

Human Physiology 653/ PHYB 401  
Respiration  
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LC55F-57F

Summary of Context #2

## PERFUSION

The pulmonary circuit is a low resistance circulation. The specific structure(s) primarily responsible for the majority of control of resistance in the resting state is controversial. As in the periphery, the majority of resistance is on the arterial side (upstream) of the the capillaries.

However, unlike the systemic circulation, this can vary considerably in response to perturbations in the system (eg: shock).

The characteristic thin-walled vessels throughout the circuit are strongly affected by intravascular and extravascular pressures, the latter influenced primarily by the alveolar and interstitial fluid environment.

Pressure inside the blood vessels themselves has the most pronounced physiological effect on pulmonary vascular resistance. Resistance varies inversely with either pulmonary arterial or venous pressure (Figure 1). This is a result of distention by intravascular pressure influencing the caliber of the vessels (radius; remember Poiseuille's Law), and increasing capillary recruitment with increased pressure. This contributes to non-uniform distribution of perfusion; in an upright individual, perfusion is highest at the base of the lung, where hydrostatic pressure is greatest (gravity). As a result of these influences, cardiac output is the primary physiological determinant of pulmonary vascular resistance.

Lung volume also influences pulmonary vascular resistance by purely mechanical effects. At low lung volumes the *extra-alveolar vessels* tend to be smaller, offering more resistance, but the capillaries are minimally affected. As lung volume increases, the extra-alveolar vessels are pulled open by radial stretch. This decreases the resistance in the extra-alveolar vessels, and pulmonary resistance falls. This phenomenon continues as the lung volume increases

Figure 1

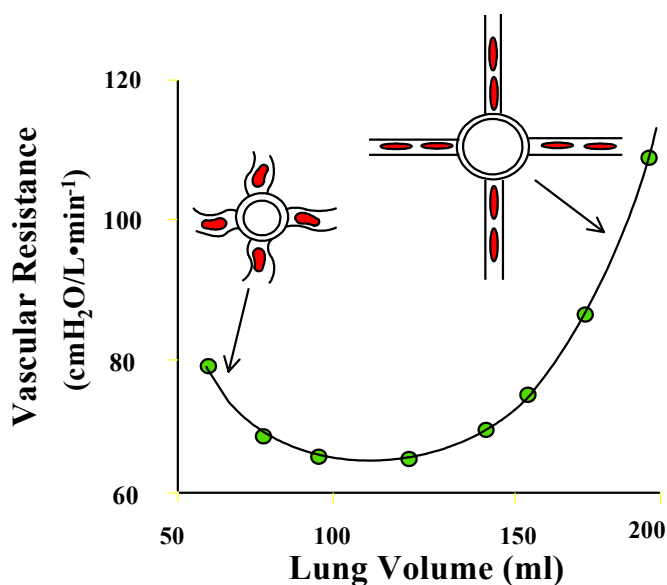
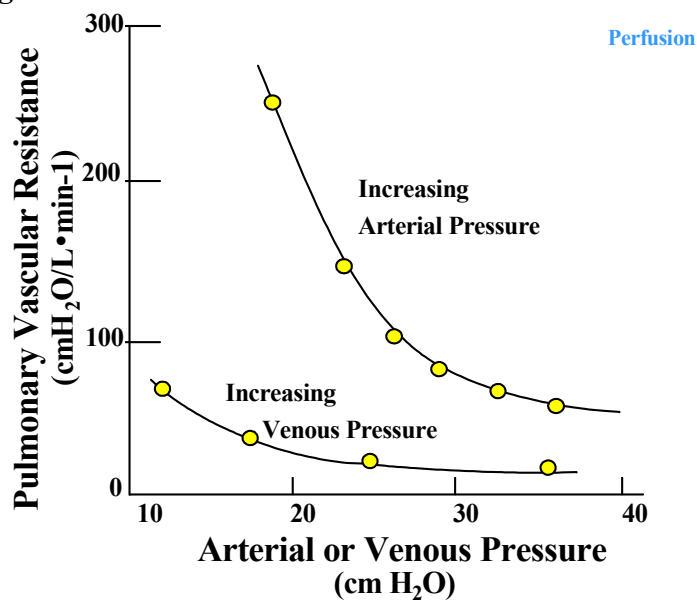


