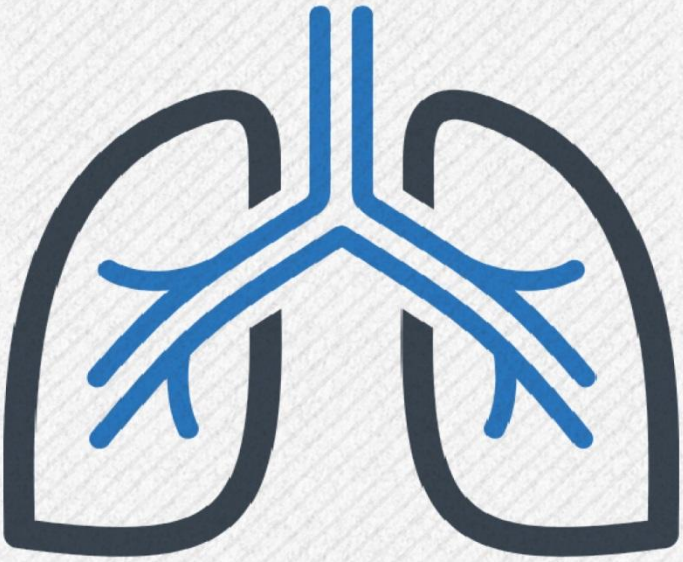

Respiratory system physiology

sheet handout slides

Number	8
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Last lecture we talked about the blood flow to the lungs. We will now continue then start with a new concept.

Blood Flow to the lungs is the cardiac output. Flow is the product of 2 things: the driving force and the resistance which opposes it. The driving force is **the pressure difference** between the pulmonary artery and the left atrium (the pulmonary circulation). The resistance is the **pulmonary vascular resistance**.

Remember:
This is the same concept as in the CVS where:

$$CO = \frac{\text{Aortic pressure} - \text{ pressure in the right atrium(RAP)}}{\text{TPR}}$$

And since we consider the RAP=0, then:

$$CO = \frac{\text{Aortic pressure}}{\text{TPR}} \rightarrow So, aortic\ pressure = CO * TPR$$

When someone is hypertensive, we lower his/her pressure either by lowering CO (which equals HR*SV) or by lowering TPR (by increasing the radius of arteries because other factors affecting resistance are fixed and cannot be manipulated).

So in the pulmonary circulation:

Pulmonary pressure = CO * pulmonary vascular resistance

At rest: CO= 5L/min, pulmonary pressure= 14 or 15mmHg
(CO in the right heart is the same as in the left heart)

During severe exercise the CO increases from 5 to 25L/min (5 times more). However, the pulmonary arterial pressure hardly reaches 30 (2 times more).

The heart doesn't like high pressure (afterload) because it is an extra load on the right ventricle; the lower the better (it is a bad guy in the "eyes" of the heart). But at the same time it is the driving force for blood flow. If pressure is low, blood can't reach capillaries (It is a good guy in the "eyes" of the capillaries). If pressure is too high, the right ventricle suffers. If it is too low, pulmonary capillaries suffer. We don't want either to happen.

So when the CO increased 5x, the pressure *only* increased by 2x. *How is that??*

→ Because <u>resistance in the vascular bed has decreased</u> by 2 ways:

1. First, by the opening of new capillaries. Normally, only one third of the capillaries in the lungs are open. So you recruit more capillaries during exercise so that the pressure doesn't rise too much. This is called ***capillary recruitment***. When you recruit more capillaries, blood has more routes to go to and the cross-sectional area increases. The more the cross-sectional area the less the resistance.

2. By distending the existing capillaries. It is not like vasodilation. Distension is passive.

Remember:

