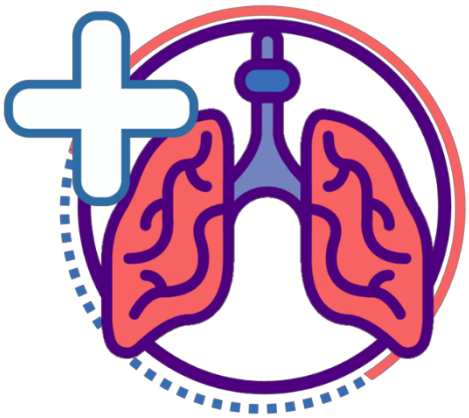


RESPIRATORY SYSTEM

Physiology

Sheet Slide

Number:	-11
Done by:	-2015
Corrected by:	- Renad
Doctor:	-Yanal

Edited by 019

⚠️⚠️⚠️⚠️⚠️**There is an important note at the end of the sheet you must read it before you start.**⚠️⚠️⚠️⚠️⚠️

**you'll see that this sheet is basically 2015's sheet with extra editing , enjoy! :)

We'll continue talking about control of breathing ;

The CNS is composed of three parts:

- The brain

- The spinal cord

- The brain stem (which is the bridge between the brain and the spinal cord)

** The medulla oblongata is located in the brain stem. Above it, we have the pons.

**Any collection of neurons in the CNS which have related (related not the same) functions is called a center. So we have respiratory centers in the medulla.

Respiratory centers are categorized into two groups:

1. Dorsal respiratory group: located dorsally. These are inspiratory neurons; they stimulate the diaphragm. **They work at rest**

2. Ventral respiratory group: located ventrally. These are inspiratory and expiratory neurons. **They don't work at rest**

-During quiet breathing (at rest), there are no expiratory muscles working (expiration is passive) meaning that the dorsal group is responsible for stimulation of phrenic neurons (between C3-C5) which stimulate the diaphragm.

While during forced inspiration or expiration, ventral neurons come to action.

*Dorsal center for ~~passive~~ inspiration → **There is no passive inspiration inspiration is always active**

*Ventral center for active -forced- inspiration and expiration.

→ In addition to the respiratory center in the medulla,

we have accessory respiratory centers located in the upper and lower thirds of the pons:

1. Apneustic center in the lower third: This is the "on" switch of the dorsal neurons.

2. Pneumotaxic center in the upper third: This is the "off" switch of the dorsal neurons.

**If we cut just below the pneumotaxic center we'll have prolonged inspiration with occasional expiration (apneusis).

So, the dorsal center is not its own boss; the accessory center controls it. During quiet breathing, the dorsal group is switched on and sends impulses for 2 seconds, then it's switched off (it stops firing) for 3 seconds. And the cycle is repeated. As a result, the duration of inspiration (contraction) is 2 seconds, and the duration of expiration (relaxation) is 3 seconds, resulting in a respiratory cycle of 5 seconds. Respiratory rate= 60/5=12 breaths/minute (respiratory cycles).

Quick recap:

-The purpose of the respiratory control center is to maintain normal ABGs.
-The tools are increased and decreased ventilation
- The feedback system is the ABGs: ↓ $PaCO_2$, ↑$PaCO_2$, ↓ PaO_2 (below 60 mmHg), ↓ H+, and ↑H+. These three elements will feedback to the respiratory center, which will increase or decrease ventilation.

Dorsal repiratory group recieve input from :

1.accessory neurons

2.the periphery (9^{th}(glossopharyngeal) and 10^{th}(vagus) cranial nerves)

3.neighbouring cellls from the medulla called chemosensitive receptors, these are stimulated by too much/too little H^+ **Exposed to CSF**

**In acidosis , inspiration is stimulation in order to wash out CO_2.

$CO_2+H_2O \longrightarrow H_2CO_3 \longrightarrow H+ + HCO_3-$

*Too much acids like in diabetic ketoacidosis or like in case of ingesting a lot of Aspirin.

these high levels of acid stimulate respiratory system;

(Acidosis ⟶hyperventilation ⟶Hypocapnia (low CO_2))

**Hyperventilation and increased ventilation aren't the same!
-Hyperventilation is when arterial PCO_2 decrease.
**During exercise: Alveolar Ventilation and CO_2 production increase while arterial CO_2 remains the same (NOT HYPERVENTILATION) !!

Acidosis can be because of a decrease in [HCo3-] or an increase in [Co2] or both.
Alkalosis is the opposite.