Figure 2

further, but the *alveolar vessels* (primarily capillaries) demonstrate different characteristic changes. Alveolar vessels become stretched tangentially along the interalveolar axes, but compressed perpendicular to this (think cross-section perpendicular to the long axis of the vessel) into non-cylindrical shapes. The resulting decrease in radius due to this compression results in higher resistance. Both the extra-alveolar vessel and the alveolar vessel responses are displayed in figure 2. Because the pattern of volume changes in the lung are not uniform from apex to base (see below), these lung volume effects on perfusion are also exerted in a non-uniform distribution pattern.

### WEST ZONES (Figure 3):

When external influences have such a profound influence on vascular resistance, the areas wherein resistance is manifested are referred to as Starling resistors. The resistance through these resistors is determined by the net intra/extravascular pressures along the length of the vessel. The net effect of these external forces on pulmonary vascular resistance in an upright individual results in perfusion zones that are defined by the factors influencing the Starling resistor properties of the vessels: pulmonary arterial and venous pressures ( $P_a$  and  $P_{pv}$  respectively) and alveolar (or extravascular) pressure ( $P_A$ ). These zones are classically known as the West zones.

Because the pulmonary circulation is a low pressure system, the hydrostatic pressure due to the column of blood from apex to base of the lungs in a standing individual has a substantial influence on perfusion characteristics. The average pulmonary arterial pressure can raise a column of blood to a height of 34 cm (~13 inches), and average pulmonary venous pressure can raise blood to a height of 8 cm (~3 inches). Where pulmonary arterial pressure and pulmonary venous pressure are greater than the alveolar pressure (on average equal to atmospheric pressure; 0 mmHg),

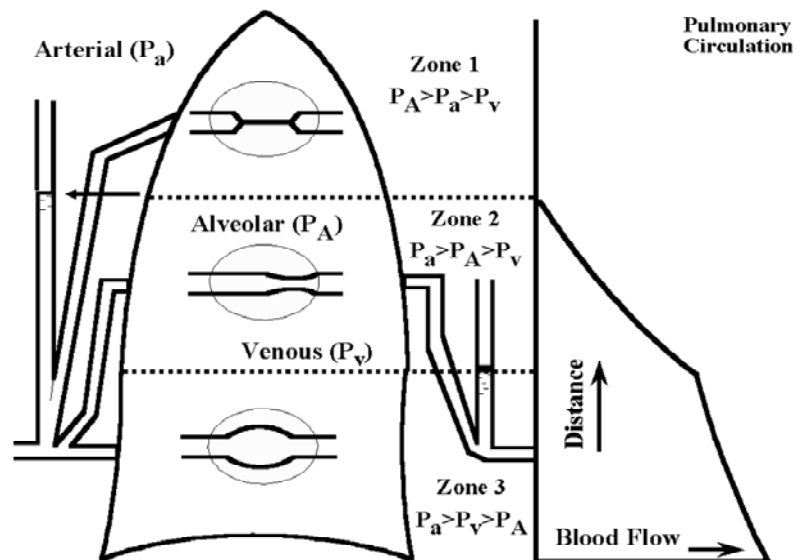


Figure 3

blood flow is driven by the pressure differential  $P_a - P_{pv}$ , and alveolar pressure has no effect. This is referred to as West Zone III. By definition, this zone is framed by the bottom of the lungs (below the heart level) up to the height to which pulmonary venous blood pressure will raise a column of blood (*SHAM* average ~3 inches). Above this level,  $P_{pv}$  is sub-atmospheric, and the relatively higher  $P_A$  will compress vessels on the venular side of the circulation. Under these “West Zone II” conditions, flow is driven by the  $P_a - P_A$

gradient, and  $P_v$  has no influence. When  $P_a$  is lower than  $P_A$  (West Zone I), there would be no flow. Physiologically, this does not exist, as normal, average *SHAM*  $P_a$  can raise a column of blood above the level of the top of the lungs. However, under circumstances where  $P_a$  may fall,  $P_A$  rises, or both, a zone I region can become manifested. The common diagram of these zones depicts them as equally distributed vertically across the lungs. In reality, the upper and lower limits of Zone II (and consequently, limits of zones I and II as well) are defined by the relative  $P_a$ ,  $P_v$ , and  $P_A$  pressures at any moment, or under a given set of circumstances.