$$R \propto \frac{1}{r^4} \; or \; \frac{1}{A^2}$$

R: resistance

r: radius

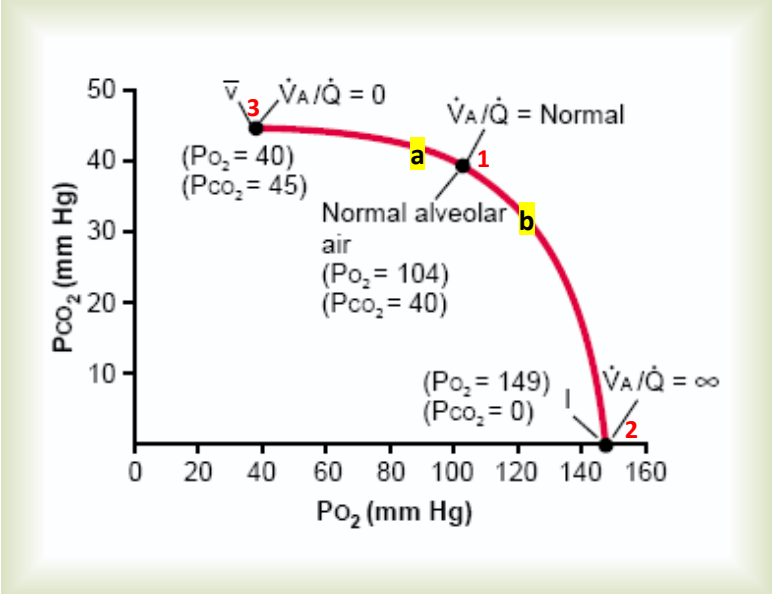
A: area

Recall from last lecture:

The ventilation perfusion ratio ($^{V}/_{Q}$) is different in different regions:

- In the apex: $^{V}/_{Q} > 1$
- In the base: $^{V}/_{Q} < 1$

P_{O_2}-P_{CO_2} diagram:



Point1 → **Normally**, P_{O_2} in the alveoli is ≈100mmHg and P_{CO_2} is 40 mmHg

*Where would the base and the apex of the lung be on this diagram (above or below normal)?

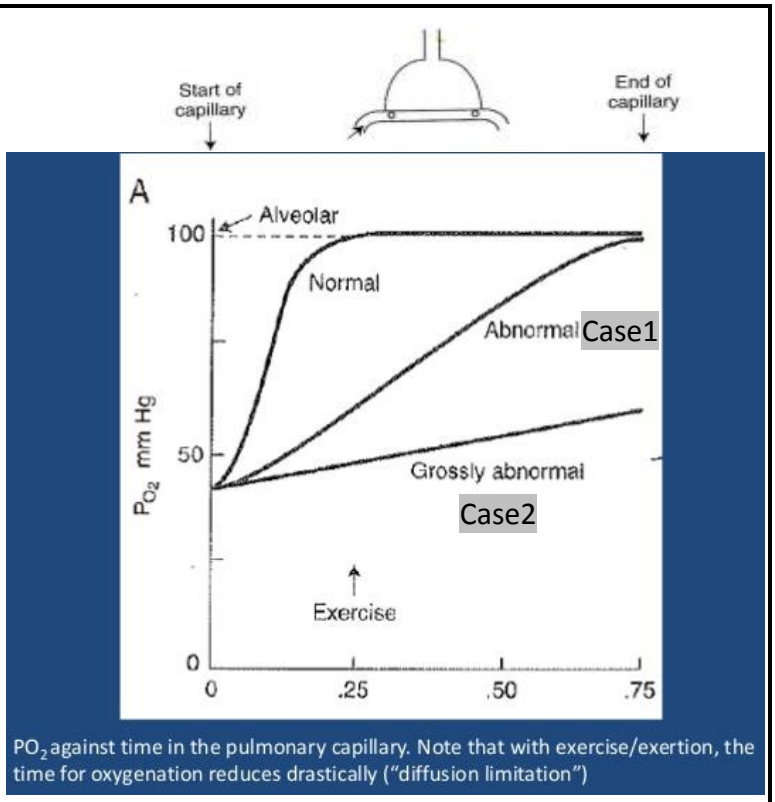
- Base is above point1 because P_{O_2} =90 mmHg and P_{CO_2} > 40mmHg (a in the diagram)

- Apex is below point1. (b)

Point2 → When $^{V}/_{Q} = \infty$ (there is **no perfusion**), alveolar P_{O_2} will be equal to the atmospheric pressures (150 mmHg). Here, there is **wasted volume** (air enters but there is no blood!).

Point3 → P_{CO_2} = 45 and P_{O_2} = 40 mmHg means that $^{V}/_{Q} = 0$. There is **no ventilation**. That's why alveolar P_{O_2} equals venous P_{O_2} (40).→ **wasted perfusion**

PO_2 versus time:



PO_2 against time in the pulmonary capillary. Note that with exercise/exertion, the time for oxygenation reduces drastically ("diffusion limitation")

Normally→ In the start of the capillary, PO_2 is 40 mmHg. It then becomes 100mmHg and stays 100 till the end of the capillary.