Because H+ is charged it is hard for it to cross the BBB and the CSF Barrier

But There is no barrier to CO_2 (it crosses any membrane), so CO_2 in the blood can cross the blood-brain barrier. **and the CSF Barrier**

In the CSF, it combines with H_2O forming H_2CO_3 which dissociates into HCO_3 - and H+.

** When we ask someone to hold his breath (no more ventilation), what happens??

The cerebral cortex(center of consciousness), which is known to control voluntary respiration, will send impulses to phrenic neurons inhibiting them. Inhibition means no contraction and thus no breathing.

As a result, 2 things happen:

a. PO_2 decreases from 100 to 80, this is not too dangerous and this decrease won't be sensed by any neuron.

b. PCO_2 increases from 40 to 50, 50 is a lot (dangerous) which will diffuse into the CSF and produce more H+ there.

When H+ in the CSF (cerebrospinal fluid) increases, it will stimulate the chemosensitive cells in the medulla. These cells will stimulate the dorsal respiratory neurons and these in turn will stimulate phrenic neurons and drive ventilation.

That's why no one can kill himself by holding his breath. PCO_2 cannot be raised to more than 50 in a normal individual.

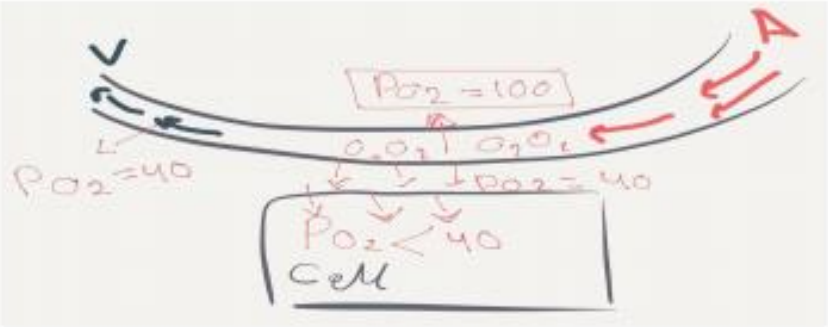
Main goal of control systems is to maintain normal ABGs

	CSF	blood
pH	7.32	7.4
Proteins	45ml/dl	6-8g/dl
HCO3-	24	26-28

*Proteins are buffers and buffers are compounds that resist pH changes in solutions whether it was an acidic or basic change so any addition of H+ to the blood will shift the pH insignificantly while adding the same amount of H+ to CSF will shift the pH markedly(a very tiny amounts of proteins are there).

We only care about Co2 because it gives us H+.
(Chemoreceptors only sense H+)

To maintain normal ABGs, we need to "see" what is going on inside peripheral arterial blood through chemoreceptors .



If I want to put sensors (the brain's "eyes") to detect ABGs, where to put them?

These sensors are in the carotid arteries (mainly) and the aorta (major arteries). They're called carotid and aortic bodies, respectively and we consider them chemoreceptors because they detect chemicals like H+, CO_2, O_2 but **they mainly detect O_2 changes in arteries.**

How are the carotid and aortic bodies going to be able to tell the dorsal respiratory neurons about the levels of arterial PO_2?

Cells receive arteries → capillaries→ drain into veins

Arterial PO_2 is 100, interstitial PO_2 is 40 and inside cells it is less than 40. If this cell is one of the carotid body's cells, it has an axon that reaches the dorsal respiratory neurons. cells cannot see arterial PO2; it can only see what is around it (the interstitial). If this was the case in carotid bodies (i.e. interstitial PO_2 is 40), they will always tell the respiratory center that PO2 is low where it is actually not (arterial PO_2 is 100-normal)!

So how will these cells be able to sense ABGs and relay them to the brain?!

There is something different about carotid bodies that is not found anywhere else. That is, the interstitial PO_2 in carotid bodies is equal to arterial PO2 so they can send the brain a massage about arterial PO_2. And If arterial PO_2 decreases, interstitial PO_2 also decreases. How is this possible?

There are 2 ways:

1. The cell is metabolically inactive and does not consume O_2 at all. This means PO_2 in the artery, capillary, and interstitium is the same. However, carotid body cells are the most active cells in our body, so this theory won't work with carotid bodies, which takes us to the second point.

2. Bringing an extremely high blood flow (and thus high amounts of O_2) to these cells so a very little proportion of O_2 is consumed (despite the high activity). Which means the partial pressure of oxygen does not drop significantly as blood is passing through the carotid body.

Blood flow to carotid bodies is the highest in our bodies; it equals 20mL/g tissue weight. Carotid bodies weigh 25mg but still they have their own artery (carotid body artery).

