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Instead of a course textbook, all the modules contain links to excellent information that can be found on the internet. It is important that you visit these links to get more background on the topics. These also may be printed out to read in more detail later, or to be saved for future reference.

If you have any difficulty in accessing any of the links within these modules please send an email to jwilliams@robarts.ca. Sometimes the sources of the links change and adjustments will be made to correct this.

When you have finished the module, please go to Module 7 Quiz.
Dr. David Steinman, a Robarts scientist who is a leading authority on computational modeling of vascular biomechanics, provided most of the content for this module.

Some content came from the following sources:


**Video Clips**

I wanted to show video clips in this module, but it proved to be impossible to configure them to show properly, so I have made links to the originals on Dr. David Steinman’s website.
The objectives of this module are fairly simple. As vascular hemodynamics is a complicated branch of hydraulics, involving the unique properties of blood and the geometric and dynamic qualities of the vascular tree, only the basic principles are touched on. This module is designed to help students understand the processes involved in vascular hemodynamics and, as with all our transdisciplinary courses, to provide them with sufficient basic knowledge to be able to follow a scientific talk on the subject in question.

Students in the biological fields have a head start on vascular hemodynamics, because they are already familiar with the properties of blood and with the vascular system.

This module starts with a brief history of hemodynamics and atherosclerosis and goes on to describe the basic principles; how blood flow patterns are diagnosed and interpreted, and the imaging methods that are used to visualize flow.

As most of the students taking this course have a strong biology background, the module does not explain topics such as arterial and venous blood pressure, as it is assumed that students will understand these concepts. For students who would like a quick refresher on cardiovascular physiology, try the following website, written by Richard E. Klabunde:

**Cardiovascular Physiology**
Vascular hemodynamics deals with the physical factors that govern blood flow within the circulatory system. The general physical principles will be explained briefly in this module. However, it should be borne in mind that a living vascular system is much more complex than mechanical systems, and while it can be thought of as the body’s “plumbing”, applying mathematical equations to a highly variable system is very difficult.

Coronary artery disease is responsible for more deaths in the developed world than any other disease, and there is excellent evidence implicating blood flow patterns and the geometry of blood vessels in its development. However, this link is as yet unproven, mostly because of the difficult technical challenges associated with quantifying coronary artery hemodynamics, particularly wall shear stresses, *in vivo*.

Once the broader principles that govern vascular hemodynamics have been explained, the local forces that contribute to coronary artery disease are more easily understood.

Local hemodynamics are important in vascular disease because potentially they can help us understand the development of atherosclerosis, and the assessment of stroke risk.

Doppler sonography is the main imaging technique used clinically to measure blood flow velocity. This information is only helpful from a clinical perspective if it shows where the blood flow is disturbed due to abnormal morphological changes. It is important to have a basic understanding of hemodynamics to help interpret blood flow velocity as visualized by Doppler sonography.
The idea that hemodynamics might play a role in atherosclerosis wasn’t formulated until the late 1960’s. Fry (1968) published the first paper suggesting that endothelial damage to the vessel walls was caused by the force exerted by flowing blood within the vessel. This force is called wall shear stress (WSS).

In 1971, Caro et al. noticed that early atherosclerotic lesions occurred in regions of low WSS, suggesting that low shear stress increases the adhesion and infiltration of macromolecules into the vessel wall. A few years later, Friedman et al. reported that spatial variations in WSS might be more important in causing atherosclerosis, rather than whether the WSS was low or high.

It wasn’t until the 1980’s that researchers started to produce evidence on the hemodynamic control mechanisms of vascular function when it was shown that the morphology of endothelial cells were affected by local hemodynamics.

It was around this time that traditional engineering flow visualization techniques were used to explore the relationship between WSS and atherosclerosis. Friedman and his colleagues used an imaging technique called laser-Doppler anemometry (LDA) which suggested that vessel geometry might be a significant independent risk factor for atherosclerosis due to the flow dynamics induced by certain vascular configurations. This established the “geometric risk” hypothesis of atherosclerosis that is still to be fully validated at the present time.

