WCHP Respiratory Physiology 2009-2010
PULMONARY BLOOD FLOW

Clinical rationale and overall goal:

Disorders affecting the distribution of blood flow within the lungs and pressures within the pulmonary circulation have serious adverse effects on pulmonary gas exchange. The overall goal of this classroom session is to provide the student with an understanding of the magnitude and distribution of pulmonary blood flow and pulmonary vascular pressures and the concept of shunt flow (venous admixture), which must be understood in order to appreciate the pathophysiology of arterial hypoxemia in a patient with respiratory disease.

Sources of information:

The sources of information that will be sufficient for the individual student to master the specific objectives listed below include the following:

- Guyton & Hall, *Textbook of Medical Physiology, 11th edition*), Chap. 38;
- Handouts, URLs, reprints or other supplementary materials provided by department faculty;
- Lecture notes

Nota bene: Students are expected to be prepared for class by having read the relevant sections in the text(s) prior to the classroom sessions on individual topics, to take their own notes during classroom sessions, to participate actively in any large-group or break-out group activities, and to try all online quizzes. Students are encouraged to contact the instructor via email (jnorton@une.edu) with any questions. Students are strongly discouraged from using class notes provided by a note service as the sole or even the primary source of information in this course.

Learning objectives:

Following study of the required reading from the assigned texts (or similar sections in other texts available to the student) and attendance at the lectures and/or discussions on this topic, the student should be able to meet the following learning objectives:

1. Define or otherwise indicate an understanding of the following words or phrases: pulmonary blood flow; anatomical shunt; intrapulmonary shunt; physiological shunt; shunt equation; hypoxic vasoconstriction; hydrostatic pressure gradients within the lung; zones I, II, and III; orthopnea; pulmonary artery wedge pressure; pulmonary interstitial fluid dynamics;

2. Differentiate among zones 1, 2, and 3 in the lung with respect to the relationship among pulmonary vascular pressures (arterial and venous), airway pressure, and patterns of pulmonary blood flow;

3. Demonstration an understanding of *anatomical shunt*, *intrapulmonary shunt* and *physiological shunt*, clearly distinguishing among the three;

4. Demonstrate an understanding of the derivation of the shunt equation, shown below:

$$\dot{Q}_S = \dot{Q}_T \cdot \frac{C_i O_2 - C_a O_2}{C_i O_2 - C_v O_2}$$

5. Demonstrate an understanding of the control of fluid balance within the lung in a normal healthy human subject and in a patient with elevated pulmonary vascular pressures, in terms of the *Starling Equilibrium equation* for capillary exchange, shown below:

$$J = K_f \cdot [(P_c - P_{isf}) - \sigma(\Pi_c - \Pi_{isf})]$$

6. Differentiate between the pulmonary and systemic circulations with respect to each of the following: total flow rate, blood volume, vascular compliance, vascular pressures and total vascular resistance;

7. Demonstrate an understanding of the relationships among *left atrial pressure*, *pulmonary capillary wedge pressure*, and *left ventricular end diastolic pressure*;

8. Compare and contrast the airway smooth muscle and vascular smooth muscle control mechanisms that help maintain a normal ventilation-perfusion ratio;

9. Recognize the *effect of pulmonary edema* on pulmonary diffusion capacity and the ability of oxygen and carbon dioxide to diffuse across the respiratory membrane, relating this effect to the factors regulating the rate of simple diffusion;

10. Demonstrate an understanding of the regulatory mechanisms controlling pulmonary blood flow and its regional distribution within the upright lung of a healthy human subject, including *hydrostatic pressure gradients*, the phenomenon of *hypoxic pulmonary vasoconstriction*, and the effects of *autonomic innervation*;

Pulmonary Blood Flow:

The purpose of pulmonary blood flow is to bring deoxygenated blood that has returned from the peripheral tissues into close contact with alveolar air within the lung, for the purposes of excreting excess carbon dioxide and replenishing the oxygen content. The same types of questions can be asked of pulmonary blood flow as were asked of pulmonary ventilation in a previous handout, namely:

- How does blood flow?
- How much blood flows?
- How fast does blood flow?
- Where does the blood go?

