ALVEOLAR - BLOOD GAS EXCHANGE[1]

Summary: These notes examine the general means by which ventilation is regulated in terrestrial mammals. It then moves on to a discussion of what happens when someone over or under ventilates. A large number of problems are presented; please attempt these before class, as they will be very important to the discussion of this material.
Note: the equations that you should know are #s 1, 2,3,5,14 and 25. You should definitely understand the relationships between gas consumption or production, metabolic rate, ventilation, and *R* but you need not memorize those equations. You must understand the last graph in these notes.

I. REGULATION OF RESPIRATION:

II. VENTILATION AND GAS EXCHANGE:

A. Introduction:

A. <u>Introduction</u>: We have just seen that relatively small disturbances in CO_2 can have large effects on minute volume, $\dot{V}_E$. In this section, we will take a more detailed look at gas exchange between the lung and environment and we will see what happens when things are not exactly matched. We will start with a consideration of where the air we breathe actually goes and whether or not it is even involved with gas exchange.

B. Alveolar Ventilation and Dead Space

1. We have previously shown that the lung normally always contains a certain amount of air. At the end of a normal tidal expiration, the amount of the air remaining is called the **<u>FRC and it is normally about 3 to 3.5 liters for a 70 kg person</u>**.

a. The act of **<u>ventilation merely removes a portion of the FRC and adds a portion of fresh air</u>**. Since a **typical resting V_E** (also called V_t or TV) is **about 0.5 L**, then a **tidal inspiration adds about 10% to the volume of air in the lung**[2] (FRC + V_E) and the **expiration removes a similar amount**[3]. During the inspiration and expiration, the "old" air is mixed with the new.

1\. Not all of the air that is breathed enters the **<u>ALVEOLAR</u> <u>SPACE</u>** where gas exchange is occurring. As air is inspired in a normal breath, all air must first travel through a **<u>DEAD</u> <u>SPACE</u>** that is made up of <u>air conducting tubes including the nose, sinuses mouth and pharynx</u>. Eventually (in a normal breath) most of the inspired air will travel to the alveolar space but some (the last part of the tidal volume) must remain in the dead space and will not undergo exchange. Thus:

$$1.\ V_E = V_D + V_A$$

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[2] If you are a quick calculator and critical thinker you will have realized that 0.5/3.5 is not 10%! The reason is that not all of the air goes to the lungs -- as we are about to see, only about 0.35 of such a

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[3] Another little correction here -- as you will hopefully realize by the end of the packet, the amount of air you exhale doesn't necessarily, even when averaged over a few breaths, equal the amount you inspired! In fact , expired is usually a bit less than inspired!! Why would that be? You should know from earlier in the course.

where V_E is the tidal volume, V_D is the dead space volume, and V_A is the amount of air that actually enters the alveolar space.

? Where does the last bit of air to leave the lungs end up? What is the oxygen percentage (dry gas) of the first bit of expired air? CO_2 percentage?
Where does the first air to enter the alveoli come from? Is it fresh air? Explain.

2. A similar version of this equation deals with **INSPIRED, DEAD, AND ALVEOLAR MINUTE VOLUMES**:

2. $f\{V_E = V_D + V_A\}$

3.

where **f** is the breathing rate, $\dot{V}_E$ is the inspiratory (or expiratory) minute volume, $\dot{V}_D$ is the dead space minute volume (also called the dead space minute ventilation) and $\dot{V}_A$ is the alveolar minute volume (also called the **ALVEOLAR VENTILATION**).

3. Obviously, the dead space is fairly constant and will not change much with different sized inhalations.

? Why did I say that V_D would not change <u>very</u> <u>much</u>? Can V_D change? How?

However, the amount of <u>alveolar ventilation will change greatly depending on how deeply the subject breathes</u>. If the breathing rate remains constant but V_E increases then $\dot{V}_E$ increases and $\dot{V}_A$ will increase but $\dot{V}_D$ will remain roughly constant.

! Very different happens if the tidal volume remains constant and the breathing rate increases or if the alveolar ventilation is kept constant and ventilation rate changes. What should happen to dead space minute ventilation in each of these two cases? How about alveolar ventilatory volume?

b. IS IT POSSIBLE TO CALCULATE $\dot{V}_A$ and $\dot{V}_D$?