1982 saw the development of an idealized model of the carotid bifurcation derived from post-mortem measurements to study hemodynamics in vessel walls. This was the Bharadvaj, or Georgia Tech model that is still in use today. Use of this model helped to establish the current most popular theory of atherogenesis, which is the “low and oscillating” shear hypothesis.
It wasn’t until the early 1990’s that computational fluid dynamics (CFD) became a viable alternative to experimental techniques for investigating blood flow dynamics. Desktop workstations were then powerful enough to be used to generate three-dimensional simulations of pulsatile flow. These advances made it increasingly clear that the dynamics of blood flow in vivo are much more complex and varied than previously suggested by idealized models.

More recent advances have been the increasingly sophisticated in vitro techniques used to elucidate the underlying molecular and genetic mechanisms of endothelial phenotypes, while at the same time, significant advances in medical imaging made it possible to study responses of individual atherosclerotic lesions to specific therapeutic challenges.

More movies can be found on Dr. David Steinman’s excellent website at David A. Steinman PhD.

Click on the image to go to the website and select the matching thumbnail.

Image courtesy of Dr. David Steinman, University of Toronto.

Computational imaging of pulsatile flow in a normal human carotid bifurcation. Magnetic resonance imaging (MRI) of a live subject provides the boundary conditions (i.e. geometry and flow rates) for a computational fluid dynamic (CFD) simulation of the blood flow patterns. In the above video clip, streak length and color intensity are proportional to the blood velocity. Color distinguishes particles exiting the external and internal branches.
Blood flow through an organ or any vascular network is driven by a pressure gradient or perfusion pressure that is normally represented by the difference between the arterial and venous pressures across the organ. The actual blood flow at any given pressure gradient is determined by the resistance to blood flow. The relationship between flow, pressure, and resistance is given below:

\[
F = \frac{(P_A - P_V)}{R}
\]

Where:
- \(F\) = Flow Rate (sometimes denoted by \(Q\))
- \(P_A\) = Mean arterial pressure
- \(P_V\) = Mean venous pressure
- \(R\) = Vascular resistance to flow

N.B. \((P_A - P_V)\) is sometimes denoted as \(\Delta P\).

\(\Delta P\) is called the perfusion pressure.

For example, renal blood flow is determined by the renal perfusion pressure (mean arterial minus mean venous pressures) divided by the renal vascular resistance. Resistance is explained on the following page.
Resistance to blood flow within a vascular network is determined by:

- The length and diameter of individual vessels;
- The organization of the vascular network;
- The physical characteristics of the blood, and,
- The extravascular mechanical forces acting upon the vasculature.

Of all these factors, changes in the vessel diameter are most important quantitatively for regulating blood flow within an organ, as well as for regulating arterial pressure.

Changes in vessel diameter, particularly in small arteries and arterioles, allow organs to adjust their own blood flow to meet the metabolic requirements of the tissue. So if an organ needs more oxygen, it can adjust its blood flow by making cells surrounding these blood vessels to release vasoactive substances that can either constrict or dilate the resistance vessels.

Image and video courtesy of Dr. David Steinman, University of Toronto.

**Pulsatile flow in two models of the stenosed carotid bifurcation**

We observed different patterns of post-stenotic recirculation in models having the same stenosis severity but different stenosis geometries. Since such flow patterns may provide ideal conditions for the formation of the blood clots that cause many strokes, we are currently investigating whether geometric or hemodynamic information can help us better identify patients at risk of stroke.
Kinetic Energy and the Bernoulli Principle

- The Bernoulli principle can be applied to the vascular system, as it is based upon the energetics associated with flowing fluids, or in our case, blood.

- Blood flow is a function of total fluid energy. Total fluid energy is a function of pressure (potential) energy and velocity (kinetic) energy. The relevant pressure in this case is perfusion (driving) pressure, the difference between the transmural pressures at two points in a conduit.

- Kinetic energy is a function of the square of the flow velocity. Thus when velocity doubles, the kinetic energy portion of total fluid energy increases 4-fold.

- For a more detailed description of the Bernoulli Principle go to:

  Bernoulli Principle by Richard E. Klabunde

- It is the high kinetic energy of the blood during ventricular ejection that keeps the aortic valve open during the latter part of this phase of the cardiac cycle. Thus, it is possible for flow to occur in the seemingly strange manner of taking place from an area of lower to one of higher pressure.