A full discussion of these questions will lead the student through the hemodynamics of pulmonary blood flow, the distribution of pulmonary blood flow within the respiratory system, and the actions of vascular smooth muscle within the pulmonary vasculature. The following discussion is only an attempt to provide the student with a framework for understanding and integrating facts and concepts related to pulmonary blood flow, and *the information in this is not meant to substitute for attendance in class or completion of the assigned reading in the required textbook*.

How does blood flow? How much blood flows? How fast does blood flow?

The answers to these first few questions are relatively simple. Blood flows through the pulmonary vasculature because of the pressure gradient between its proximal end, the pulmonary artery, and its distal end, the left atrium. The pressure and flow through the pulmonary vasculature is provided by the pumping action of the right ventricle. Typical pulmonary artery pressures during the cardiac cycle are 25/10 mm Hg, significantly lower than the corresponding typical systemic arterial pressures of 120/80 mm Hg. The pulmonary vessels are generally larger in diameter than their systemic counterparts, and the overall length of the pulmonary vascular tree is shorter, resulting in a lower overall vascular resistance. The lower pulmonary vascular resistance is associated with the lower perfusion pressure gradient.

The right and left ventricles constitute two separate pumps arranged in series, so the total blood flow through the pulmonary circulation is equal to the systemic blood flow, or cardiac output. The only qualification involves the relatively small right-to-left anatomical shunt flow, consisting of a small amount of bronchial venous blood that mixes with the oxygenated blood in the pulmonary veins and a small amount of deoxygenated blood from the coronary circulation (Thebesian veins) that empties directly into the left ventricle. Although insignificant with respect to overall hemodynamics, the anatomical shunts have a measurable effect on the differences between alveolar and arterial values for PO_2, as will be discussed in the handout and lectures on pulmonary gas exchange.

The volume flow rate through the pulmonary circulation for a typical, 70-kg, healthy human subject is approximately 5 L/min. The velocity of blood flow is most important with respect to gas exchange in the pulmonary capillaries. Normally, blood spends about one second within the pulmonary capillaries, and diffusional gas exchange of oxygen and carbon dioxide is usually complete within about 0.25 seconds. Conceivably, cardiac output would have to increase more than four times above its resting value in order before there would be an inadequate time for complete equilibration between alveolar gas and pulmonary capillary blood. Since blood flow within the lung is more evenly distributed with increased cardiac output (see a more complete discussion of this below), and because more pulmonary capillaries are recruited with increased pulmonary blood flow, healthy human subjects usually do not experience an exercise-induced arterial hypoxemia, although this may occur in world-class athletes with very high levels of cardiac output.

Where does the blood go?

The answer to this question is somewhat more complicated, and involves a consideration of the overall elastic properties of the lung and its vasculature, gravity, the relationships among pulmonary arterial pressure, pulmonary venous pressure, and alveolar pressure, and reflexes involving the action of pulmonary vascular smooth muscle.

The lungs are soft, spongy, highly compliant organs, which move freely within the pleural cavities because of the slippery layer of fluid between the visceral pleura and the parietal pleura lining the inside of the thoracic wall.