Total area of the respiratory membrane = **50-100 m^2**

It is huge because of the large number of alveoli. If we have only one sphere, its surface area would be much smaller.

Case1: If one fourth of the area of the respiratory membrane is available (75% has been destroyed or less), oxygen is still not diffusion limited.

*How can we know if oxygen is diffusion limited?

- If we reached the end of the capillary and there is a difference between capillary and alveolar PO_2 (i.e. PO_2 in capillary is less than 100), then oxygen is diffusion limited.

In this case, PO_2 still reaches 100 at the end of the capillary, so oxygen in case1 is not diffusion limited.

Case2: In this case, PO_2 didn't reach 100 (it equals 80mmHg at the end). This is because more than 75% of the respiratory membrane has been destroyed.

Here we considered the cardiac cycle =0.8 seconds (normal). It equals the time that blood takes to cross the capillary.

But when heart rate increases, the duration of the cardiac cycle decreases as follows:

	Heart rate	Systolic duration	Diastolic duration	cardiac cycle duration
Normal	75	0.3	0.5	0.8
-1-	150	0.2	0.2	0.4
-2-	300	≈0.1	≈0.1	0.2

When heart rate increases, the duration of the cardiac cycle decreases but the diastolic duration is affected more than systolic (in -1- diastole decreased by 0.3 while systole decreased by 0.1!). I.e. Most of the shortening is in the expense of diastole. This is very dangerous because coronary blood flow occurs mainly during diastole.

Now we go back to the previous diagram: How does this affect PO_2 in pulmonary capillaries?

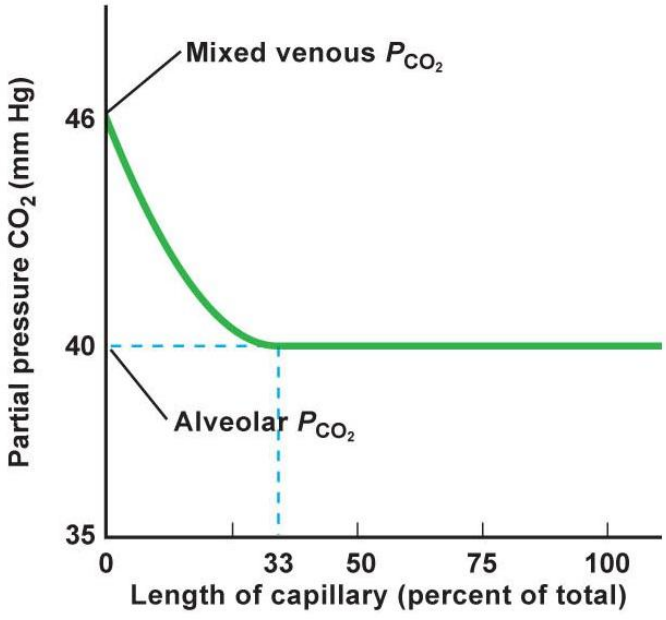
The effect of increased HR during exercise on PO_2 in pulmonary capillaries:

-1- When the HR =150 and the duration of the cardiac cycle is 0.4s, we still equilibrate (we reach 100mmHg). → the diagram will look like that in case1

-2- However, when cardiac cycle = 0.2s, there is a problem! We don't reach 100mmHg → the diagram will look like that in case2

The function of the heart is to eject blood. In order to eject, you need to fill and in order to fill you need time. When HR increases, time for diastole decreases (time for filling), so ejection is decreased. But things don't stop here; respiration is also affected. When the duration of the cardiac cycle is decreased, time is not enough for exchange so PO_2 in pulmonary capillaries doesn't reach 100mmHg.

PCO_2 versus time: The PCO_2 diagram looks very much the same but it is inverted.



Diffusion Capacity

We breathe to bring oxygen in and CO_2 out. We consume **250mL** of O_2 each minute.

How to calculate O_2 consumption/min:

1. If you know CO:

- CO = 5 L/min = **50 dL/min**
- Every dL of blood contains 20mL of O_2 but we only use **5mL/dL blood**
- So, O_2 consumption = 5 mL/dL blood * 50 dL/min = **250 mL/min**

If you know the CO you can calculate O_2 consumption and if you know O_2 consumption you can calculate CO.