The existence of West Zones can become important in the common clinical practice of estimating left heart filling pressure (an index of left heart preload) by obtaining pulmonary arterial wedge pressures (PAWP; also variably referred to as pulmonary capillary wedge pressure [PCWP] or pulmonary arterial occlusion pressures [PAOP]). This parameter is measured from the right heart side of the pulmonary

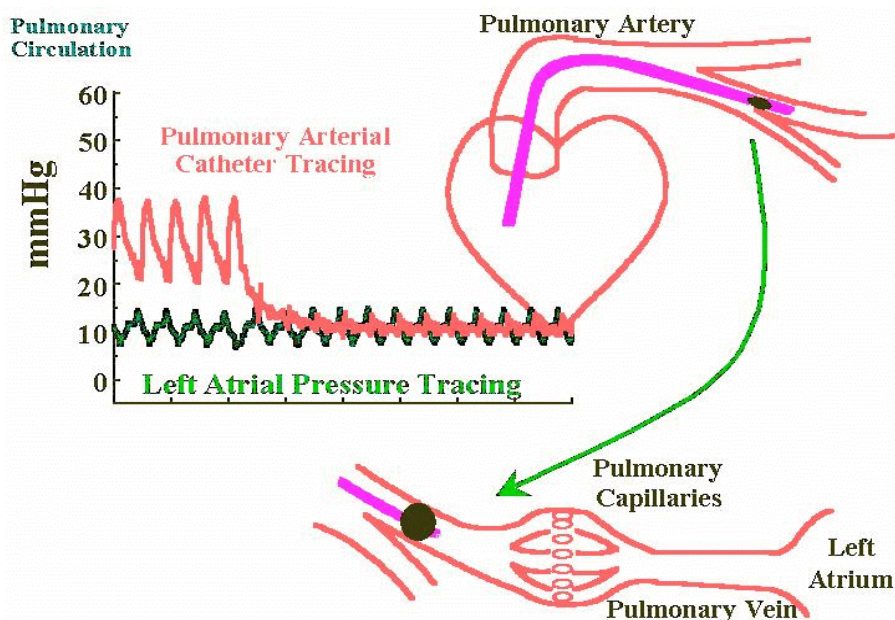


Figure 4

circulation, and is based on the assumption that there is a clear conduit from the pulmonary artery to pulmonary veins (and left atrium) across which one can measure pulmonary venous pressure as an index of left heart preload. For this parameter to be accurate, the measurement *must* be made in Zone 3. In Zone 3, when the balloon is inflated at the tip of the catheter, the pressure at the tip of the catheter will fall to equal pulmonary venous pressure (Figure 4). If the catheter is in a West Zone II environment, when the balloon is inflated at the tip of the catheter, the pressure at the tip of the catheter will fall to the pressure surrounding the alveolar or extra-alveolar vessels rather than to pulmonary venous pressure.

Other factors influencing pulmonary vascular resistance:

- Neural/humoral influences Vasoactive substances are generally less effective here, due to the smaller amount of smooth muscle in the pulmonary vessels compared to the systemic vasculature. However, these substances can exert unique changes. Both serotonin and histamine, for example, are constrictors in the pulmonary circulation, but serotonin acts primarily on the arterial side, while histamine is more effective in the pulmonary venous vessels.
- Alveolar PO<sub>2</sub>: If alveolar PO<sub>2</sub> is low, the vessels perfusing that alveolus constrict. This phenomenon is unique to the lung, and may provide a survival advantage by reducing physiologic shunt flow (see shunts), but the mechanism is poorly understood.
- Anatomy: The right pulmonary artery comes off at an acute angle. Because this alteration in direction consumes potential energy (pressure), more blood subsequently flows through the left lung.