- Ordinarily in the arterial circulation kinetic energy is only a small fraction of pressure energy, since the pressure is so high; however, in veins where pressure is low, kinetic energy may become a significant fraction of total fluid energy.
Normal blood flow throughout most of the circulatory system is laminar flow. It is made up of even concentric layers of blood moving in parallel down the length of a blood vessel and maintaining a constant distance from the vessel wall. In cross section, laminar flow shows a parabolic velocity profile with the highest velocity (Vmax) in the middle of the vessel, and the lowest velocity (V=0) next to the vessel wall. This occurs because the blood cells closest to the vessel walls tend to stick to the walls and the layers in the centre move over them at a faster rate. (Bear in mind is that purely laminar (or parabolic) flow is a commonly used, but gross approximation of reality. Blood flow is generally non-turbulent, but not necessarily completely laminar).

Diagram of the concentric layers in laminar flow. Each layer is made up of blood cells and it has a velocity separate to other layers. The layers do not mix.
A Doppler flowmeter measures this parabolic flow velocity, but calculates the average velocity of a cross-section of the vessel, not the maximal velocity found in the centre of the vessel.

When laminar flow becomes disturbed it may lead to turbulent flow and more energy loss within the vessel, although disturbed laminar flow is not necessarily turbulent. Disturbed flow is usually referred to as deterministic, while turbulent flow implies randomness.

Pulsatile flow in an idealized normal carotid bifurcation

In this animation, particles shaded blue represent blood flowing to the left, highlighting the region of recirculating blood in the carotid bulb. This is where atherosclerotic plaques commonly occur, suggesting a link between hemodynamics and vascular disease.

Image courtesy of Dr. David Steinman, University of Toronto.
**Turbulent Flow and the Reynolds Number**

Turbulence is irregular flow that forms swirling eddy currents that cause significantly more flow resistance than laminar flow. It develops where the normal laminar flow becomes much faster, or in flow that has passed an area of significant stenosis. So it appears distal to stenoses in arterial vessels, or anywhere there is a sudden change in a vessel's diameter.

The likelihood of turbulent flow increases in direct proportion to the diameter of the vessel (2r), the flow velocity (v) and the density of the blood (ρ), but it is inversely proportional to the blood viscosity (η). The relationship of these quantities is expressed by a parameter called the Reynolds number (Re) as follows:

\[
Re = \frac{2rv\rho}{\eta}
\]

Where:

- \(2r\) = vessel diameter,
- \(v\) = flow velocity,
- \(\rho\) = blood density, and
- \(\eta\) = blood viscosity

There is a Reynolds number, called the critical value, which is the transition point where laminar flow becomes turbulent flow. This number is usually between 2000 and 2200 in smooth-walled vessels.

There are a very few areas in the body where turbulent flow occurs normally. One of these is in the ascending aorta, just below the aortic valve.

Turbulent flow flattens the *velocity profile* described on the previous page. The higher the Reynolds number the flatter the profile.

For a more detailed description of turbulent flow, including an explanation of blood viscosity, please go to the following link on the [Cardiovascular Physiology Concepts](#) site written by Richard E. Klabunde, Ph.D.

**Turbulent Flow**
Disturbed flow. There is disruption of the orderly laminae (layers) within the region of narrowing (mild flow disturbance), and disorganized, multidirectional flow vectors distal to the stenosis (turbulent flow).

The Properties of Blood - Viscosity

- Viscosity is a fundamental property of fluids and it affects the flow of liquids through tubes – or in our case, blood traveling through vessels.

- Viscous fluids are made up of adjacent layers all traveling together (it is a stratified structure), but the layers create an internal friction, one layer against another.

- Viscosity can be defined as the internal resistance of these layers, as well as the friction generated between the blood and the vessel wall. It is this friction that contributes to the resistance to flow.

- Isaac Newton was the first person to describe this effect, “which he called “a lack of slipperiness”.