To compare: The kidney 4mL/g (the 2nd highest flow) Skeletal muscles receive 0.03mL/g.

Blood Flow to Different Organs

Tissue	Blood flow (ml/g/min)	A-V difference Vol%
Heart	0.8	11
Brain	0.5	6.2
Sk muscles	0.03	6
Liver	0.6	3.4
Kidney	4.2	1.4
Carotid bodies	20	0.5

As a result, these cells are the only cells in our bodies that are exposed to arterial PO_2. They sense arterial PO_2; whenever it decreases they can sense this and tell respiratory centers so when we calculate arterial-venous PO_2 difference it'll be 0.5 which makes it very sensitive to any change in arterial PO_2.

Around these cells —> gases in veins ≈ interstitial fluid ≈ Arteries

Also 1/7 the ability to sense o2

These bodies are also sensitive to any increase/decrease in H^+ and CO_2 BUT its equal to only to 1/7th of central effect, but its response is 5x faster than the central response.

When Po2 is less than 60 mmHg they begin sending more impulses to the Respiratory centers.

The more the decrease below 60 the more the number of impulses.(strength of the signal = number of impulses).

The effect of high altitudes on ventilation

If somebody ascended to high altitudes, what will happen?

PO_2 levels at high altitudes is low , this will result in peripheral stimulation.

①At the level of the Dead Sea (-350m): Ventilation will not be affected because as we said if PO2 increases above 100, there will be no suppression.

②When you ascend until 3000m As long as your PO_2 is higher than 60, ventilation will not be affected because respiratory centers are not stimulated when PO2 is higher than 60.

③At higher altitudes PO_2 is lower than 60 → hyperventilation. What is going on!?

-PO2 is lower than 60 → increased ventilation.

Increased ventilation affects ABGs as follows: ↑ PO2, ↓ PCO2, ↓H+ (↑pH) (alveolar) So, hypoxia stimulated ventilation.

- But at the same time, he now developed hypocapnia (decreased PCO2) because of increased ventilation

Hypocapnia should decrease ventilation.

According to Hasselbalch equation below, at high altitudes →↓ PCO2 → ↑pH → alkalosis → alkalosis suppresses ventilation by suppressing central chemoreceptors

Henderson Hasselbalch equation

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

So, now there are 2 antagonizing effects (opposing stimuli):

One: peripheral stimulation which drives ventilation (hypoxia), and another that decreases ventilation (hypocapnia).These opposing stimuli hinders the ability of low PO_2 to express its decrease fully.

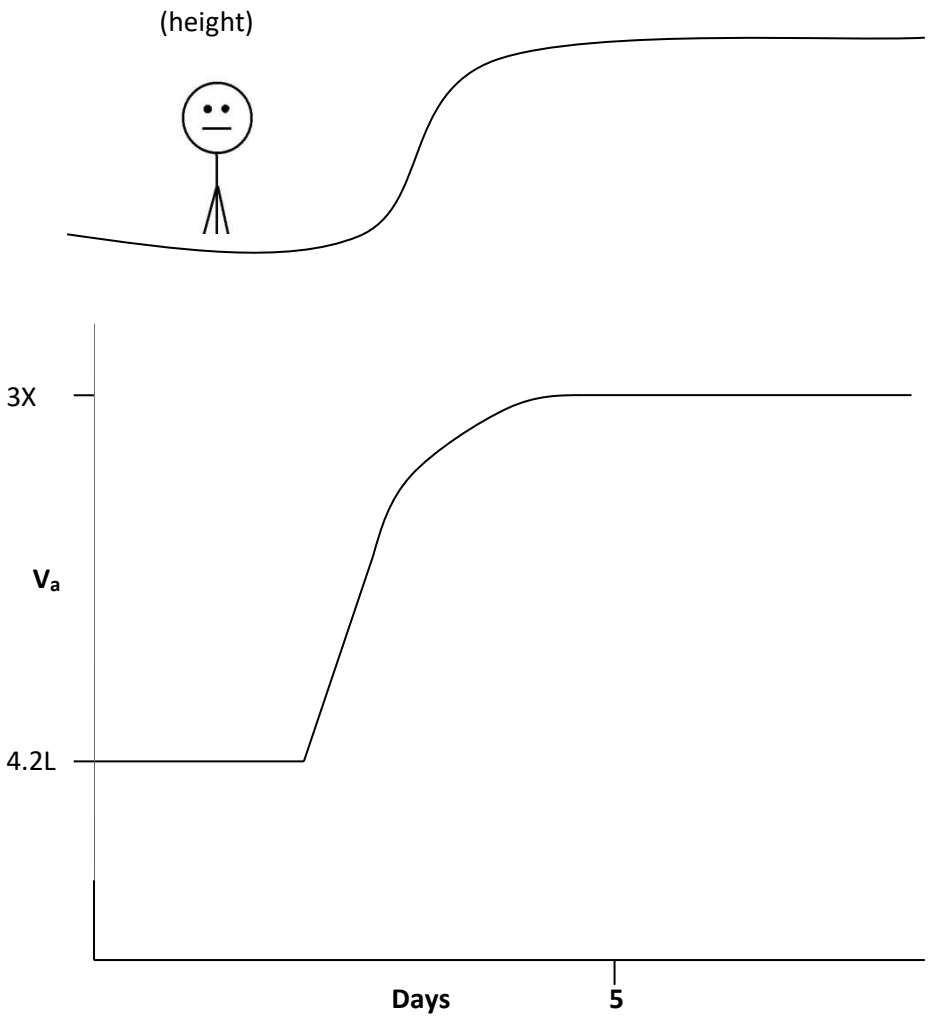
At 4000m above sea level, I expect that ventilation triples. However, when someone is at 4000m above sea level, ventilation actually doubles because of the effect of hypocapnia. Hypoxia stimulated ventilation, but hypocapnia makes this stimulus moderate; hypoxia was unable to fully express its effect in term of ventilation.