2. If you don't know CO or want to calculate it:

To find the O_2 consumption you let the patient breathe through a bag with a known amount of oxygen. After 10min, you see how much O_2 was consumed. To find the O_2 consumption in one minute you divide the result by 10. Now, since you know the O_2 consumption you can calculate the CO.
Note: We took the equation in the CVS and it is in Dr.Yanal's slides.

*How much CO_2 is produced/min?
If we only consume sugar (glucose = $C_6H_{12}O_6$), CO_2 production will equal O_2 consumption according to the following equation:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$$

But in real life we don't only eat sugar; we also eat lipids and proteins. Lipids and proteins are not totally metabolized. So, the ***respiratory exchange ratio (respiratory quotient)*** is less than 1.

$$\textbf{\textit{Respiratory exchange ratio}} = \frac{\textbf{\textit{CO}}^{\textbf{2}}\ \textbf{\textit{production}}}{\textbf{\textit{O}}^{\textbf{2}}\ \textbf{\textit{consumption}}}$$

Respiratory exchange ratio for different foods:

- ✓ Carbohydrate only =1
- ✓ Protein only= 0.8
- ✓ Lipids only =0.7
- ✓ Mixture of food around 0.8

So normally we produce **200mL of CO_2/min** → respiratory exchange ratio = $\frac{200}{250} = 0.8$

The area of the respiratory membrane = **50-100 m^2**.

***How much is the *capacity* of this membrane to pass O_2?**

Let's talk about 2 scenarios:

1. When someone wants to run a marathon for example, O_2 consumption increases to **5L/min** (20 times normal). Before he can run the marathon, his lungs must be able to provide this amount of O_2. How to know if this applies to him?

VO_2max is the maximal O_2 consumption during maximal exercise. O_2 consumption increases from 250mL at rest to 5L/min in marathon runners (20x).

2. People who are continuously exposed to dust or those who work in phosphate factories inhale a lot of foreign substances which make their respiratory membrane thick and diffusion decreases. If we wait until symptoms appear it's too late because symptoms don't appear until more than 75% of the diffusion through the respiratory membrane is lost, before that they stay in good shape. How can we monitor/screen those people? How can we detect changes in the respiratory membrane before the appearance of symptoms?

In both scenarios, we calculate the ***diffusion capacity*** of the lung for oxygen.

Diffusion capacity: how much oxygen can diffuse from the alveoli to the blood per min for a pressure difference of 1mmHg

According to Ohm's low: $flow = \frac{driving\ force}{resistance}$

When applying this low to oxygen:

$$oxygen\ consumption\ (VO2) = \frac{pressure\ difference}{resistance} = (alveolar\ O2\ pressure - O2\ pressure\ in\ the\ capillary) * K$$

Resistance is a measure of difficulty. K is the permeability (how easy is to flow) and it equals the reciprocal of resistance ($\boldsymbol{K = \frac{1}{R}}$). By rearranging the equation we get:

$K = \frac{VO2}{\Delta PO2}$; The unit of K is **mL/min/mmHg**

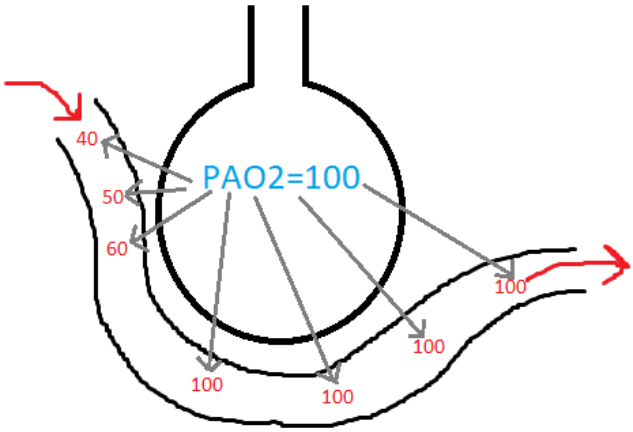
So, K is how many mL of oxygen can diffuse per min per mmHg pressure difference.

To be more specific, we call the permeability ***the diffusion capacity*** of the lung for oxygen (DLO_2).

$$\mathbf{DLO2} = \frac{\boldsymbol{VO2}}{\boldsymbol{\Delta PO2}}$$

We can easily calculate VO_2 (mentioned previously in this sheet). But what about ΔPO_2?

