CIRCULATORY PHYSIOLOGY SECTION 4: THE VASCULAR SYSTEM*

I. Anatomy and Histology of the Vascular System

A. **Arterial (High Pressure) Side** --

1. Characterized by

a. thick walls which helps result in

b. relatively low compliance and low **capacitance** (ability to hold a certain volume of blood for a given pressure -- a synonym for compliance used in vascular physiology) compared to veins they have

c. **in some cases** they have more ability to undergo **active changes in diameter**,

d.) no significant exchange occurs between them and the tissues they pass through (diffusion distances are great, area for volume is small).

2. Types of arteries

a. Great Arteries: (e.g. aorta, pulmonary artery)

b. Arteries: branches from above, e.g., coronary, carotid etc.

c. Arterioles: major resistance component of the arterial side; largest drop in pressure occurs in these small but variable diameter vessels -- this means that they are the main source of resistance that the heart must work against; changes in their diameter are a major factor in regulating blood flow.

d. Precapillaries and A-V shunts: essentially special cases of arterioles -- in one case they regulate the flow through groups of capillaries while in the other (shunts) they are paths where blood moves directly from the arterial to venous side and by-passes the capillary bed.

B. **Exchange bed – Capillaries**

1. Extremely thin-walled vessels that are the only place where exchange occurs with the tissue (with the **exception of heat exchange** which can occur in a variety of situations -- for instance, in retes the vessels may be arteriole size).

2. This is also the site of formation of lymph (see lymph notes) in animals with closed circulations.

3. Finally, they represent the second most important site of pressure decrease (and *therefore the second most important source of resistance that the heart faces*) in the vascular system, -- second only to the arterioles. By the time blood leaves the capillary beds in the systemic circulation, it is at very low pressures.

C. **Venous (Low Pressure) System**:

1. Characterized by

a. thin-walled vessels with little smooth muscle

b. high compliance, high capacitance, .

c. Pressures throughout this part of the vascular system are low and variable; much of the pressure required to move blood may come from accessory pumps (see packet C-3) and blood may commonly pool in certain regions and not flow at all. Changes in posture may even cause venous blood to temporarily flow backwards (away from the heart)

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although valves in veins tend to prevent too much of this type of backflow. Generally, the majority of the blood is in the venous system at any moment in time.

d. no significant exchange occurs between them and the tissues they pass through (diffusion distances are great, area for volume is small).

e. some venous elements (venules) can undergo radius change and thereby alter the flow of blood -- venule regulation is especially important in filtration in the kidney.

2. Types:

a. venules: receive blood from the capillaries and A-V shunts, these are the only veins that can undergo active changes in diameter due to changes in smooth muscle tonus.

b. veins: larger diameter, relatively thin walled and highly compliant structures that hold much of the circulation's blood.

c. great veins (e.g., venae cavae and pulmonary veins); large veins that return blood to the heart.

D. **Summary comments on blood vessel anatomy.**

Dimensions of Typical Vessels[1], in mm:

