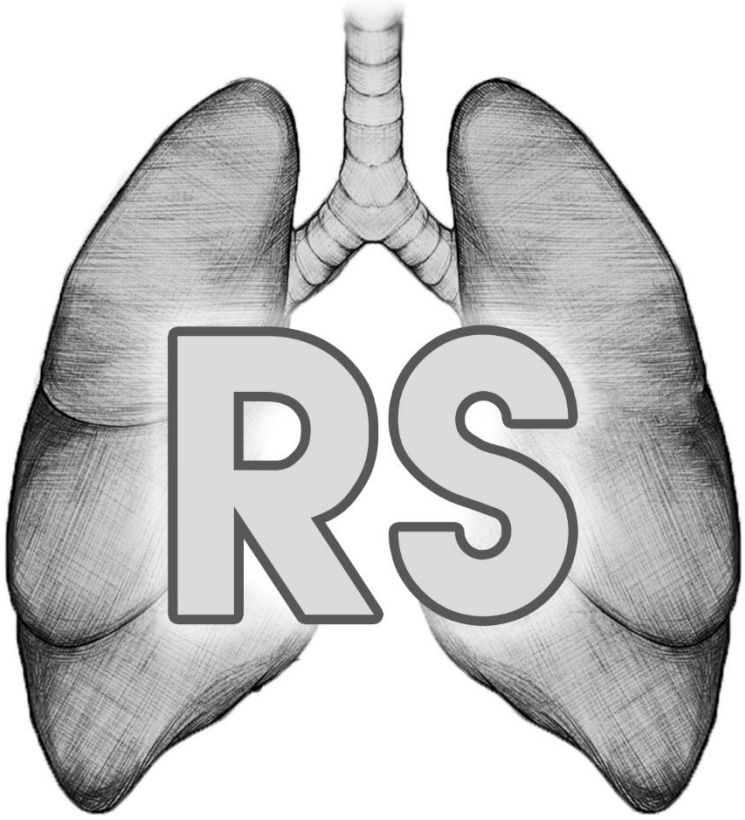


PHYSIOLOGY

☑ Sheet ○ Slide ○ Handout

Number

10

Subject

Control of breathing 2.0

Done By

Omar Saffar

Corrected by

Mohammad Qussay Al-Sabbagh

Doctor

Dr. Yanal Shafagoj

Date: 00/00/2016

Price:

بسم الله الرحمن الرحيم

- This sheet was written according to section 2 recording.
- The sources used making this sheet are (Guyton & Costanzo) .
- Try to enjoy

Introduction

- In the previous lecture we talked about how do we control our breathing, and we saw how Alveolar Ventilation affects blood gases.
- In this lecture we are going to see how blood gases affects our ventilation.

How do gases affect alveolar ventilation?

- Blood conc. Of 3 gases work together to control our breathing; PO_2, PCO_2 and H^+ "pH".
- The conc. Of these gases are sensed through deferent mechanisms and chemoreceptors, discussed in the previous lecture.
- We know that normal alveolar ventilation is 4.2L, an increase or decrease in this volume is our normal response to any change the blood gases.

Note: how do we know that minute alveolar ventilation is 4.2L?

Minute alveolar ventilation = (Vt-ADS) × RR = 500-150 ×12 = 4.2 L

So let's talk about these gases:

A. The first gas that regulates our respiration is **Oxygen**. Remember that oxygen regulation mechanism is half tailed; PO_2 doesn't affect ventilation if it goes above **100mmHg**, its decrease also doesn't affect our ventilation as long as it's above **60mmHg**, However, when PO_2 goes below 60 mmHg, strong activation of **Peripheral** chemoceptors will lead to increased ventilation, Best known example of this is when you ascend to mount tops.

B. The second regulator of ventilation is **H^+**, usually, CO_2 and H come together, but not always!.

Now how do we measure pH?