1. Obviously, we can measure $\dot{V}_E$. However, finding either $\dot{V}_A$ or $\dot{V}_D$ is tricky.

2. <u>**CALCULATION OF $\dot{V}_A$**</u>**:**

(i) The <u>total amount of CO_2 that is expired must equal the sum of the CO_2 in the volumes of air from the dead space and the alveolar space</u>; i.e.,

(ii) the volumes of these spaces times the concentration of CO_2 in each of these compartments.

Therefore, we know that the **total EXPIRED CO_2** must be given by the following equation:

4. $$\dot{V}_{\mathrm{CO_2}} = \dot{V}_E * F_{ECO2} = \dot{V}_D * F_{DCO2} + \dot{V}_A * F_{ACO2}$$

where F_{ECO2} is the fraction of expired air that is CO_2, F_{DCO2} is the fraction of the dead space air that is CO_2 and F_{ACO2} is the alveolar CO_2 fraction.

(iii) Next, we must realize that F_{DCO2} is essentially 0 since the air residing in the dead space at the end of a tidal inspiration is filled with atmospheric air. Thus, since we know that **F_{ICO2} is 0.0003**, a very small number, **we can <u>assume</u> that normally F_{DCO2} is 0**. (There are cases where F_{ICO2} and F_{DCO2} could be non-zero (important), but they are very unusual.) Equation 4 becomes:

5. $$\dot{V}_{\mathrm{CO_2}} = \dot{V}_A * F_{ACO2}$$

We can re-arrange this equation to find the alveolar minute ventilation:

6. $$\dot{V}_{\mathrm{A}} = \frac{\dot{V}_{\mathrm{CO_2}}}{F_{ACO2}}$$

Next, we can find **dead space minute ventilation** by the following:

7. $$\dot{V}_D = \dot{V}_E - \dot{V}_A$$

? How would you find the dead space volume?

3. We can **<u>find DEAD SPACE</u> in another, more direct way**. Starting again with eq. #7, if we now substitute the alveolar ventilation equation (#6) for $\dot{V}_A$ in eq. 7, we get:

8. $$\dot{V}_D = \dot{V}_E - \frac{\dot{V}_{\mathrm{CO_2}}}{F_{ACO2}}$$

Now since $\dot{V}_{\mathrm{CO_2}} = \dot{V}_E * F_{ECO2}$

9. $$\dot{V}_D = \dot{V}_E - \frac{(\dot{V}_E * F_{\mathrm{ECO_2}})}{F_{\mathrm{ACO_2}}}$$

by subtracting the terms on the right:

10. $$\dot{V}_D = \frac{(\dot{V}_E * F_{ACO_2})}{F_{ACO_2}} - \frac{(\dot{V}_E * F_{ECO_2})}{F_{ACO_2}}$$

re-arranging:

11. $$\dot{V}_D = \dot{V}_E \frac{(F_{ACO_2} - F_{ECO_2})}{F_{ACO_2}}$$

and the dead space can then be found by:

12. $$V_D = \frac{\dot{V}_D}{f}$$

There is a rule of thumb that is often used to <u>approximate</u> what the dead space volume is for a healthy subject: the subject's lean weight in pounds is <u>roughly</u> equal to their dead space volume in ml. REMEMBER THAT <u>THIS SHOULD NEVER TAKE THE PLACE OF A CALCULATION IF THE DATA FOR SUCH A CALCULATION ARE AVAILABLE</u>. (i.e., don't ever use this on a test or where you can calculate dead space.

--- A Couple O'Tough Problems:

? What is the effect of breathing through a long snorkel on dead space? Assume that a subject breathes 12 breaths per minute whether or not they use the snorkel. Also assume that they both inspire and expire through the snorkel.
Assume that their dead space is 150 ml and that they normally need to exchange 350 ml with the alveolar space per breath (in other words, their tidal volume is 500 ml). The snorkel has dimensions such that it has a volume of 5 ml per cm in length.
Finally assume that the person's vital capacity is 6 liters.
What is the longest snorkel they can breathe through at 12 b/m? What will their effective dead space be at this length?

ANS: They must be able to totally exchange at least 350 ml per breath. Since their maximum breath is 6000 ml, then if they breathe through a snorkel with a volume of 5500 ml their total dead space will equal 5500 + 150 = 5650 ml. Thus, the snorkel could be 5500/5 = 1100 cm! (about 35 feet!!).
Don't fall into the trap that they exchange 350 - 150 = 200 ml since the dead space is filled with alveolar air after an expiration and the first part of an inspiration must therefore be alveolar air from the last breath. This is true, but the total volume of air that actually enters the alveoli is 500 ml just as the total amount of air that enters the dead space is also 500 ml. Its just that only 350 ml

of the breath represents "fresh air" (the other 150 ml is "stale air" from the dead space). Likewise for the dead space.

