady, not pulsatile, and the velocity at the wall is zero (no slip at the wall).



INLET LENGTH. Flow entering a side branch results in skewed profile. It takes a certain inlet length before the velocity develops into a parabolic profile again.

In curved vessels and distal to branching points the velocity profile is not parabolic and the blood flow profile needs some length of straight tube to develop, this length is called inlet length. The inlet length depends on the Reynolds number (Re, see Chapter 4) as:

$$l_{inlet}/D \approx 0.06\,Re$$

with D vessel diameter. For the aorta mean blood flow is about 6 l/min, and the diameter 3 cm, so that the mean velocity is ~ 15 cm/s. The Reynolds number is therefore ~ 1350. This means that l_{inlet}/D is ~ 80, and the inlet length ~240 cm, which is much longer than the length of the entire aorta. In the common iliac artery the Reynolds number is about 500 and diameter 0.6 cm giving an inlet length of ~18 cm. In other, more peripheral arteries the inlet length is much shorter but their length is shorter as well. Clearly, a parabolic flow profile is not even approximated in the arterial system. Nevertheless, the law of Poiseuille can be used as a concept relating pressure drop to flow.

A less detailed and thus more general form of Poiseuille's law is $Q = \Delta P/R$ with resistance R being:

$$R = 8\eta \cdot l/\pi r_i^4$$

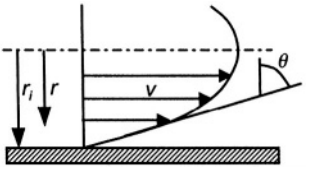
This law is used in analogy to Ohm's law of electricity, where resistance equals voltage drop/current. The analogy is that voltage difference is compared to pressure drop and current to volume flow. In hemodynamics we call also it Ohm's law. Thus:

$$\Delta P/Q = R$$

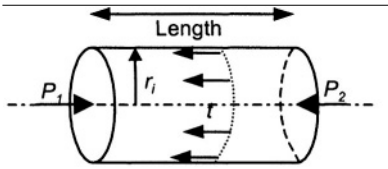
This means that resistance can be calculated from pressure and flow measurements.

Calculation of wall shear stress

The wall shear rate can be calculated from the slope of the velocity profile near the wall (angle θ in the figure above), which relates to the velocity gradient, $\tan\theta = dv/dr$, near the wall (see Chapter 1). The derivative of the velocity profile gives the shear rate $\gamma = (\Delta P/l) \cdot r/2\eta$. Shear stress is shear rate times viscosity $\tau = (\Delta P/l) \cdot r/2$. The shear rate at the vessel axis, $r = 0$, is zero, and at the wall, $r = r_i$, it is $\tau = (\Delta P/l) \cdot r_i/2$, so the blood cells encounter a range of shear stresses and shear rates over the vessel's cross-section.



THE SHEAR RATE at the wall of a blood vessel can be calculated from the 'rate of change of velocity' at the wall, as indicated by angle θ.



SHEAR STRESS at the wall can also be calculated directly by the balance of pressure and frictional forces.

The shear stress at the wall can also be calculated from basic principles. For an arterial segment of length l, the force resulting from the pressure difference $(P_1 - P_2) = \Delta P$, times the cross-sectional area, πr_i^2, should equal the opposing force generated by friction. This frictional force on the wall equals the shear stress, τ, times the lateral surface, $2\pi r_i \cdot l$. Equating these forces gives $\Delta P \cdot \pi r_i^2 = \tau \cdot 2\pi r_i \cdot l$, and

$$\tau = (\Delta P/l) \cdot (r_i/2)$$

This formulation shows that with constant perfusion pressure an increase in viscosity does not affect wall shear stress.

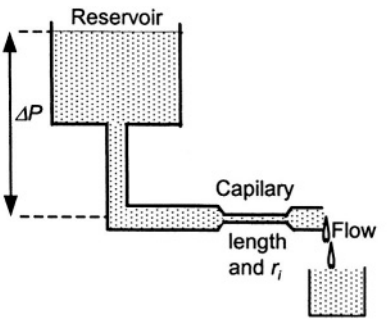
The wall shear stress may also be expressed as a function of volume flow using Poiseuille's law

$$\tau = 4\eta \cdot Q/\pi r_i^3$$

this is a more useful formula for estimating shear stress because flow and radius can be measured noninvasively using ultrasound or MRI, whereas pressure gradient cannot.

Example of the use of Poiseuille's law to obtain viscosity

A relatively simple way to obtain viscosity is to use a reservoir that empties through a capillary. Knowing the dimensions of the capillary and using Poiseuille's law viscosity can be calculated. Even simpler is the determination of viscosity relative to that of water. In that case only a beaker and stopwatch are required. The amounts of blood and water obtained for a chosen time are inversely proportional to their viscosities. The practical design based on this principle is the Ostwald viscometer.



A WIDE BORE RESERVOIR maintaining constant pressure, provides the blood flow through a capillary. The application of Poiseuille's law, or comparison with water, gives absolute or relative viscosity, respectively.

Murray's law

Murray' law (1926) was originally proposed by Hess in 1913 and assumes that the energy required for blood flow and the energy needed to maintain the vasculature is assumed minimal [1]. The first term equals pressure times flow and, using Poiseuille's law, this is $P \cdot Q = Q^2 \cdot 8 \cdot \eta \cdot l/\pi r_i^4$. The second term is proportional to vessel volume and thus equals $b \cdot \pi r_i^2 l$, with b a proportionality constant. The total energy, E_m, is:

$$E_m = Q^2 \cdot 8\eta \cdot l/\pi r_i^4 + b \cdot \pi r_i^2 l$$

The minimal value is found for $dE_m/dr = 0$ and this leads to:

$$Q = (\pi/4l) \cdot (b/\eta)^{0.5} \cdot r_i^3 = k \cdot r_i^3$$