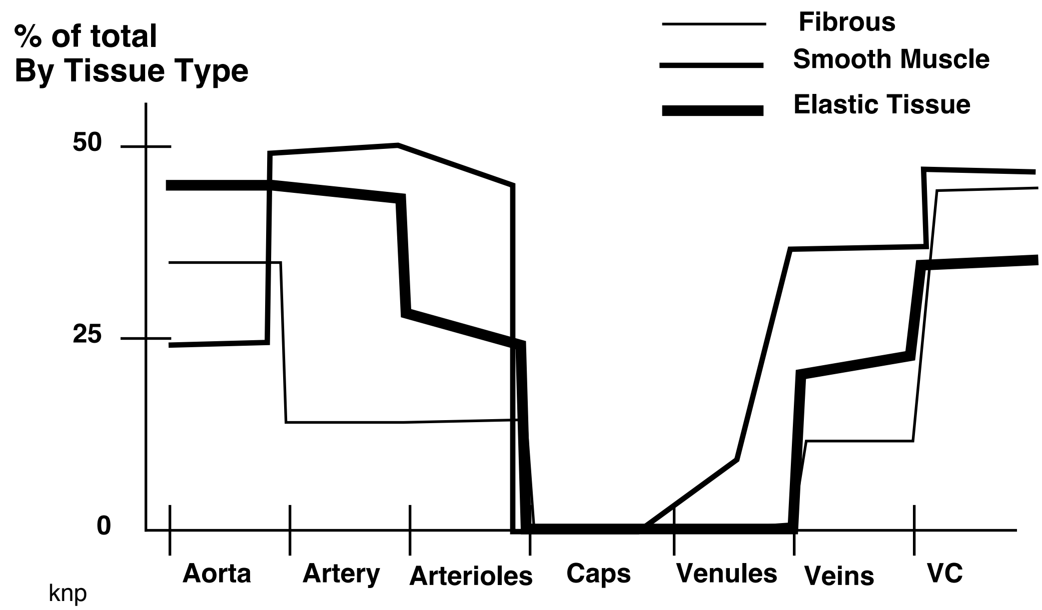
Vessel -->	Aorta	Artery	Arteriole	Precap-Sphincter	Cap.	Venule	Vein	Vena Cava
Wall	2	1	0.02	0.030	0.001	0.002	0.5	1.5
Lumen	23	3	0.01	0.005	0.007	0.018	4.5	28.5
Total	25	4	0.03	0.035	0.008	0.020	5.0	30
X- Section vs. Vena Cava x-section	0.65	0.011	1E-7	3E-8	6E-8	4E-7	0.025	1.0
% Lumen	92%	75%	33%	14%	88%	90%	90%	95%

Notes related to the data on the table above:

- The **lumen** makes up the smallest portion of the total volume in the high resistance arterial vessels -- the arterioles and pre-capillary sphincters. These vessels experience relatively high pressure since they are on the arterial side, furthermore, their relatively small lumen correlates with their high resistances to flow.
- There is a tremendous decrease in size as one moves from the great veins or arteries to the capillaries. But keep in mind that this decrease in diameter tells only part of the story -- there are also far greater numbers of the small vessels. We will return to the interaction between the number of vessels and their diameter in the next couple of figures.
- Finally note that although the veins of a given generation are somewhat larger in diameter than are the corresponding arteries, nevertheless they are not hugely different in size. However, their **cross sectional area** (a major determinant of volume), **equal to πr^2**, **is considerably larger** and this explains in part the larger volume of blood in the venous system (the higher capacitance of the venous veins also is important in this explanation).

Tissue composition of vessels: The graph below shows the rough proportion of each major type of tissue found in blood vessels:

[1] Wall and total data source: Berne and Levy, *Physiology* , 1983, C.V. Mosby, fig. 26-1



- Note that smooth muscle is very important in arteries and arterioles (and pre-capillary sphincters -- not shown). This shouldn't be surprising -- but the fact that, of the tissue present, it also makes up a large portion of the veins and vena cava may be surprising.
- Elastic tissue (fibrin, elastin) is nearly absent from the capillaries and venules as is very stiff fibrous tissue
- Keep in mind that the above graph tells proportions, not absolute values. From the table above the graph, you can see that the walls of arteries is thicker than in veins and therefore the total amounts of the tissues found in each are different and therefore the elastic and contractile properties are different even though the proportional composition is the same.

II. Pressure, flow, particle velocity, and vessel tension in different types of blood vessels

A. Some general observations:

1. In moving from the great arteries to the capillaries, the number of vessels increases and the average radius of the vessel decreases; the opposite happens in the venous side.

2. on the other hand, the **total cross-sectional area, A,** increases as one approaches the capillaries. Total cross sectional area is calculated as:

1. $A = r^2 * \pi *$ (# vessels of a certain type)

where r is the average radius of those vessels.