Do you think that a person could actually breathe through a 35-foot long snorkel if they went under water to a depth of just under 35 feet? At this depth, the ambient pressure is two atmospheres (plus a little). Go back to the R-4 notes and find the maximum pressure (force) that the inspiratory muscles can generate.

C. About the Size of the Function Reserve Capacity (FRC)

1. Recall that the FRC is about 40% of the total lung capacity.
2. You should now be able to see that each breath at rest normally exchanges about 10% of this volume -- in exercise the percentage exchanged is much greater (it may even be greater than 100% of the FRC).

? Why should the FRC be so large? Why does it make up about 40% of the total lung capacity? Give several reasons beyond biomechanical ones. Put another way, what are the proximate and ultimate causes of the size of the FRC?
How could alveolar ventilation be larger than the FRC?
? If F_{AO2} (oxygen fraction of alveolar air) = 0.155 at then end of a tidal expiration, <u>what does it equal at the end of a tidal inspiration</u> for a person with $V_E = 0.5$ L, $V_D = 0.15$ L, and FRC = 3.5 L?
<u>Ans.</u>: 0.542 L O_2 in FRC, 0.073 ml O_2 per V_A = 0.615 L O_2 in 3.85L volume (=FRC + V_A) at top of inspiration so 0.615L O_2/3.85 L air = 0.160 = F_{AO2} at top of inspiration.

? Most people breath about 12 times a minute at rest. Therefore, a typical ventilatory cycle is 5 s. Make a plot of F_{AO2} for a typical ventilation cycle.

? Make a similar plot for this person's arterial blood -- that is, the blood leaving their lungs and heading into the systemic circulation except **express the oxygen as P_{aO2}**. Assume that P_{H2O} in the lung is 47 torr and P_b = 760 torr. Assume that the **P_{aO2} is the same as the F_{AO2}** -- i.e., alveolar gas and blood leaving the lungs are in equilibrium. (Thus, for this calculation, you do not need Fick's Law (step 1) to figure out the P_{aO2} -- if you only consider the finished product (when then, would Fick's Law be useful?))

? Make plots of the amount of oxygen dissolved and bound in arterial blood for the conditions in the last question. Assume <u>solubility of oxygen in arterial blood is 0.03 mlO2/(dl blood * torr)</u>, <u>pH is 7.4</u>, and <u>use the O_2 dissociation curves at the end of packet R-7</u>. **Do the fluctuations in P_{aO2} result in changes in %S_{aO2}?**

D. Respiratory Steady and Non-Steady States.

1. Introduction: Now that we know a little about where the air goes when we take a breath, let's see what the effects of different sized breaths or breathing rates (different minute volumes) will be on the amounts of O_2 and CO_2 in the alveolar space if we assume that tissue demand for O_2/CO_2 elimination is constant and circulation is constant.

2. Hyper- and Hypo-ventilation:. Increasing the expiratory minute volume ($\dot{V}_E$) over the amount required to maintain steady-state conditions of O_2 and CO_2 exchange between each of the respiratory conductances is termed **HYPERVENTILATION**. Decreases in minute volume below what is required to maintain steady-state for the conductances is called **HYPOVENTILATION**.

3. We will consider hyperventilation in detail: hypoventilation will simply be the opposite. Hyperventilation eventually will have the following effects (some of these effects are more prompt than others):

a. increased P_{AO2} , P_{aO2} , P_{vO2}, and P_{tO2}
b. decreased P_{ACO2}, P_{aCO2}, P_{vCO2}, and P_{tCO2}

We will now look specifically at the effects of hyper- (or hypo-) ventilation on F_{AO2} and F_{ACO2}.

4. The **derivation of an equation that describes the effects of ventilation on F_{ACO2}:**

We know that **essentially all CO_2 that is exhaled comes from the alveolar space** of the lungs (see eq. #4). **Thus:**

13. $$\dot{V}_{\mathrm{CO_2}} = \dot{V}_A * F_{ACO2}$$

We can re-write this eq. for P_{ACO2}, the partial pressure of alveolar CO_2 by using the relationship :

14. $$F_{ACO2} = \frac{P_{\mathrm{ACO2}}}{(P_b - P_{\mathrm{H2O}})}$$

(Note: we prefer to use partial pressures since gases move down partial pressure gradients, not concentration (fraction) gradients).