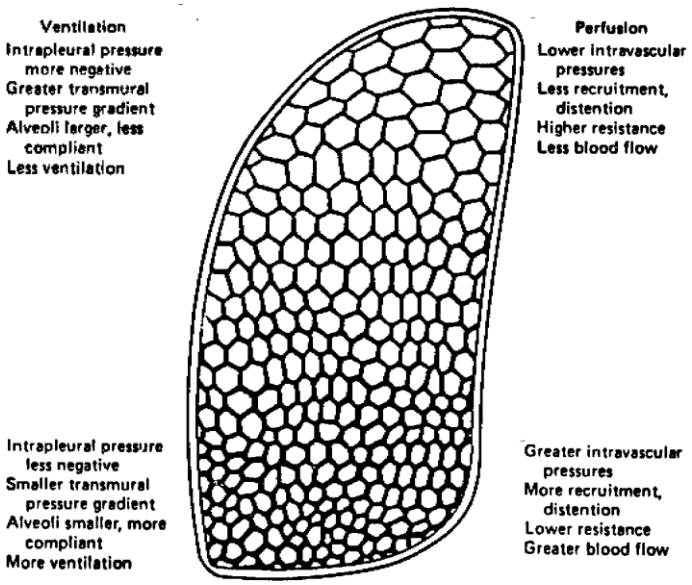
The lungs stay inflated within the pleural cavities because of the negative pressure within the intrapleural space. But a blood-filled lung can, and does, sag within the pleural cavity due to the weight of the blood within it, stretching our the alveoli at the top of the lung, and compressing the alveoli at the base. The height of the lungs in a healthy human subject standing upright is large enough to cause significant hydrostatic pressure differences between the apices and bases of the lungs. The vascular pressures in the apices are about 15 mm Hg lower than the vascular pressures at the hilus (with systolic arterial pressures of 10/-5 mm Hg), and those at the base are about 15 mm H higher than the hilar pressures (with systolic arterial pressure of 40/25 mm Hg). There is about a 30 mm Hg vertical pressure gradient between intravascular pressures at the apex and the base in an average-sized human subject.

This difference in hydrostatic pressure between the apex and the base of the lung has hemodynamic consequences. First, more blood is located in the base of the lung than the apex, because the higher intravascular pressures at the base of the lung stretch the highly compliant pulmonary vessels, increasing their diameters and their volume. Secondly, the larger vascular diameters produce a lower vascular resistance at the base, and more blood flows through the base of the lung than through the apex, even though the overall pressure gradient promoting flow is the same for both locations. The uneven distribution of the blood within the lung and the sagging of the lung within the pleural cavity affects ventilation in the different regions of the lung, which will be discussed next.

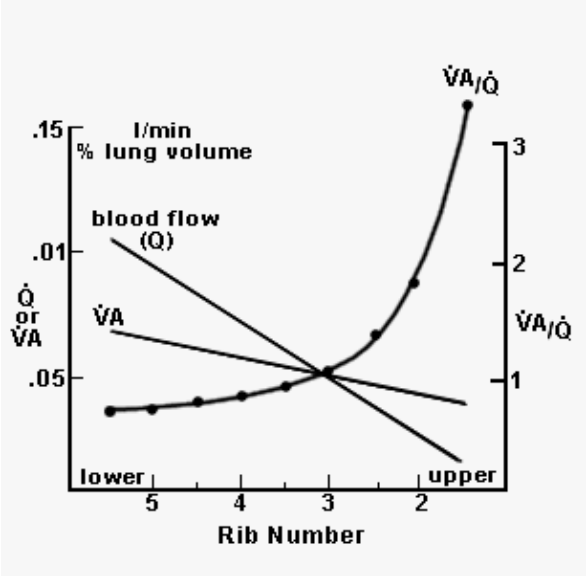
Below is an excellent diagram illustrating the gradients in ventilation and perfusion that exist in the lung of a healthy human subject standing upright. In this diagram, the polygons represent alveoli, the size of the polygons indicate the size of the alveoli, and the thickness of the lines outlining the polygons indicating the amount of blood in the vessels surrounding the alveoli.

The weight of the blood in the pulmonary circulation causes the lung to sag within the pleural cavity, compressing the alveoli at the base of the lung, and stretching the alveoli at the apex of the lung. This is indicated in the diagram by the increased size of the polygons representing the alveoli at the apex. The stretched alveoli at the apex have a reduced compliance, and change their volume less during inspiration than do the more compliance alveoli at the base of the lung. *Ventilation is therefore greater at the base of the lung than the apex* in a healthy human subject standing upright.