First of all, normal H^+ concentration is 40 nM *"nano-molar"*

➔ [H] 40nM, which equals $4 * 10^{-8}$ M → $\log 4 * 10^{-8} = \log 4 + \log 10^{-8}$

➔ $= 0.6 + (-8) = -7.4$

➔ we take the negative log (- log) so as the results will be positive, this is called "pH"

➔ $-\log 4 * 10^{-8} = 7.4$ → p is – log , H^+ is 40nM

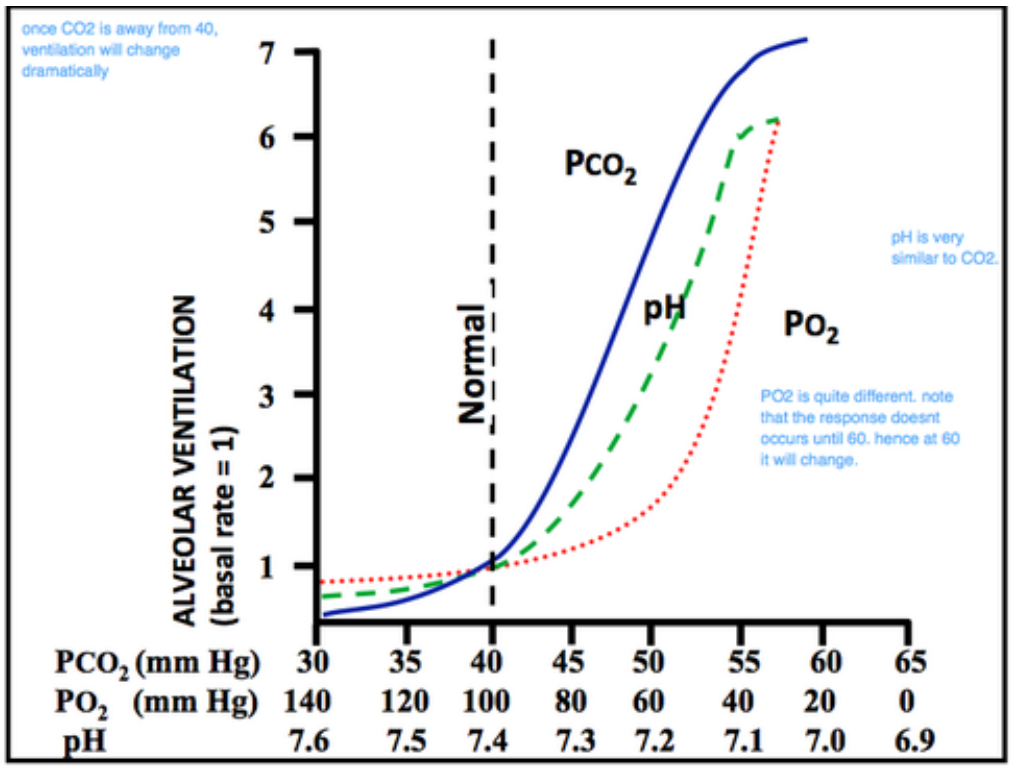
➔ So more [H] will result in more ventilation *to get rid of excess H^+*.

So in general, higher H conc. → lower pH → more acidic blood → increased ventilation.

On the other hand, lower H → higher pH → more alkali blood → decreased ventilation

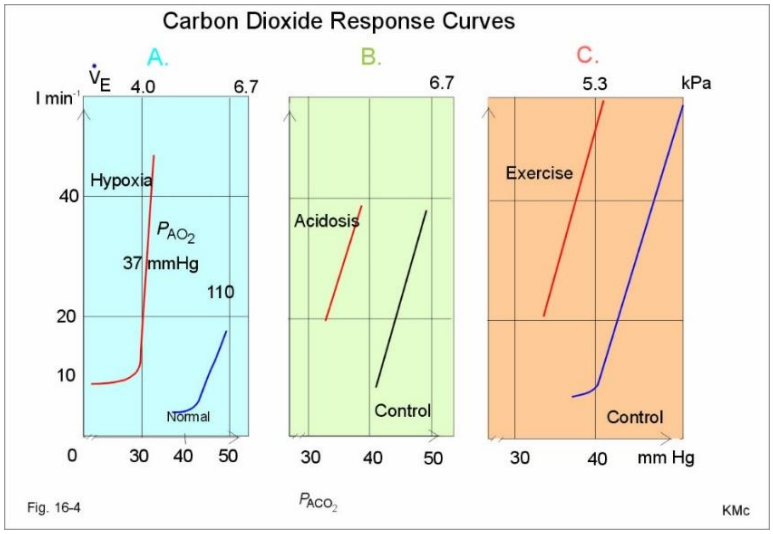
C. The 3rd gas that affects ventilation is **CO_2**, there's a <u>linear</u> relation between CO_2 levels and ventilation. increased CO_2 levels will increase ventilation, while decreased CO_2 levels will decrease ventilation