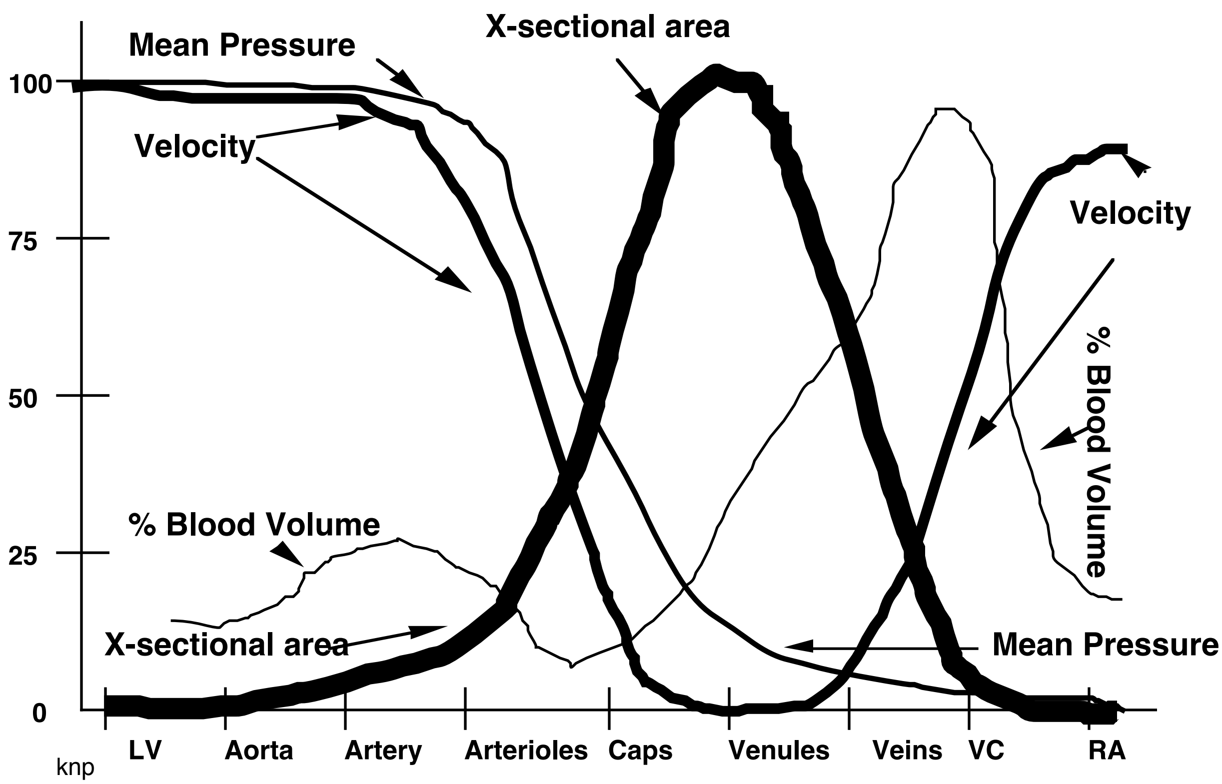
3. Pulsatile flow diminishes such that by the time the blood leaves the capillaries, flow is non-pulsatile (continuous -- or not at all).

4. Pressure decreases on the arterial side as the vessels narrow. This is due to effects of resistance. In the large arteries there is little resistance (review the Poiseuille equation) due to their relatively large diameter. On the other hand when the radius decreases significantly in the arterioles, pre-capillary sphincter regions, and capillaries, energy is consumed by the increased resistance and pressure drops.

? Look at the table presented on page 2. By what factor will the resistance per vessel increase in the arterioles and capillaries as compared to the aorta?
? From what you have learned earlier in the course, does total resistance of a "stage" of the arterial system necessarily have to increase in going from the arteries to the arterioles? Explain.