- This led to the concept of Newtonian fluids, which are fluids that retain constant viscosity regardless of the flow rate and applied force and measurement method (i.e. fluid which is not dependent on shear rate and time). Low molecular weight fluids such as water, benzene, etc. are usually regarded as Newtonian. Plasma generally behaves as a Newtonian fluid.

- Any fluid that does not obey the Newtonian relationship between the shear stress and shear rate is called non-Newtonian. High molecular weight liquids which include liquids in which fine particles are suspended, such as blood, are usually non-Newtonian.
Viscosity continued

- The higher the percentage of erythrocytes in the blood (the hematocrit) the higher the blood viscosity. If the hematocrit is 50% above the normal value, blood viscosity will increase by about 100%.

- Viscosity is dependent on the hematocrit (the percent of whole blood that is comprised of red blood cells), the temperature, and the flow rate.

- The viscosity of most fluids, including blood, increases as temperature falls (i.e. they become more viscous).

- Low flow rates increase the cell-to-cell and protein-to-cell adhesive interactions that can cause erythrocytes to stick to each other, raising the blood viscosity.

- As discussed in laminar flow, the blood in the vessels has a parabolic velocity profile, with the highest velocity in the centre of the vessel and zero at the vessel wall.

- The force required to move the layers over one another (also called the stress), is proportional to the velocity gradient.

- The greatest work the heart must perform is to overcome the viscous resistance to keep the layers of blood moving through the vessels.

- Poiseuille’s Law (more on the following page) tells us how viscosity (and length and diameter) affect the flow rate for a given perfusion pressure. The standard unit of viscosity is the poise (pronounced ‘pwaz’ after the French pronunciation of Poiseuille).

- The velocity gradient is affected by the viscosity. The more viscous the blood, the flatter is the shape of the parabolic velocity gradient. This reflects the fact that the higher the viscosity, the lower the flow rate for a given applied pressure. This is explained in more detail on the next page.
Poiseuille’s Law

How much blood flows through an individual blood vessel at the local level and what are the factors that affect the rate of blood flow? Poiseuille (1797-1869) was a French physician, who was interested in blood flow through vessels. He carried out experiments on capillary tubes ranging from 0.03mm to 0.15mm in diameter and made two observations:

1. Flow is proportional to the radius of the cylindrical tube raised to the 4th power.
2. Flow is inversely proportional to the length of the tube and the liquid viscosity.

He developed the formula which became known as Poiseuille’s Law. Poiseuille's Law relates the rate at which blood flows through a small blood vessel (Q) with the difference in blood pressure at the two ends (P), the radius (r) and the length (L) of the artery, and the viscosity (n) of the blood. This formula shows that the radius of the blood vessels is the most important factor in determining the amount of blood flow.

According to the formula, if the radius of the coronary artery doubles, the blood flow through it will increase 16 times.

To understand the relationship of the flow and the viscosity, think about drinking different liquids through a straw. Flow in this case is the amount of liquid that flows into your mouth in a given period of time. The pressure difference is provided by your lungs sucking on the straw. If the liquid is water, doubling the radius of the straw will result in 16 times more liquid flowing through the straw. However, if the liquid was honey, whose viscosity is much higher than water, the flow would be much less. The other factor governing how much liquid will come through the straw is the length – the longer the straw, the less the flow.

All these factors have an important bearing on blood flow. For example, vessels in which the radius is decreased by 50% by atherosclerosis will have 16 times less flow than a normal vessel.
Elasticity of Vessel Walls

Blood vessel walls are made up of different tissues, each having its own special properties. The various tissues are:

- Smooth Muscle
- Endothelial Cells
- Connective Tissue
- Bands of Elastin
- Collagen Fibres

The smooth muscle is the physiologically active element, while the other components are essentially passive. The distensibility of the vessel wall is dependent on the proportions of all these components, and on how contractile is the smooth muscle.

Although vessel walls contain both active and passive elements and so are not homogeneous, their elasticity can be studied by applying classical mechanical principles.