- All 3 above mechanisms are true if each gas taken alone, but this doesn't apply in real life, because 3 gases work <u>together</u> at the same time to determine the resultant increase or decrease in alveolar ventilation.
- For example, regarding point 2, the magnitude of response to decreased H^+ is much lower than the response to increased H^+, This is due to the fact that the decreased H^+ → high pH → alkalosis, and we respond by suppression of ventilation which results in decreased PO_2, and by now we know that a PO_2 below 60 mmHg will result in increased alveolar ventilation, antagonizing alkalosis.
- However, increasing ventilation results in higher PO_2 which does NOT suppress ventilation (As the Oxygen-Hemoglobin dissociation curve is sigmoidal). So a one unit decrease in H^+ has less effect than a one unit increase in H^+, due to the antagonizing effect of **hypoxia**.



Gases effect on Ventilation

❖ From previous example, we can build up other conclusions to understand the relation between each two gases and all 3 gases together:



1- CO_2 levels and pH go usually together, So, Hypercapnia and acidosis are additive to each other.
2- In many cases, hypoxia will lead acidosis, and fortunately, the effect of acidosis and hypoxia on the lung is additive.
3- Hypoxia potentiate the effect of hypercapnia (the resultant effect is higher than both effects on the lung)

"Chronic End stage Renal failure and Potentiation"

To clarify the idea of potentiation we will talk about this clinical case:

- Chronic End stage renal failure results from destruction of kidney parenchyma due to **DM, HTN**, or most commonly, both.
- As you know, DM increases the risk of HTN, So many DM patients will end up having HTN.
- HTN is diagnosed as Systolic 140 or more OR diastolic 90 or more OR both.
- If a patient that has DM develops HTN, he will reach end stage renal failure **faster**.
- Actually, 90% of DM patients that develop end stage renal failure has HTN.
- So Diabetes and HTN potentiate each other in destruction of the kidney *"like the idea of 3+4=10 not 7 due to potentiation"*

- So to sum up, conditions that favor increased ventilation works together, which means in hypoxic conditions, the patient will have acidosis and hypercapnia too, all these conditions work in the same direction.
- However, if the patient is in a condition that favors decreased ventilation, there are some limitations.
- So if a patient suffers from alkalosis, he will suffer also from hypocapnia, these two factors will try to reduce his ventilation. However, hypoxia will develop an antagonizing effect of both alkalosis and hypocapnia on the lungs

The best way to appreciate the effect of our respiratory controlling system is to think about practical examples,

- 3 examples will be discussed; **COPD, high altitudes** and **exercise**.

To be continued…

1- COPD

- A person with COPD has permanently elevated PCO_2 with low PO_2, What's the response of his control system?
- To estimate his response, we have to talk about each type of receptors.
- Regarding central receptors, these receptors respond to CO_2 and H levels (pH), actually, these receptors are highly sensitive to pH. But less sensitive to CO_2. So they sense low CO_2 levels by sensing the pH due to Henderson Hasselbalch equation :

  $H_2O + CO_2 \leftrightarrows HCO^3 + H^+$

  $pH = 6.1 + \log [HCO_3] / [CO_2]$

  Henderson Hasselbalch equation

  $$pH = 6.1 + \log \frac{[HCO_3^-]}{0.03 \times paCO2}$$

  Arterial conc. of HCO_3 = **24 mM,** while CO_2 = **40mmhg**

  So CO_2 should be multiplied by 0.03 (conversion factor) to be mM → = 1.2 mM

  So 24/1.2 = 20 → log 20 =1.3 → pH = 6.1 + 1.3 = 7.4!