FACTORS INFLUENCING NON-UNIFORM VENTILATION

- ***Increased expansion at base and outer parenchyma: intimate association with diaphragm and ribcage muscle dynamics.*** Due to the intimate association of the diaphragm and ribcage with the base and lower portions of the lung, the base is expanded more than the apex upon inhalation. These influences also provide for more expansion in the aouter parenchyma than in the inner portion of the lung.
- ***Differences in resting radius of alveoli (base vs. Apex)***
- ***Weight of the lung and blood at the base*** results in less negative pleural pressure at the base (favors expansion of apical regions)

Summary:

Ventilation resulting from these factors is generally highest at the base of the lung, and lowest at the apex.

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## VENTILATION-PERFUSION

Gas exchange function at the lung depends upon both ventilation and perfusion. That is, the equilibrium of gas partial pressures between the alveoli and capillaries perfusing them is a function of both ventilation and perfusion. This relationship can be made clear by the analogy presented in figure 5. In it, a mixing chamber is shown with an inflow and outflow tract at the bottom, representing perfusion rate ( $Q$ ). A dye is being added at the top, representing ventilatory renewal ( $V$ ). The final concentration of the dye in the mixing chamber ( $V/Q$ ) will be dependent on both the rate of perfusion, and the rate at which the dye is added to the chamber. If the rate at which the dye is infused into the system decreases, while perfusion rate remains constant, the concentration of the dye in the chamber will decrease. In a similar fashion, if the perfusion rate decreases, but rate of introduction of the dye is unchanged, the concentration of the dye will increase. Other variations on this theme can be considered by variable changes in the relationship of  $V$  to  $Q$ . The equilibrium partial pressures for blood gases is similarly vitally linked to the ratio of  $V/Q$ .

On average, alveolar ventilation is  $\sim 4\text{L}/\text{min}$ , while pulmonary blood flow equals  $\sim 5\text{L}/\text{min}$  (cardiac output). This yields an average  $V/Q$  of 0.8 (because ventilation and perfusion are both expressed in  $\text{L}/\text{min}$ , the ratio has no units). However, knowing these two values does not tell one all that is needed to assess a situation. To be effective, flow must go to regions that are ventilated! *Matching* of  $V$  and  $Q$  determines the final alveolar/end-capillary  $\text{PO}_2$  and  $\text{PCO}_2$  (assuming a perfusion limited condition). At an alveolus where there is all ventilation and no perfusion,  $P_{\text{A}}\text{O}_2$  will equal