5. Velocity tends to decrease as one goes towards the capillaries and then increase again in the veins. Since pressure drops throughout the system, this may be surprising but review the fluid dynamics notes. Those notes tell you that the reason for this pattern has to do with cross-sectional area. In a steady-state, roughly the same amount of blood must flow through each type of vessel (e.g., artery, aorta, capillaries, etc.) per unit time. Since that blood is divided into more and more paths (as measured by increased cross-sectional area) as the capillaries are approached, then the average velocity must drop; likewise, as the blood collects again into a smaller venous cross-sectional area, the velocity in each vein must increase!

6. Finally, **more total blood is found in the venous system** than in the capillaries or arteries, at least at rest (things change a bit in exercise). The reason for this is that the v**eins are very complian**t, **normally have large radius** and are **long (the one thing that arterioles and capillaries, even though they have a greater cross sectional area, are not!).** So, veins have a greater volume and a greater ability to accept (or donate blood) than do arteries. One result of this is that velocities in the venous system are always less than in a comparable part of the arterial system (principally due to the larger diameter of veins).



Above: Plots of % mean blood pressure, % blood velocity, %cross-sectional area, and % total blood volume as a function of vessel type in the systemic circulation. Note that in each case 100% refers to the peak value for that particular variable.

(i) **Pressure** decreases little in the aorta and arteries since their radii are large and therefore resistance is very low. However, as radius decreases in the arterioles and capillaries, the pressure drops rapidly. Then, as the vessels begin to widen again pressure decreases at a lesser amount. All of these pressures are taken in a situation where gravity is not an important factor.
(ii) **Total cross-sectional area** is the sum of the cross sectional areas of all vessels of a certain type. Even though the arterioles, capillaries and venules have the smallest diameters per vessel, they are so numerous that the x-sectional area is maximal in these regions. Note that *cross-sectional area is not the same as volumes since it does not contain a length factor*; nor does it include changes in cross section when large amounts of blood are briefly forced into the vessel.
(iii) **Velocity:** since the same amount of blood must flow through each generation of vessels during a steady-state, then if it is divided up into a large area, as it is in the capillaries, and venules then the velocity must drop in these areas. This is useful to maximize diffusion in the capillaries as the blood spends a relatively long period of time there.
(iv) **% Blood Volume:** the increase in number and cross section of the arteries compared to the aorta coupled with the fact that they are distended as blood is injected into them results in high volumes; by contrast the small size and length and low pressures found in the capillaries and arterioles means that little of the total of the blood is found there while **the high compliance and large radii of the veins causes the majority of the blood to pool within these vessels**.

B. Blood Pressure and Wall Tension:

1. The **tension found in the walls of capillaries** is determined by a version of the **Law of Laplace**:

2. $$T = P * r$$

where ***T*** is the tension in the blood vessel walls, ***P*** is the pressure difference between the blood on the walls and the surrounding tissues (which is usually 0) and is called the **transmural pressure** and ***r*** is the radius of the vessel.

We will see the law of Laplace again when we consider the operation of lung alveoli.

a. **Capillaries** must be extremely thin-walled because of the needs of diffusion. They have only thin cellular/elastic material in their walls – no muscles to give tension.

i. Capillary wall tension is always relatively low since the radius is very low (see earlier table). T**his is important since capillaries must be very thin-walled but they also must not rip open when pressures are increased.**

ii. However, note that if the diameter and pressure do increase somewhat (due the combined action of pre- and post-capillary flow regulation, see below), the tension changes elastically (within limits).

iii. Larger vessels. *As lumens increase in diameter*, *especially where pressures are high (arterial side), tensions could easily become very high*. To counteract this, the **walls are made thicker** and the tension (result from compliance and transmural forces interacting with radius) is spread throughout the thick wall. The law of Laplace no longer fully explains the tension as some of it is generated actively by vascular smooth muscle.
A measure of tension normalized to one unit of wall thickness is called the **wall stress,** σ :

3. $$\sigma = \frac{T}{w_d} = \frac{P * r}{w_d}$$

where σ is the wall stress, ***T*** is the tension, $\boldsymbol{w_d}$ is the wall diameter, ***P*** is the transmural pressure and ***r*** is the radius. The total tension acting on such a vessel is the sum of the tensions acting on each unit thickness (essentially an average tension).