The increased vascular pressures at the base of the lung cause more blood to be located at the base of the lung and dilate the highly compliant pulmonary vessels, decreasing vascular resistance. Therefore, *perfusion is greater at the base of the lung than the apex* in a healthy human subject standing upright, as indicated in the diagram below by the increased thickness of the walls of the polygons.



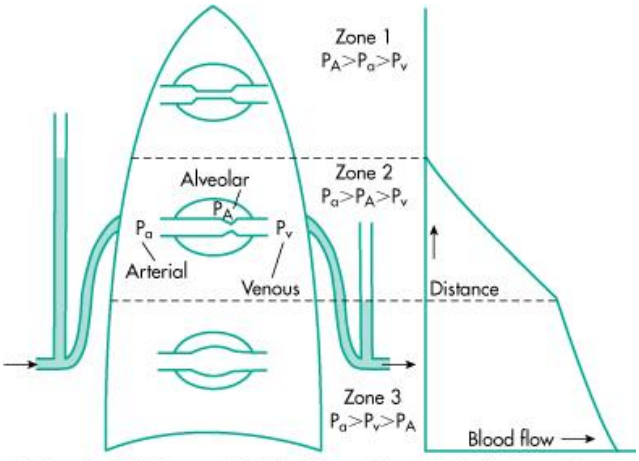
Even though both ventilation and perfusion are higher at the base of the lung, the relative change in perfusion from apex to base is greater than the relative change in ventilation from apex to base, as illustrated in the diagram below by the slopes of the lines labeled " $\dot{Q}$ " (blood flow, L/min) and " $\dot{V}_A$ " (alveolar ventilation, L/min).



Because perfusion, $\dot{Q}$, is relatively greater at the base than is alveolar ventilation, $\dot{V}_A$, the ratio of ventilation to perfusion, the ventilation/perfusion ratio, or $\frac{\dot{V}_A}{\dot{Q}}$, is low. On the other hand, at the apex of the lung, ventilation is relatively greater than perfusion, even though both are lower than at the base, and the ventilation/perfusion ratio is high. These regional differences in ventilation/perfusion ratios within the lung of a healthy human subject are inconsequential, but ventilation/perfusion ratio disturbances in patients with pulmonary disease are the most common cause of hypoxemia, or low arterial PO_2, as will be seen in discussions of the mechanisms of arterial hypoxemia.

Pulmonary blood flow "zones"

Another factor, in addition to gravity, that determines the distribution of blood flow within the lung is the relationship between vascular pressures and alveolar pressure. The diagram below shows vascular pressures within the pulmonary arteries (P_a) and pulmonary veins (P_v), and alveolar pressure (P_A) exerted by the air within the alveoli. The diagram shows three zones, defined by the relative magnitudes of these pressures.



In Zone 1, the alveolar pressure, P_A, is greater than either the pulmonary arterial pressure, P_a, or the pulmonary venous pressure, P_v. The vessels are therefore collapsed, and there is no flow. In healthy human subjects standing upright, this zone is very small or non-existent, but it can develop and increase if pulmonary vascular pressures are low, such as in shock, or if alveolar pressures are elevated, such as in positive-pressure ventilation. In Zone 2, the pulsatile pulmonary arterial pressure rises above alveolar pressure, allowing intermittent flow through the vessels. The amount of flow in Zone 2 is determined by the difference between the arterial pressure and the alveolar pressure. Zone 2 occupies approximately the upper third of the lung of a healthy human subject standing upright. In Zone 3, all pulmonary vascular pressure are higher than the alveolar pressure, blood flow is continuous, and the magnitude of the flow is determined by the difference between the pulmonary arterial and venous pressures. Zone 3 occupies the lower two-thirds of the lung of a healthy human subject standing upright.