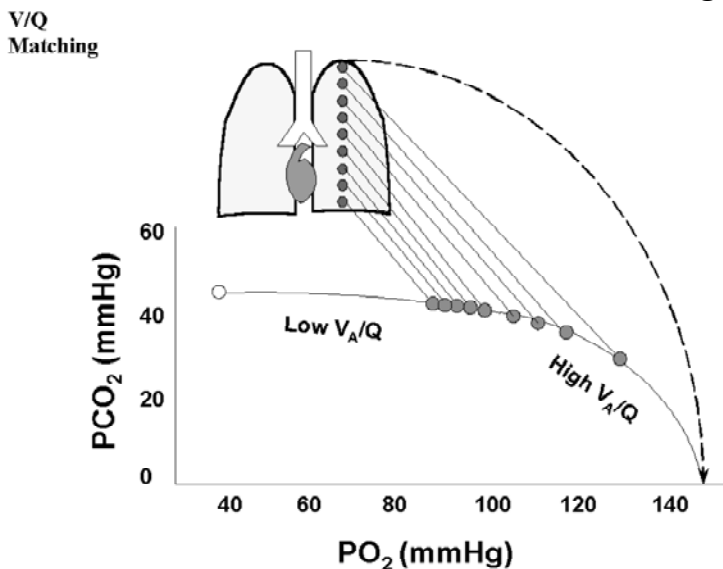


Figure 6

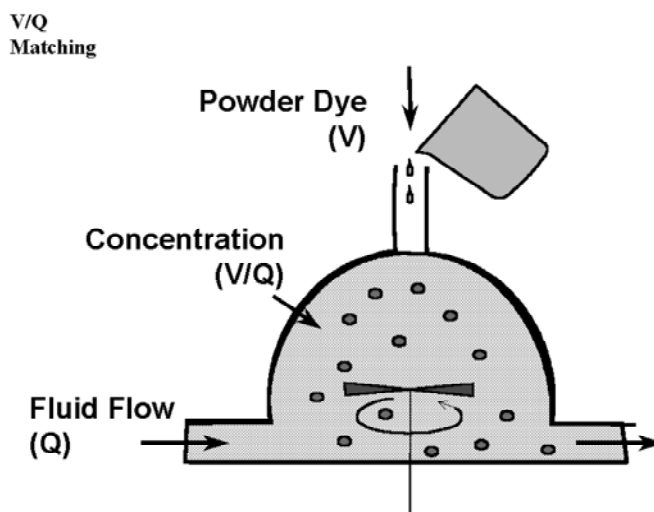


Figure 5

150mmHg. At an alveolus where there is blood flow, but no ventilation, the  $P_{A}O_2$  will equal the  $PO_2$  of mixed venous blood ( $P_{mv}$ ). All alveolar values for  $PO_2$  and  $PCO_2$  (assuming a normal respiratory quotient of 0.8) will fall upon the line shown in Figure 6. At the apex of the lung, under conditions where one might find ventilation with no perfusion (West zone 1) the  $P_{A}O_2$  will equal 21% of air (adjusted for water vapor), and  $PCO_2$  will also be that of air ( $\sim 0$ ). As one moves into regions that are better perfused, the  $P_{A}O_2$  will fall, and  $PCO_2$  will rise. Under conditions of all perfusion and no ventilation, the  $P_{A}O_2$  and  $PCO_2$  will equal those of mixed venous blood. Gradations of this are found from apex to base due to the relative changes in  $V/Q$ .

Both ventilation and perfusion increase as one moves from the apex to the base of the lung. However, the equilibrium value of alveolar/blood gases is determined by the  $V/Q$  ratio, *not wherever either ventilation or perfusion are highest*. The changes in ventilation, perfusion, and their ratio to each other are shown in figure 7. One finds a value for  $V/Q$  highest at the apex, and lower at the base of the lung, due to the fact that the relative increase in perfusion lower in the lung is greater than that of ventilation. As a result of this, the alveolar and blood gases (and other parameters) going from the apex to the base of the lungs are affected, as shown in Figure 8. Because the  $V/Q$  ratio is higher near the apex, the  $PO_2$  is higher, as is the pH, and  $PCO_2$  is lower. The opposite effect is seen at the