? Why is increasing the strength of the walls of an artery (that allow it to withstand very high pressures) by adding more fibers in parallel like making a muscle stronger? Explain

C. Exchange and Flow Through the Capillaries:

1. General: The walls of capillaries are largely lipid-based but they c**ontain pores that will allow materials up to a molecular weight of about 80,000 to pass.**

a. Small non-polar molecules simply pass the lipid portion of the membrane; they also move through the pores.

These pores should not be confused with protein channels – they are far, far larger and less specific.

b. Small polar molecules easily pass through these pores,

c. With large molecules, such as proteins, passage becomes increasingly difficult.

2. The size of these pores can be increased by elements of the immune system -- this allows antibodies and lymphocytes to get out the blood and into the interstitial fluid. In addition, injury may also increase the size of pores.

3. **In general, the rate of flow of small polar molecules is set by:**

a. the concentration difference across the wall and

b. by blood flow - higher blood flows result in more diffusion. We say that these molecules are **flow limited**.

4. On the other hand, diffusion of larger, lower permeability polar molecules from capillaries to the tissues is such that only a few of those that are present are able to pass through the pores.

a. Thus increasing the blood flow does not affect the rate at which they arrive in the tissues as strongly as with small molecules.

b. We say that these particles are **diffusion limited** since it is a limitation on diffusion that determines how much is delivered, not a limitation on blood flow. Note that diffusion here is not very free, unlike small polar and non-polar substances.

4. **Non-polar substances (e.g., oxygen, fatty materials) have no trouble moving across the capillary walls through their surface and pores**.

? Why should higher blood flow result in more diffusion in small polar molecules? How about in small non-polar ones? Are non-polar molecules diffusion or flow limited?

III. The Regulation of the Microcirculation: What Regulates the Rate of Flow Through Capillaries?

A. General:

1 **Microcirculations** are the blood flows through single or groups of capillaries.

2. This contrasts to **macrocirculation** that is the entire circulation or the circulation to entire organs.

3. In mammals, typical capillaries are about 0.5 to 1 mm long and have blood that flows at highly variable speeds from zero to several mm a sec.

a. It will be minimal when blood flow to the capillary is blocked; this is a common occurrence and will be explained below.

b. It reaches maximum velocities in situations of low blockage and high pressures.

c. The **average velocity is about 1 mm/s and therefore when blood is flowing it is in capillaries for an average of 0.5 to 1s,** although since flow is often stopped it is often there for a much longer period of time.

B. **Flow is largely determined by the resistance produced in pre- and post-capillary vessels.**

1. These vessels **include the arterioles, precapillary sphincters** (when present – precapillary sphincters are thick areas of smooth muscle just before the capillary) and **venules**.

2. All of these vessels can undergo considerable changes in radius (called **vasomotion**) because of the large amounts of smooth muscle they contain.

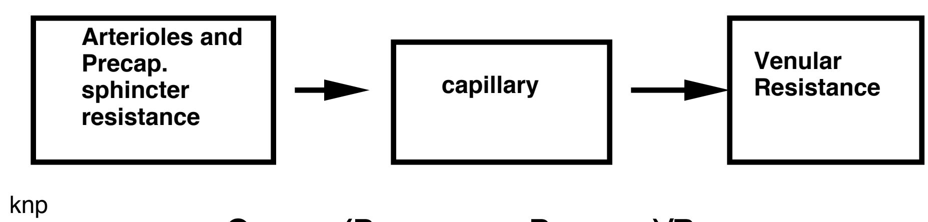
3. The actual flow through a capillary is caused by a difference in pressure across the capillary; this is the result of the interaction of the pre- and post arterial side.

a. Thus for a certain blood flow through the arteriole resistance (determined largely by radius of the arterioles at some moment in time) the pressure difference can be found; one of these pressures is the one at the upstream end of the capillaries.