Pulmonary capillary exchange

Exchange of fluid and solute across the walls of the pulmonary capillaries is governed by the same principles that determine fluid exchange across any capillary, which were outlined by Ernest Starling in his equation for capillary exchange:

$$J = K_f \cdot [(P_c - P_{isf}) - \sigma(\Pi_c - \Pi_{isf})]$$

In the above expression, J is the net rate of fluid movement, K_f is the capillary filtration coefficient, P_c is the pulmonary capillary pressure, P_{isf} is the pulmonary interstitial fluid pressure, Π_c is the pulmonary capillary oncotic pressure, and Π_{isf} is the pulmonary interstitial oncotic pressure. Since pulmonary capillary pressures are lower than capillary pressures elsewhere in the body, and capillary oncotic pressure is the same as elsewhere in the body, there is a substantial "safety factor" within the pulmonary vasculature that diminishes the likelihood of edema as pulmonary vascular pressures rise. Pulmonary capillary pressures have to approach capillary oncotic pressures (~24 mm Hg) before edema develops. Since, in the upright lung, pulmonary vascular pressures are higher at the base than the apex, pulmonary edema due to general elevations in pulmonary vascular pressures will first develop at the lung bases.

Pulmonary edema adversely affects oxygen exchange, by increasing the diffusion distance within the lung. Ironically, the hydrostatic pressure gradient within the upright lung can be used to improve gas exchange in a patient with elevated pulmonary vascular pressures and pulmonary congestion. If such a patient is lying horizontally, vascular pressures are relatively even (and elevated) throughout the lungs, affecting gas exchange everywhere. If the patient is raised toward an upright position, vascular pressures decrease at the lung apices; The extent of the edema at the apices will therefore be less, and gas exchange may improve in these regions. This phenomenon – improvement of gas exchange in the upright position – is described as *orthopnea*. Patients with elevated pulmonary vascular pressures due, for example, to congestive heart failure often discover this principle on their own, and sleep better while propped up on one, two, or even three pillows. Many find relief only when sleeping nearly upright in a chair. Orthopnea can be roughly quantified by the clinician, based on a careful patient history, as the number of pillows required to sleep comfortably – two-pillow orthopnea, three-pillow orthopnea, *etc*.

Pulmonary shunts

In respiratory physiology, the word "shunt" has a very specific meaning. It refers to blood that enters the left side of the heart without having been oxygenated in the lung. Some shunt flow is normal and "*anatomical*", caused (as described above) by mixing of bronchial venous blood with oxygenated blood from the pulmonary capillaries. Other forms of shunt flow are abnormal, and can be caused, for example, by blood that perfused alveoli that are fluid-filled, collapsed, or otherwise non-ventilated. This blood passes by the diseased or damaged alveoli, does not pick up oxygen or give off carbon dioxide, and is subsequently mixed in the pulmonary venous circulation with well-oxygenated blood from normal alveoli. These are described as "intrapulmonary" shunts. The term "*physiological shunt flow*" *encompasses both anatomical and intrapulmonary shunts*, and simply describes all of the non-oxygenated blood, from all sources, that is mixed with the oxygenated blood in the pulmonary circulation or in the left side of the heart. Some congenital cardiac malformations (but not all!) allow mixing of deoxygenated blood from the right side of the heart with oxygenated blood in the left side of the heart. These are described as *right-to-*

left shunts and usually produce arterial hypoxemia and cyanosis. Indeed, congenital heart diseases can be separated into two groups – *cyanotic* and *acyanotic* – depending on whether the malformation increases physiologic shunt flow.