- This occurs in normal conditions, from this equation, we can see that there's another player on the relation between CO_2 and pH, which is <u>HCO_3</u> levels, and if the lung is responsible for CO^2, kidney is responsible for HCO_3.

Henderson-Hasselbalch equation

$$pH = pK\alpha + \lg \frac{\uparrow [HCO_3^-]}{\uparrow [H_2CO_3]} \rightarrow dCO_2 = \alpha \times PaCO_2 \downarrow \text{dissolubility}$$

$$= pK\alpha + \lg \frac{[HCO_3^-]}{\alpha \cdot PaCO_2}$$

$$= 6.1 + \lg \frac{24}{0.03 \times 40}$$

$$= 6.1 + \lg \frac{20}{1}$$

$$= 7.4$$

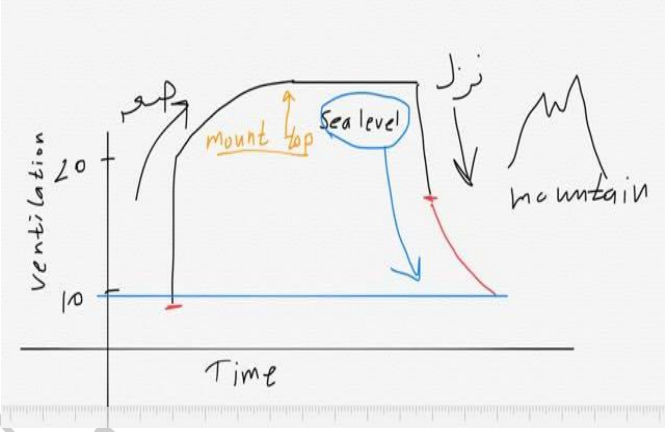
$pK\alpha = 6.1$
$\alpha = 0.03$
$[HCO_3^-] = 24 mmol/L$
$PaCO_2 = 40 mmHg$

- So we can say that Henderson-Hasselbalch equation is about kidney/lung → $pH = 6.1 + \log K_{idney}/L_{ung}$
- In this patient, the CO_2 is high but the kidney work to compensate and increases HCO_3 formation, making pH less dependent on CO_2.
- Which results in high CO_2 & high HCO_3, and pH is normal!
- So everything is cool now, despite suffering from hypercapnia, his blood pH is normal, which desensitize his <u>central</u> receptors (or elevate its set point).
- In this condition, his respiratory centers are regulated <u>only by oxygen</u> through **peripheral chemoreceptors** (he has low PO_2, and this drives his respiration)
- But what If he had flu and came to the hospital, suffering from severe hypoxia (remember from pathology, COPD patient will have severe hypoxia if they have RS infection)

- If we gave him pure O_2, this will elevate his PO_2, decreasing the drive for ventilation and will cause suppression of respiration, so CO_2 will accumulate more and more and repository failure will occur.
- So it is <u>contraindicated</u> to give pure O_2 to COPD Patient, We only give 42% O_2 and in intermittent phases instead