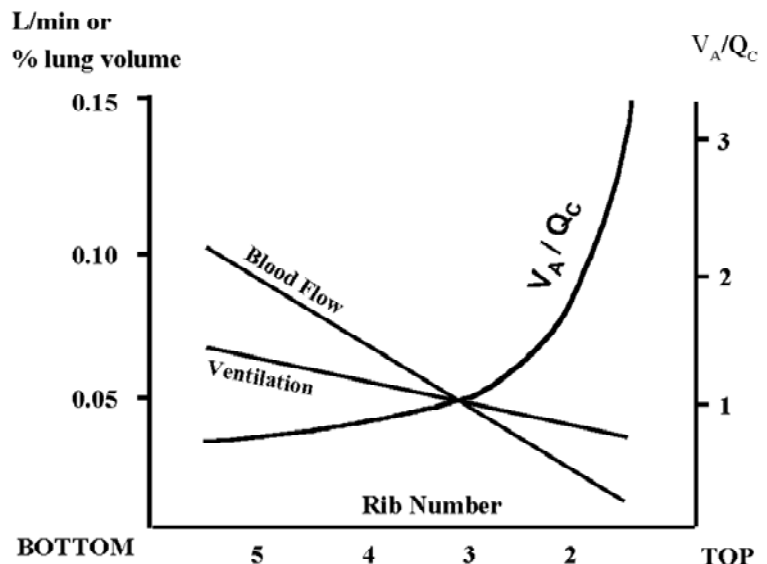
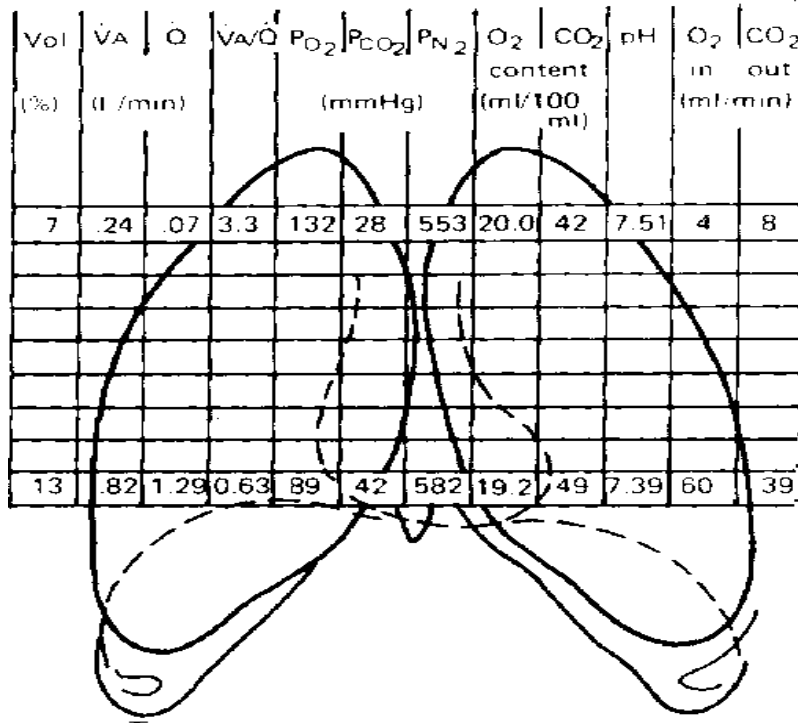


Figure 7



base, where the V/Q ratio is lower.

Figure 8

### VENTILATION/PERFUSION MATCHING: THE $PAO_2$ - $PaO_2$ DIFFERENCE

The final concentration of oxygen in arterial blood is dependent upon the relative V/Q of all regions of the pulmonary circulation, and their respective influences on oxygen content. In the example given in Figure 9 three alveoli with three different V/Q ratios (0.1, 1, and 10) yield oxygen contents of 16, 19.5, and 20 Vol%, respectively. The first feature to note here is that despite the relatively equivalent increases in V/Q ratios (10-fold each) there is little change in  $O_2$  concentration of blood coming from the middle alveolus and the far right alveolus. This is due to the shape of the oxyhemoglobin dissociation curve at higher  $PO_2$  values.

Increases in  $PO_2$  above 100 do not substantially alter the  $O_2$  content of the blood. The second feature is that the average oxygen content in arterial blood must take into account the oxygen concentration in all contributing blood sources, and the quantity of blood represented by those sources.