b. Notice that if arterioles constrict, less blood flows and the pressure at the arterial end of the capillaries drops.

c. On the other hand, if resistance in the venules increases due to their constriction, less blood passes through. If the pressure at the distant end of the venules (venous pressure) remains constant, the pressure on the capillary end either remains high or may actually increase:

$$Q * R_{arteriole} = P_{arteriole} \qquad Q * R_{vemule} = P_{venule}$$



$$Q_{cap} = (P_{arteriole} - P_{venule})/R_{capillary}$$

d. As a result of changes in these two pressures, the blood flow through the capillaries may increase or decrease.

e. An additional set of factors also enters. If the arterial - side pressure increases (before the arterioles) the pressure at the arterial side of the capillaries will increase if there is no change in arteriole resistance. By contrast, an increase in venous pressure after the venules absent a change in venule resistance will increase the pressure at the end of the capillary and decrease flow.

C. What factors cause the arterioles (usually) and venules (occasionally) to change size?

1. **<u>Autonomic Nervous System</u>** activity (go back and review the autonomic NS packet):

a. **<u>adrenergic stimulation</u> (NE or E)** tends to cause **<u>vasoconstriction in most tissues</u>**. Interestingly, the way it operates is that

i. the total number of open paths is decreased and all of the blood passes through this fewer number of paths in accordance with the flow equations.

ii. Blood apparently does not go through special shunts (at least not in skeletal muscles).

b. **<u>cholinergic (parasympathetic) stimulation</u>** to vascular smooth muscle generally causes **<u>vasodilation</u>**;

i. the result is an increased perfusion but interestingly, only through the capillaries that were opened before the parasympathetic stimulation!

ii. In other words, the resistance of already opened vessels was decreased and flow increased in them but vessels that were closed remained so and so there was no change in flow in these vessels.

2. How then are the other vessels (arterioles and therefore also capillaries) ever opened?

a. **<u>Regulation by Metabolites</u>:** part of the changes that occur in the perfusion of all tissues are due to changes in metabolite concentration. In particular, **lactic acid, CO_2 and H^+** appear to be potent vasodilators.

i. Assume that a capillary has no flow because its arteriole is shut.

ii. As the tissues metabolize, at first there are no problems as metabolites simply diffuse into the still blood.

iii. However, over time the concentration of these metabolites in the blood and the tissue (including the pre-capillary tissue) increases.

iv. This induces the arteriole smooth muscle to relax somewhat.

v. Perfusion increases, the metabolites are washed out as new blood comes in, oxygen and nutrients are delivered (anaerobic metabolism, if it was present, decreases) and tissue levels (including the adjacent arterioles and precapillary sphincters) of these substances decrease. As a result, constriction begins, resistance increases and flow decreases and the entire cycle starts again.

b. **<u>Regulation by Adenosine and Certain Prostaglandins</u>:** These are known to be potent vasodilators in certain tissues (e.g., adenosine in the heart) and there is growing evidence that they may be very significant factors in the blood flow of capillary beds (certain tissues).

c. **<u>Autoregulation and transmural pressure</u>**: the <u>greater the pressure exerted on the walls of arterioles the more they tend to contract</u> and therefore the more they tend to <u>increase resistance and vice versa</u>. Notice that this tends to ensure a constant pressure and therefore flow over a wide range of pressures and is termed **<u>autoregulation</u>**.

d. **Here are some other possibilities but evidence seems to be against them:**

i. K^+, Phosphate and Osmolarity: All of these factors will cause changes in vasomotor state, and in the way that might be expected to be significant (e.g., increased osmolarity causes increased arteriole diameter). However, there is simply no good evidence that they normally change enough during the usual flow cycle of a capillary.

ii. Regulation by oxygen tension: Oxygen does cause some effects but they are not consistent -- there is no consistent negative correlation between arteriole diameter and oxygen tension.

? In exercise, parasympathetic activity is usually decreased and sympathetic activity increases. Explain how it is possible that blood flow to muscles increases in exercise. How about to the viscera?