-Later on, the kidney will start excreting HCO3 - in urine. After 5-10 days, HCO3 - decreases.

So, ↓HCO3 - → ↓CO2 → pH is back to normal.

**Normally, we cannot afford losing HCO3- in the urine because it's the "most precious" molecule in our bodies but while ascending high altitudes alkalosis occurs so we start excreting some in urine. But as you know renal regulation is slow , taking few days that's why after 5 days of being in conditions where PO2 levels are low (at high altitudes) PCO2 stops being inhibiting because H+ is back to normal.

Remember: We said that H+ is what affects respiratory centers, so as long as it is normal (even if CO2 is low), things are OK. So, after 5-10 days, CO2 is low but H+ is normal and this person has tolerated the drop in PCO2 . The kidney brought pH back to normal and removed the effect of low CO2. Now O2 alone can exert its effects and increase ventilation (even with low CO2) until it reaches the expected level (3x).



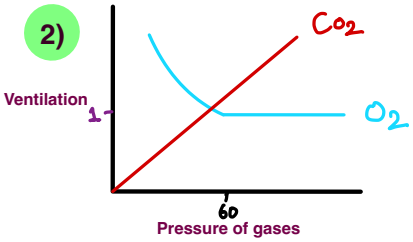
"Dulness is a disease".-Freddie Mercury

The end

The doctor explained the last 4 pages of the last sheet then he added those points:

1) When there is decrease in Co2 there will be a decrease in H+ —> alkalosis
normally ca is 50% bound and 50% free if there is alkalosis the free ca become less which lead to spasms in the muscles of the face,hand…..ex.
Thats why we give a person with spasms a bag to breath in so that [Co2] increase and consequently [H+] increase—> no alkalosis —> free ca increase —> no spasms.

2)



-If Po2 60 or more respiratory centers are not activated but When lower than 60 they get activated and ventilation is increased.
-In Co2 when PCo2 increases ventilation increases and vice versa.

3) In emphysema:
— PCo2 is increased (50-60) which should increase [H+] and cause acidosis shouldn't it?
That is not the case because emphysema is a chronic disease (it takes a longtime not overnight) thats why the Kidneys compensate the rise in Co2 by increasing HCo3- so pH is normal and as we said Co2 doesn't affect the chemoreceptors directly but by changing H+(pH).
So Normal pH—> Respiratory Centers are not affected by Co2 increase.

$$PH = 6.1 + \log \frac{\uparrow[HCO_3^-]}{\uparrow[CO_2]}$$

— Po2 decreases (55 for example) so the body tries to compensate by increasing ventilation.(The only factor affecting the centers because Co2 is being compensated for).
If a patient with this disease gets the common cold or corona or anything that would reduce his o2 levels he needs oxygen because his reserves are already low but if you but the oxygen mask without proper monitoring the only thing affecting the respiratory system is being compensated for so they will be switched off(suppressed) which leads to Apnea and death.(Monitoring includes the duration of putting the mask, taking it off and putting it back on after certain periods, the amount of oxygen).

Notes about the lecture:

1) The doctor said that only what is in the original sheet is what's required for the exam so the last points were added just in case.

2)If you want to know who the real boss is watch the record (10:25-13:48).

https://youtu.be/mY4HacYPF3o .

Good

Luck