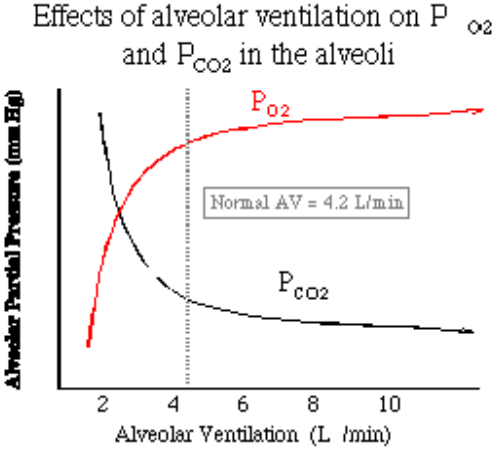
---

2-HIGH ALTITUDES



- If we take a normal person and bring him to a mountain top what will happen?
- When he was at sea level he was breathing normally.
- So his arterial PO_2 was 100 and PCO_2 was 40.
- When a person ascends to high altitudes, atmospheric pressure will drop, so PO_2 will drop, leading to hypoxia, Hypoxia drives the ventilation through stimulating <u>the peripheral chemoceptors</u>.
- But hyperventilation will lead to hypocapnia, Hypocapnia suppresses ventilation centrally in the medulla.
- So in first few days, the patient will suffer from <u>mild hypoxia</u>, and <u>hypocapnia</u>. As hypoxia and hypocapnia antagonize each other.
- In the coming 5 days in mount top, this person will tolerate CO_2 drop, but how?
- In the equation of Henderson, CO_2 will drop and HCO_3 will be decreased too to equilibrate the pH, So HCO^3 will be lost with urine, "and bicarbonate is very precious to the body, normally we cannot tolerate losing 1 molecule of carbonate in the urine!!!" *(that's what the doctor said yet I'm not sure) saffar*

"شوف... مصارله كم سنة بالطب و ديشكك بكلام الدكتور-." صباغ



- In the coming days, after tolerating low CO^2, Suppression for ventilation (alkalosis) will be removed, hypoxia will be the only driver of the ventilation,so ventilation will increase and usually successfully compensate for hypoxia.
- And this person will live in peace there for now ✌
- Now the hypoxia will not be exerting its full effect because it's opposed by the low CO_2
- Later on, In the coming few days as we said the kidney will excreting HCO_3
- So, this person's CO_2 will not be 40 mmHg, it becomes 20 and HCO_3 will not be 24 mM, it'll be 12 (normal values at mount top نوعاً ما).

Henderson Hasselbalch equation

$$pH = 6.1 + \log \frac{[HCO_3^-]}{0.03 \times paCO2}$$

- But if he suddenly descend to sea level, Here the hypoxic effect will be removed → no hypoxia.
- So ventilation will decrease, and when it's decreasing CO_2 will increase to 30, "*while normal is still 40*", this will lead to elevated H^+ concentration and a drop in pH.
- Now the kidney have to Increase HCO_3 levels again, but because kidney has a slow response, and respiratory system is fast, **acidosis** will happen, "acidosis is either due to HCO_3 decrease or CO_2 increase".
- So his breathing didn't get back to the sea level value *"original value"* right away, it will get back after few days when the kidney function will return to normal (HCO_3 excretion back to normal) .

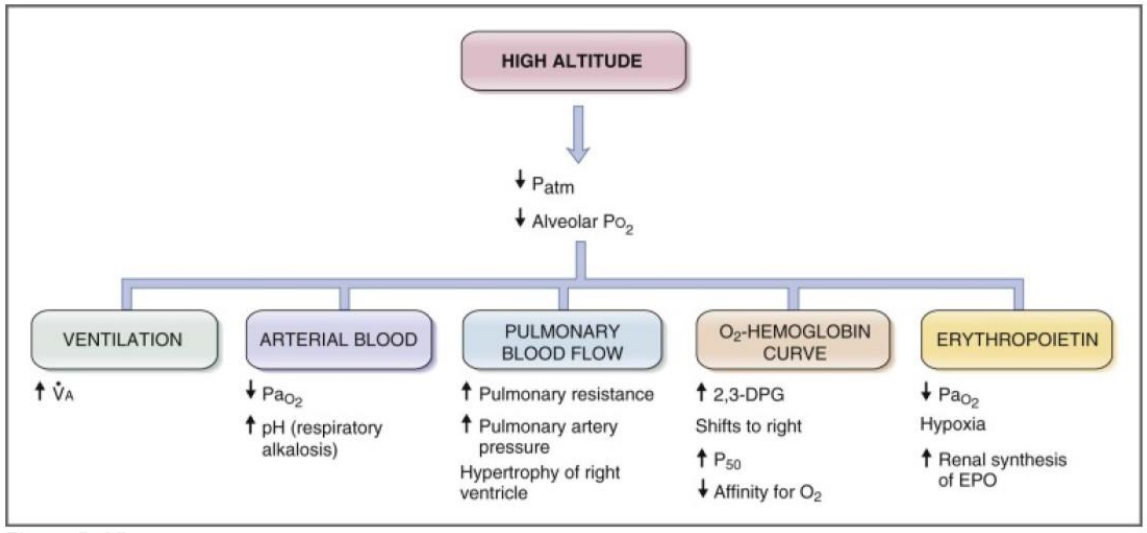
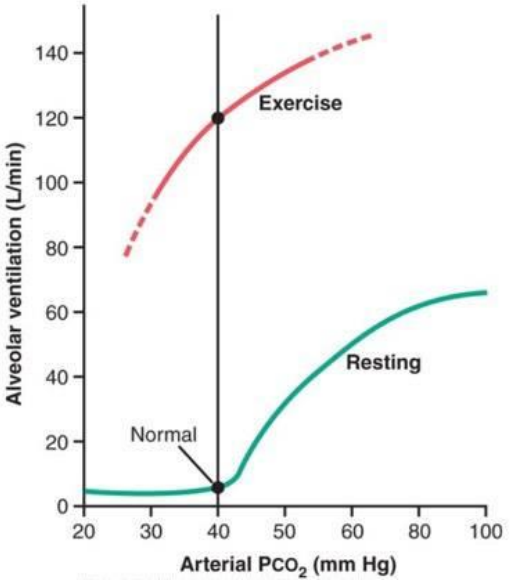