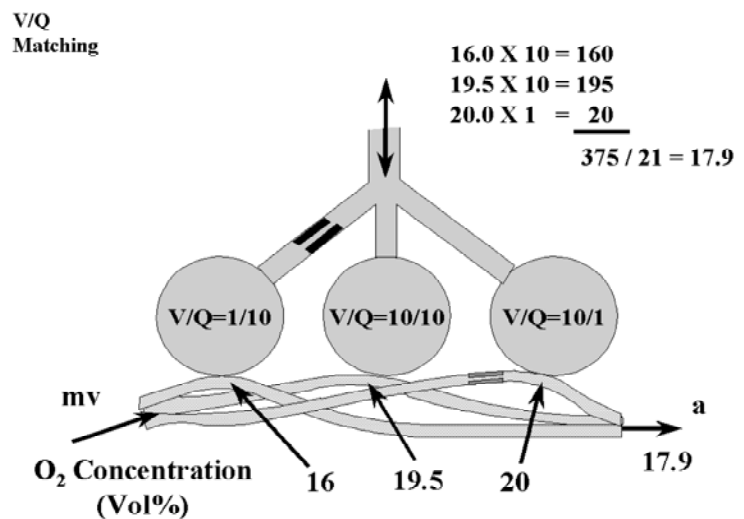


Figure 9

How well ventilation and perfusion are matched to each other can be an extremely relevant clinical assessment. As noted above, the arterial oxygen content will represent an admixture of blood from different sections of the lung with various V/Q ratios. If one were dealing with uniform distribution of V and Q throughout the lung, and all of the pulmonary blood flow passed by gas exchange regions,  $PAO_2$  would equal  $PaO_2$ . However, because neither of these are true, There will be a discrepancy between  $PAO_2$  and  $PaO_2$ . The difference between these two values can be used as an index of the adequacy of ventilation and perfusion matching.

$PaO_2$  can be determined from an arterial blood sample. To determine average, or “ideal” alveolar  $PO_2$ , the following equation must be applied:

$$P_{A_{O_2}} = F_{I_{O_2}} (P_B - P_{H_2O}) - P_{A_{CO_2}} \left[ F_{I_{O_2}} + \frac{1 - F_{I_{O_2}}}{R} \right]$$

This equation is based on the assumptions that the relative amount of  $O_2$  used to  $CO_2$  produced (respiratory quotient) affects the amount of  $O_2$  and  $CO_2$  in the ideal alveolus at equilibrium, and that blood  $CO_2$  rapidly and completely equilibrates with alveolar  $CO_2$

(CO<sub>2</sub> is perfusion limited). The respiratory quotient for most Americans is 0.8, but decreases toward 0.7 with a higher fat diet, and up toward 1.0 with more carbohydrates. The 0.8 figure is usually very accurate. Because CO<sub>2</sub> equilibrates between blood and the alveolus, PaCO<sub>2</sub> can usually be substituted for PACO<sub>2</sub>.

Plugging appropriate numbers into the equation, a person breathing air in Chicago (BP=747) who has a PaCO<sub>2</sub> of 40 would have an ideal PAO<sub>2</sub> of ~100 mmHg. The same person has a PaO<sub>2</sub> of 95 mmHg. So, why the discrepancy? Two major factors contribute to this. The first is the shape of the oxyhemoglobin dissociation curve. Remember that at the apex of the lung, where PAO<sub>2</sub> is typically ~132mmHg, the extra O<sub>2</sub> content that the blood will hold (compared to O<sub>2</sub> content at ~100 mmHg) is very little. This blood is mixed with a larger amount of blood from the base of the lungs that perfuses alveoli with a lower average PO<sub>2</sub>. The result is that the final PO<sub>2</sub> of the blood is weighted toward the lower PO<sub>2</sub> value.

The second factor contributing to the PAO<sub>2</sub>-PaO<sub>2</sub> discrepancy is the degree of shunt flow through the lungs. Shunt flow is perfusion that is not matched to regions of effective ventilation. This can be anatomical or physiological, but both effectively lower the PO<sub>2</sub> of the arterial blood relative to “ideal” alveolar PO<sub>2</sub>.