- Elasticity is the ability of a material to return to its former state after it has been deformed (stretched).
- A material with perfect elasticity will always return to its original state and size after being stretched in various directions by a force.
- Different materials have their own limit of deformation characteristics, and when they are stretched beyond this range, they will either break or become permanently elongated.
- If a body of material is uniformly elastic regardless of which direction it is stretched, it is said to be *isotropic*.
- The force that causes the deformation is called a *stress*. 
**Vessel Wall Stress**

- **Tensile stress** elongates a structure.
- **Compressive stress** shortens it.
- The **Shear rate** refers to shear deformation over time and is a type of strain rate. The shear rate is the blood-flow velocity gradient perpendicular to the vessel wall.
- **Shear stress** is the applied force per unit area needed to produce deformation in the blood. In simple terms it means that forces are applied in different directions at different points, which can result in a twisting type of movement.

Shear stress = viscosity x shear rate. In fact viscosity may be thought of as a kind of ‘modulus’ relating shear stress to shear rate.

- **Wall Shear Stress (WSS)** arises from the fact that the velocity of blood relative to the vessel wall equals zero at the wall itself.

This creates a velocity gradient in the flowing blood. In the blood vessel the velocity profile across the diameter is essentially parabolic. When this is multiplied by the blood viscosity yields the (shearing) stresses exerted by the flowing blood against the endothelial cells of vessel walls.

The following website gives a clear and easy description of the physics of how fluids behave.


The following link is to a paper that gives an excellent review of vessel wall shear stress:

Effect of Vessel Geometry on Flow

Flow separation occurs at bifurcations, plaques, stenoses, or any area where there is an expansion of the vessel lumen. Separation zones are thought to be a predisposing factor in atherosclerosis.

Changes in the velocity and pressure of blood flow caused by constrictions or widenings of the vessel walls lead to shear stresses that can slow or reverse the layers next to the vessel wall.

These changes in the velocity profile are not abnormal, but exist as a result of normal vessel geometry. The following page shows a schematic diagram of flow at a 90° bifurcation, showing the differences in the endothelial cells lining the vessel walls at the different points.

A separation point (SP) shown at the carotid bifurcation starting at the single white arrow, and reattaching at the double white arrows (reattachment point RP).

From DN Ku, DP Giddens. Arteriosclerosis 3, p31, 1983
Schematic of the flow pattern at a T-bifurcation. The straight entrance flow is concentrated in the centre of the vessel. The elongated endothelial cells lining the vessel wall are oriented in the direction of flow. At the separation zone (SP) the plasma layer is disrupted and the endothelial cells in this area are rounded and enlarged. Note that separation zones form in both branches, with reattachment points (RP) shown for each.
Doppler Flow Waveforms

The above diagram shows the time velocity spectral displays for normal and stenosed blood vessels. The spectral display shown at (a) is a small **Doppler sample volume** (see diagram) of a mid-sized artery. Only the highest velocities from the centre of the lumen appear, making the spectrum narrow and ribbon-like. The slower velocities near the vessel wall are not picked up in the small sample. At (b) the same volume of blood is forced through a narrowed (stenosed) part of the vessel, which increases its velocity. The sample volume now covers the whole blood volume and includes the whole spectrum of blood velocities from zero to maximum. This gives a broader spectral display filling the whole area under the spectral curve. Just past the stenosis (c) there is a sudden increase in the vessel diameter and the flow becomes disturbed due to slowing of its velocity. The small sample volume still encompasses most of the different blood velocities and a broad spectrum. Thus, in a Doppler examination **Spectral Broadening and increased maximum velocity** are the prime indicators of vessel stenosis.  

Hemodynamic Effect of a Stenosis

Doppler sonography can show direct and indirect signs of occlusive disease.

Direct signs can be seen with only a minor stenosis of the lumen.

Indirect signs are observed only when there is severe narrowing of the lumina.

A vessel needs to be stenosed with approximately 80% reduction in blood flow (the critical area) before a measurable decrease in flow and pressure is possible.\(^8\)

This reduced flow velocity can be detected by bilateral Doppler examination comparing both sides, as shown in the graph opposite.

The above graph comes from a landmark paper by MP Spencer and JM Reid, “Quantitation of carotid stenosis with continuous-wave (C-W) Doppler ultrasound.” Stroke 1979 May-Jun;10(3):326-30
References