15. $$\dot{V}_{\mathrm{CO_2}} = \dot{V}_A * \frac{P_{\mathrm{ACO2}}}{(P_b - P_{\mathrm{H2O}})}$$

We can remove the P_b - P_{H2O} expression by putting it into a constant that will also take into account changes in partial pressures due to various RQ values (obviously if O_2 and CO_2 are not being exchanged evenly, the partial pressure of a gas will shift according to the actual exchange rate). Thus, we will combine the barometric and vapor pressure and the effects of different RQs into one constant, C:

16. $$\dot{V}_{\mathrm{CO_2}} = c * \dot{V}_A * P_{ACO2}$$

or, solved for P_{ACO2}:

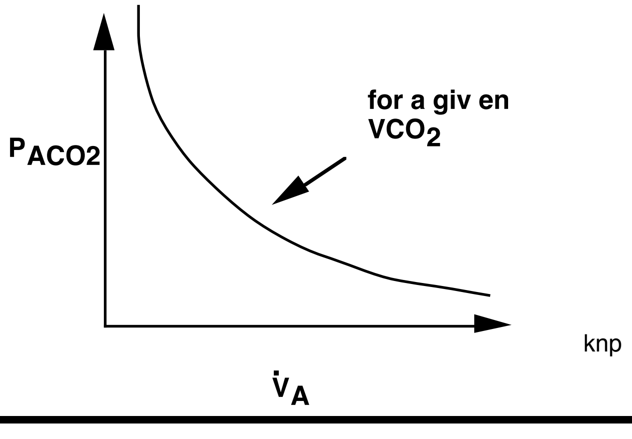
17. $$P_{ACO2} = \frac{\dot{V}_{CO_2}}{c * \dot{V}_A}$$

Thus, we can see that P_{ACO2} is:

i) directly related to the rate of CO_2 production
ii) inversely related to the alveolar ventilation

These should be intuitively obvious relationships: obviously if $\dot{V}_{CO_2}$ increases and nothing else changes, then P_{ACO2} will also increase as more CO_2 diffuses into the alveoli. Likewise, if $\dot{V}_{CO_2}$ remains constant at the tissue level but the alveolar ventilation is increased (hyperventilation), then since the rate at which CO_2 is being expelled from the lung by ventilation is greater than the rate it is being delivered to the lung by the circulation (and ultimately, greater than the rate that it is produced), the P_{ACO2} must decrease.

! Note that the behavior involved in a change in $\dot{V}_A$ that is not related to a change in $\dot{V}_{CO_2}$ is an example of non-steady state as discussed at the start of class.
Here is a graph of the results of eq. 17:



4. We can write a similar equation for O_2; here keep in mind that the alveoli are the site where O_2 is removed and therefore the difference in inspired and expired alveolar gas O_2 is what is needed (since neither is normally 0; with CO_2 F_{ICO2} is taken as 0).

18. $$\dot{V}_{O_2} \cong \dot{V}_A (F_{IO_2} - F_{AO_2})$$

once again, if we make corrections for various non-equal O_2-CO_2 exchange ratios (such as when RQ does not = 1) and also change from concentration to P_{O2}, we can define a constant C that is identical to that used in eqs. 16 and 17:

19. $\dot{V}_{O_2} = c * \dot{V}_A * (P_{IO2} - P_{AO2})$

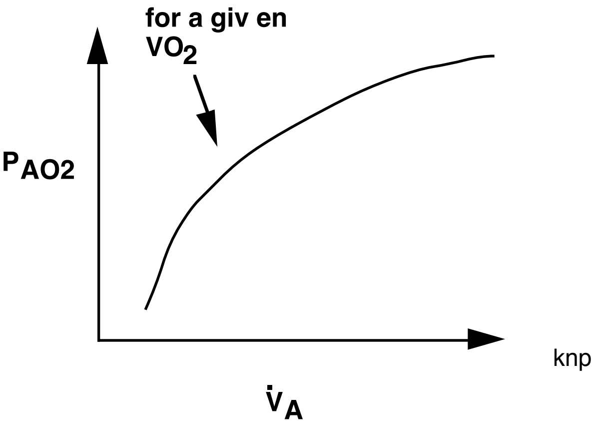
20. $P_{AO2} = P_{IO2} - \dfrac{\dot{V}_{O_2}}{c * \dot{V}_A}$

that is; P_{AO2} varies:

i) directly with P_{IO2}, $\dot{V}_A$ and C

ii) inversely with $\dot{V}_{O_2}$

These relationships should be self-evident. Here is a graph similar to that shown for P_{ACO2}:



5. Now we can inter-relate these equations into one generalized equation. We do this by solving equations 17 and 20 for C and then setting them equal to each other and solving for either P_{ACO2} or P_{AO2}:

? Why is *c* the same constant in each equation?
Ans.: *c* takes into account (P_b - P_{H2O}) and differences in inspiratory compared to expiratory volumes that will be the same for both CO_2 and O_2.