The same argument outlined previously for determining physiological dead space can be applied to the calculation of the magnitude of physiological shunt flow. The high oxygen content of the pulmonary end-capillary blood (C_iO_2, for "ideal" oxygen content) is diluted by the addition of venous (deoxygenated) blood from physiological shunts that has a low oxygen content (C_vO_2), producing an oxygen content in systemic arterial blood (C_aO_2) that falls somewhere between the two. The ratio of physiological shunt flow ($\dot{Q}_S$) to total flow ($\dot{Q}_T$) can be calculated using the dilution principle, as described in the shunt equation:

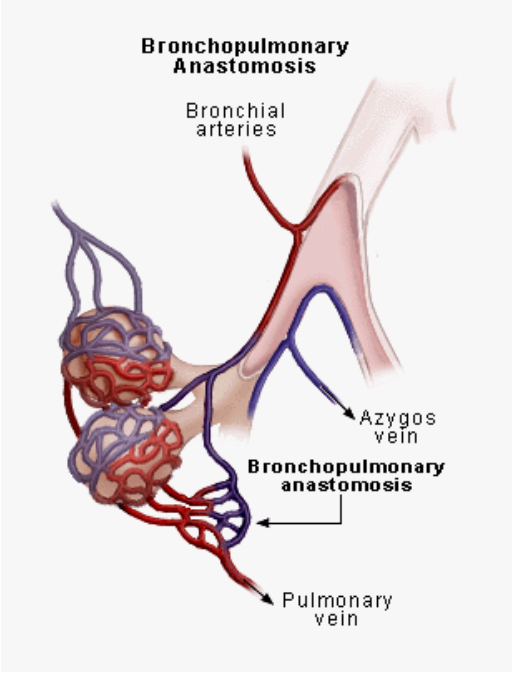
$$\frac{\dot{Q}_S}{\dot{Q}_T} = \frac{C_iO_2 - C_aO_2}{C_iO_2 - C_vO_2}$$

or

$$\dot{Q}_S = \dot{Q}_T \cdot \frac{C_iO_2 - C_aO_2}{C_iO_2 - C_vO_2}$$

Oxygen content is used in the shunt equation instead of oxygen partial pressure because the latter reflects only the chemical activity of dissolved oxygen. When oxygenated blood from ventilated alveoli mixes with shunt blood, the PO_2 changes in a non-linear fashion related to the shape of the oxygen dissociation curve. The dilution principle can therefore only be applied to total oxygen content, not PO_2.

In healthy human subjects, intrapulmonary shunts are non-existent or inconsequential, and physiological shunt flow is very close to normal anatomical shunt flow. The diagram below shows the origin of normal anatomical shunt flow from the bronchial venous circulation through bronchopulmonary anastomoses.



Hypoxic vasoconstriction

In contrast to blood vessels elsewhere in the body, blood vessels within the lungs constrict when exposed to low levels of oxygen, rather than dilate. In the rest of the body, a low PO_2 surrounding the vessels is an indication that the tissues are not getting enough oxygen, so it makes sense that low PO_2 would cause blood vessels in that region to dilate, bringing more blood and oxygen to the tissues there. In the lung, a low PO_2 surrounding blood vessels means that the region of the lung is not getting an adequate amount of ventilation. In order to maintain as normal a ventilation/perfusion ratio as possible, it would make sense in the lung to constrict vessels going to a poorly ventilated region, decreasing flow there. Blood would therefore be diverted to other, better-ventilated regions of the lung where more normal oxygenation could take place. Hypoxic vasoconstriction is therefore a useful physiological response that helps to restore ventilation-perfusion ratios toward normal, except when respiratory disease severely impairs ventilation or when a healthy human subject rapidly ascends to high altitudes where less oxygen is available for gas exchange in the lung. In these cases, the global hypoxia within the lung will produce a global hypoxic vasoconstriction, increasing pulmonary vascular resistance, increasing pulmonary vascular pressures, and increasing right ventricular workload. In high altitude pulmonary edema (HAPE), the elevated vascular pressures secondary to the hypoxic vasoconstriction promote movement of fluid out of the pulmonary capillaries into the interstitial space, causing pulmonary edema and impairing pulmonary gas exchange.