Figure 5–35

Responses of the respiratory system to high altitude. EPO, Erythropoietin.

3-EXERCISE



*The ventilation will increase depending on the intensity of the exercise or the psychological state on the curve

- During exercise, all blood gases (PO_2, PCO_2 and pH) remain normal, so what drives respiration then?!
  "From 6L/min to 30L/min", *not blood gases which drives ventilation*
- Remember that we said in previous lecture, that we have to find a way to tell our CNS that we need oxygen for extra effort, so when you exercise you give muscles Impulses from the cortex, these impulses will also affect the dorsal respiratory neurons which drives ventilation to increase.
- At the same time the moving muscle as they affect the joints (the proprioceptors), they send impulses through "afferent" fibers, these impulses go to the **medulla oblongata** to drive ventilation,
- E.g. if you move a comatosed patient muscle his vent will increase
- So anything of these but NOT blood gases to drive vent, because they are constant (100, 40) which mean the lung is very good efficient machine.

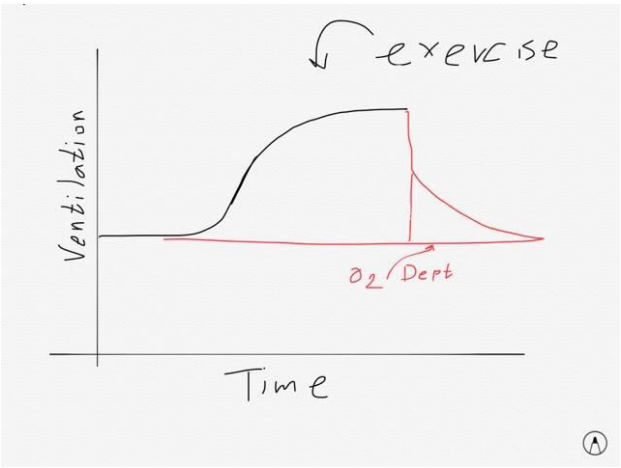
*Proprioceptor

a sensory receptor that receives stimuli from within the body, especially one that responds to position and

---

Another Q → (santa Qlause😊)

- When an athlete stops exercising, he's still having high ventilation rate & respiration for 10mins-hours *(depending on the severity of the exercise)*, why?