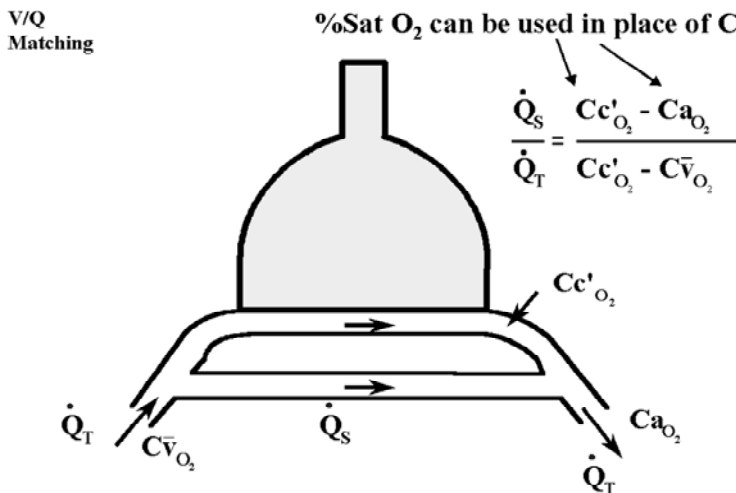


Figure 10

Pulmonary shunt is illustrated in figure 10. A percentage of the total flow ( $Q_T$ ) going through the lungs is shunted past effectively ventilated regions, and is considered shunt flow ( $Q_S$ ). The PO<sub>2</sub> of the mixed venous blood is unchanged in shunt flow, yet still combines with newly oxygenated blood to comprise the arterial oxygen content. The amount of shunt can be calculated from the equation shown in the top right corner of figure 2, where  $Q_T$  and  $Q_S$  are total and shunt flow, respectively, and  $C_aO_2$ ,  $C_vO_2$ , and

$C_c'O_2$  are oxygen contents of the arterial, mixed venous, and end-capillary blood (leaving a well ventilated alveolus), respectively. All of these parameters are easily obtained in the clinical setting, with the exception of  $C_c'O_2$ . This value must be derived from the oxyhemoglobin dissociation curve, and is estimated by calculating the oxygen content one would find in the “ideal” alveolus in a perfusion limited setting. Also recall that one can often substitute oxygen saturation (%) for oxygen content.

The effect of significant shunt flow on PaO<sub>2</sub> is readily apparent under conditions of breathing 100% O<sub>2</sub>. This is shown in figure 11. The end-capillary PO<sub>2</sub> of blood leaving

adequately ventilated regions is equal to the ideal alveolar  $PO_2$ , calculated from the equation given previously. However, the  $O_2$  content of this blood is not much higher (~22 Vol%) than it would be at a  $PO_2$  of 100 mmHg (20.5 Vol%). Thus, mixing with shunt blood from any source dramatically lowers the  $PaO_2$  as a result of the shunted blood's relatively deoxygenated hemoglobin combining with the "excess" dissolved  $O_2$  in the high  $PO_2$  blood. The amount of shunt in a normal individual is usually 5% or less, and as such, even breathing 100% oxygen, one can expect a  $PAO_2$ - $PaO_2$  difference of up to 100 mmHg. Larger values are indicative of significant shunting of blood, or severe ventilation/perfusion mismatching.

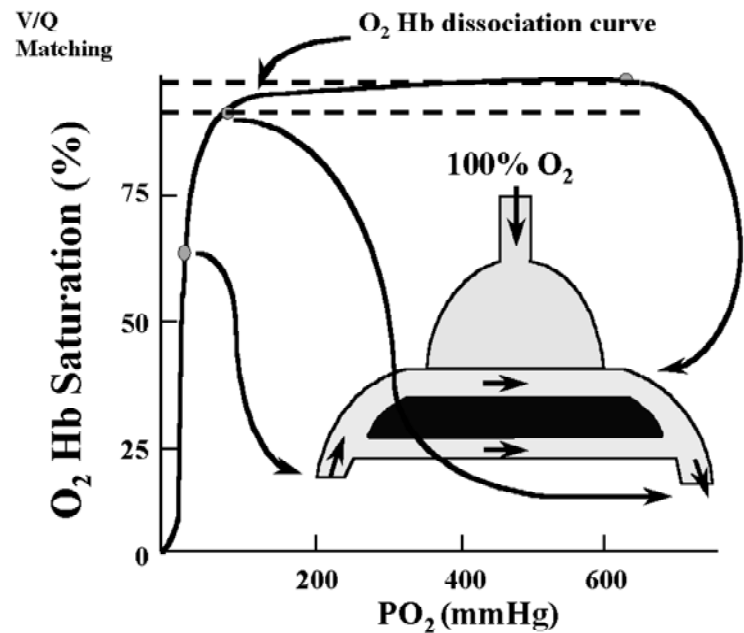


Figure 11

In addition to the shunt equation given above, one can estimate shunt fraction by assuming 1% of the CO for every 20 mmHg  $PAO_2$ - $PaO_2$  difference.