21. $c = \dfrac{\dot{V}_{CO_2}}{P_{ACO_2} * \dot{V}_A}$ and $c = \dfrac{\dot{V}_{O_2}}{\dot{V}_A * (P_{IO_2} - P_{AO_2})}$

therefore

22. $$\frac{\dot{V}_{CO_2}}{P_{ACO_2} * \dot{V}_A} = \frac{\dot{V}_{O_2}}{\dot{V}_A * (P_{IO_2} - P_{AO_2})}$$

canceling the alveolar ventilation:

23. $$\frac{\dot{V}_{CO_2}}{P_{ACO_2}} = \frac{\dot{V}_{O_2}}{(P_{IO_2} - P_{AO_2})}$$

re-arranging:

24. $$(P_{IO_2} - P_{AO_2}) = \frac{\dot{V}_{O_2} * P_{ACO_2}}{\dot{V}_{CO_2}}$$

At this point we need to define one new and important parameter that is known as the:

25. RESPIRATORY EXCHANGE RATIO, $R = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}}$

NOTICE that ***R* appears to be defined exactly as is *RQ*.** There are two very **important differences**, however.

- i) ***R* is defined at the respiratory exchange site while *RQ* is properly only defined at the tissue level.**
- ii) ***R* may vary greatly on a moment-to-moment basis: anytime non-steady state conditions exist, *R* will not = *RQ*.**
- iii) **Only during steady-state is *R* a good indicator of *RQ*.**

We can now substitute $\frac{1}{R}$ for $\frac{\dot{V}_{O_2}}{\dot{V}_{CO_2}}$ in eq. 24 and re-arrange:

26. $$P_{AO2} = P_{IO2} - \frac{P_{ACO_2}}{R}$$

Thus, notice that P_{AO2} is:

- i) directly proportional to P_{IO2}
- ii) inversely proportional to P_{ACO2}
- iii) directly proportional to ***R* for a constant P_{ACO2}**.

The most useful way to visualize a whole series of changes that occur in lung gases with various different types of gas exchange is to use a **CO_2-O_2 diagram:**

1) **CO_2 is plotted on the ordinate, O_2 on the abscissa**
2) **A point that describes the P_{IO2} and P_{ICO2} is marked on the graph as P_I (for inspired air).**

3) A point that **describes the steady-state P_{ACO2} and P_{AO2} is marked P_A** for the **alveolar gas point.**

4) The **absolute value of the slope of the line** connecting the two **represents the *R*** for the situation with a given P_I and P_A. Plot several P_A points and justify to yourself why the slopes should be different.

5) For any one *R* line, any point on the line represents a possible combination of respiratory gases that will give an *R* equal to that on the line.

6) The P_{EO2} and P_{ECO2} will also fall on the *R* line (P_E) and will be positioned according to the size of the dead space. The larger the V_D , the closer P_E will fall to P_I.

? WHY?
Derive and equation for *R* in terms of inspired and expired gas fractions. Do the same for alveolar gas fractions.
Using the concepts of dead space that were gone over earlier in this class, explain the positioning of P_E.

? Will different-sized breaths have any significant effects on the gas concentrations in the alveolar space? To answer this try the following calculation -- it asks about the relative amounts of CO_2 and O_2 in the lungs and tissues:

F_{AO2} =0.16
F_{ACO2}=0.06
FRC = 3L
average percent saturation of Hb in blood = 70%
O_2 capacity of blood = 20 ml O_2/dl
average CO_2 content in all forms -- ~ 52 ml CO_2 /dl blood
blood volume = 6 L
tissue O_2 content --- negligible
tissue CO_2 content -- similar to blood
total non blood tissue water = 45L

Questions

1. Why should tissue and blood CO_2 contents be similar?

2. Calculate the size of the stores of oxygen in the lungs and the blood. Ignore dissolved oxygen.
ANS.: lungs 0.48 L, blood = 0.84L total body store =1.44 L O_2

2b. Why should you ignore the dissolved oxygen? -- - at least two reasons.