- Because of a phenomenon called **oxygen debt**!
- when you have lactic acid *(due to muscle exercise)* you remove it by oxygen, and while you're exercising and don't have much O_2 you borrow some from the dissolved O_2 in body fluids,
- Also you consume the O_2 in myoglobin, so you have to replenish it again, so it takes time to return this borrowed O_2 → It takes time to return back to normal ventilation and homeostasis

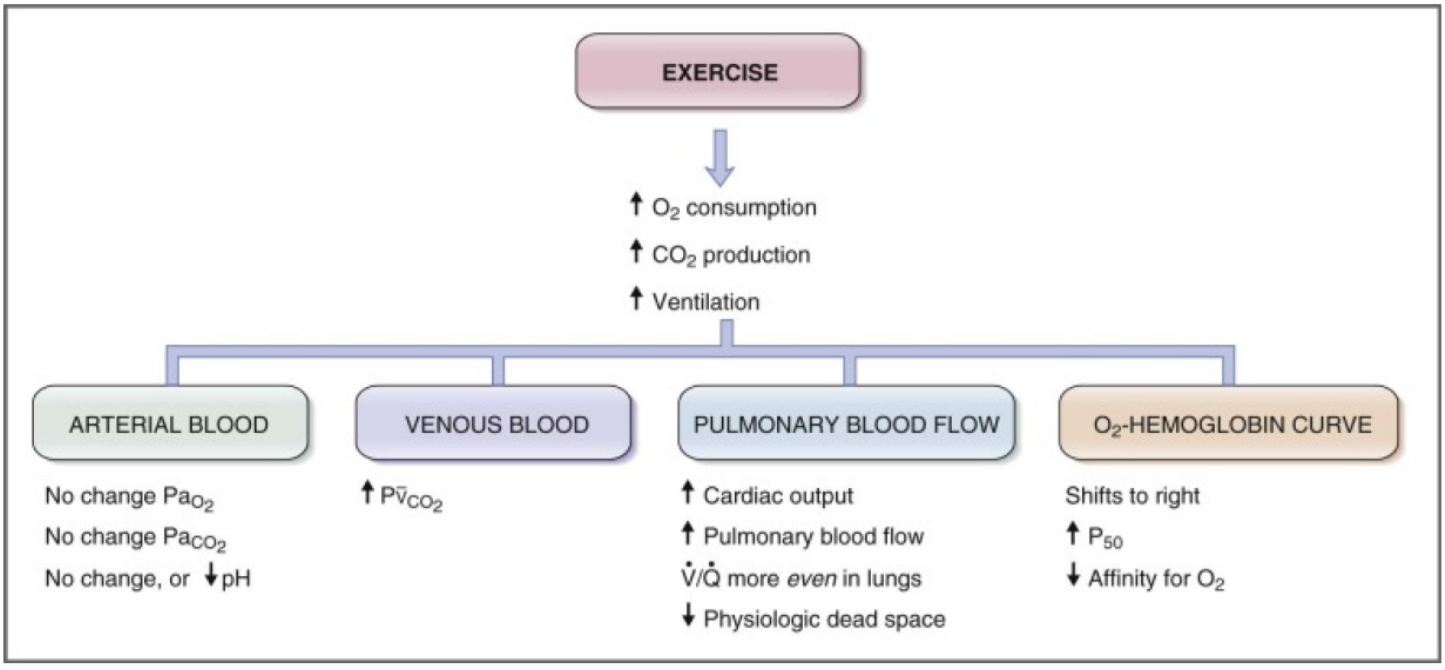
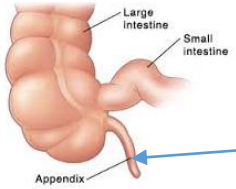


Figure 5–34

Responses of the respiratory system to exercise.

Appendix…



It was Sabbagh idea to add this figure…

I'm sorry ☹

An important قاعدة in physiology is قاعدة اللتر.. it says that, at rest, CO *"cardiac output"*, which is 5L is distributed into 5 major parts, each part takes 1 L

- Sk. Muscles 1L
- GI 1L
- Renal 1L (it's actually 1,25)
- Brain 1L (it's actually 0.75)
- Others 1L (Coronary blood flow takes 0.25)

Now during exercise, CO may reach 15L, out of these, skeletal muscles takes 8L

Le Fin.

"Words can heal, and also can kill, choose your words wisely"

O. Saffar

Done by: Omar Saffar

Revised by: Mohammad Qussay al-Sabbagh