PO_2 in the alveoli is 100mmHg but in the capillary it differs. At first PO_2=40 so the difference between the alveolus and the capillary is 60. Then PO_2=50 so the difference is 50 and so on until we reach 100. The difference will be zero. I want the difference in pressure across the whole membrane not part of it and we don't know where exactly PO_2 in the capillary reached 100mmHg* so it is very difficult to calculate ΔPO_2 across the respiratory membrane.



So, we cannot measure diffusion capacity for the lung because we cannot measure ΔPO_2 across the respiratory membrane. It is almost impossible to measure diffusion capacity for O_2 or CO_2 directly; there must be another way.

Diffusion capacity for oxygen depends on **4 factors**:
[Gradient is not a factor because it is fixed (1mmHg)]

a. **Surface area** of the membrane (A)
b. **Thickness** (dx) of the membrane: the more the thickness, the less the diffusion.

→ a and b are properties of the membrane; they are the same for different gases (for the same lung).

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*We said previously that PO_2 in the capillary reaches 100mmHg at the first third, but some people say it could be in the first fourth for example. Also, when I want to test a patient I don't know whether his diffusion is normal or not, so we cannot predict where PO_2 reaches 100mmHg in his state.

c. **Solubility** of the gas (S): how much gas is attracted to water (we don't need to calculate it because it is already calculated by the laws of physics). If the gas is attracted to water (more soluble), you get more chance for diffusion (more diffusion). If solubility is low, we reach saturation easily so diffusion is less. Solubility of CO_2 in water is 20 times more than that of O_2. So we have more chance of CO_2 to diffuse.

d. **Molecular weight** of the gas (MW). The larger the gas, the harder its diffusion. The diffusion capacity is inversely proportional to the square root of MW. This means that the MW has an insignificant role in the diffusion capacity (the least important factor).

MW of:
O_2 = 32
CO_2 = 44
CO = 28

→ c and d are properties of the gas.

$$\boldsymbol{diffusion\ capacity} = \frac{\boldsymbol{A}}{\boldsymbol{dx}}\ \boldsymbol{X}\ \frac{\boldsymbol{S}}{\sqrt{\boldsymbol{MW}}}$$

The solubility and the MW are properties of the gas and we can put them as one unit called the ***diffusion coefficient*** (**d.c**) → $\mathbf{d.c} = \frac{\boldsymbol{S}}{\sqrt{\boldsymbol{MW}}}$

To simplify the equation we use the diffusion coefficient of O_2 as a standard so we say that d.c for:

- O_2 =1 (standard)
- CO_2 = 20
- CO = 0.8

Now we can calculate the diffusion capacity for the different gases (the membrane is common between different gases but they differ in the diffusion coefficient).

We usually measure the diffusion capacity of the lung for CO.
Why?

Remember:
Hb-CO = carboxy-Hb
Hb-CO_2 = carbamino-Hb
Hb-O_2 = Oxy-Hb

We give the patient a small concentration of CO. Then CO diffuses to the blood. Hemoglobin loves CO 250 times more than oxygen, so CO is immediately captured by hemoglobin forming carboxyhemoglobin. It is like CO in the blood stays zero (PCO capillary = 0) and CO in the alveoli equals the amount we give.
So: ΔPCO = PCO alveolar – PCO capillary = PCO alveolar
I don't need to worry about CO in blood because any amount of CO that goes to

blood is immediately captured. That's why we use CO.
Diffusion capacity of the lung for **CO = 17mL/min/mmHg**. And since:

$$\boldsymbol{diffusion\ capacity\ = \frac{A}{dx}\ X\ d.c}$$

We can calculate $\boldsymbol{\frac{A}{dx}}$:

$$\boldsymbol{\frac{A}{dx} = \frac{diffusion\ capacity}{d.c} = \frac{17}{0.8} = \ 21}$$

Now to calculate the diffusion capacity of the lung for CO_2:

$$\boldsymbol{diffusion\ capacity\ = \frac{A}{dx}\ X\ d.c = 21\ X\ 20\ \approx 400}$$

And for O2 it equals **21 mL/min/mmHg**.

By calculating the diffusion capacity, we can now know how much the lungs can provide me with oxygen. During exercise DLO2 increases 3 times (from 21 to 63) because all capillaries open and the entire lung becomes zone3.

GOOD LUCK

THE END