3. Calculate the size of the stores of CO_2 in the lungs and blood.
ANS.: lungs 0.18 L, blood = 3.1 = 3.28 L CO_2
non-blood fluid = 23.4 L CO_2
total body stores (Lungs+Blood+non-blood) = 26.68 L CO_2

4. Holding one's breath -- will it have a greater affect on the alveolar and arterial partial pressures of which gas -- O_2 or CO_2 will they change the same? Why?

Will both gases be affected to the same extent by changing ventilation pattern? Think back over the last three classes in making your answer. We are about to see what happens.

5. Problem: Keep in mind what you have just learned about the sizes of gas stores in the body. Now, assume that someone has an **RQ of 1.0**.

a. If **P_{IO2} = 150 torr** and **P_{AO2} = 110 torr**, **what is P_{ACO2}?**

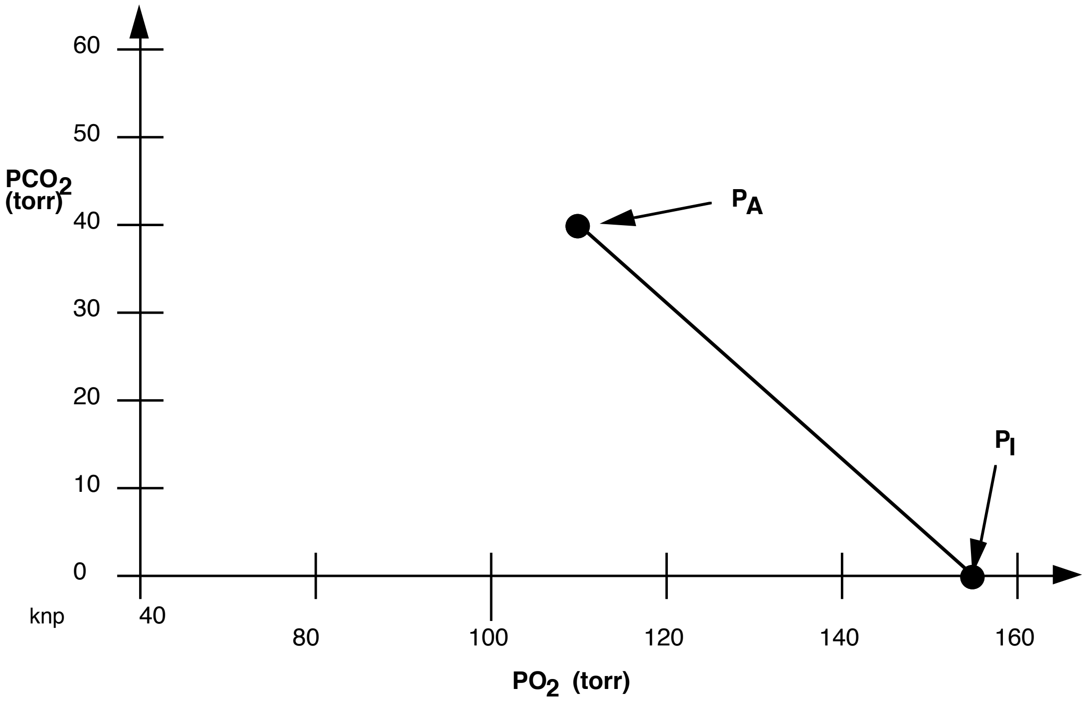
Graph this point and label it P_{alv} on the CO_2- O_2 diagram on the next page.

b. Assume that the person begins to hyperventilate; that is, their ventilatory conductance exceeds their other conductances . **Graph what will happen to their alveolar O_2 and CO_2.**

HINT: THE TWO WILL NOT CHANGE AT THE SAME RATE. KEEP IN MIND THAT THERE ARE RELATIVELY FEW O_2 STORES IN THE BODY AND THAT THERE ARE LARGE CO_2 STORES (see problems above).

c. Finally, will the person ever come to a new steady state? If so, **where will it be located?** How will the person ever get back to P_A? Describe what they would need to do and how their alveolar gases would change.

CO2 - O2 Diagram of Respiratory Exchange



Final note: this diagram is very useful and far more can be done with it that we have done. For instance, a very complete description of gas exchange can be made if plots for blood gas and ventilation/perfusion ratios are added. Those who take graduate level work in respiratory physiology will learn about these; they are covered in any good pulmonary or medical physiology text.