Respiratory system physiology

sheet handout slides

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Control of Breathing

What is the purpose or the final goal of the control system?

The goal of the **respiratory center** in the medulla oblongata is to maintain normal ABGs (arterial blood gases) which are **PO_2 =100**, **PCO_2 = 40**, and **pH =7.4**.

The p in pH means –log
For example:
$pCa^{+2} = -\log [Ca^{+2}]$

What are the tools that the respiratory controller system uses to achieve this goal?

It either decreases or increases ventilation. It will work on muscles and either cause more contraction → hyperventilation OR less contraction → hypoventilation

Hyperventilation is when alveolar ventilation is MORE than CO2 production → decrease P_aCO_2 and increased P_aO_2
Hypoventilation is when alveolar ventilation is LESS than CO2 production → increase PaCO2

1. Oxygen

❖ **P_aO_2 depends on:**

1. O_2 delivery to alveoli (Alveolar Ventilation VA).
2. Rate of O2 absorption to blood (O2 consumption VO2).

So **P_aO_2 = (VA/VO_2).**

❖ **When P_aO_2 increases:**

If P_aO_2 increased to 200 for example, the control system does nothing. This is because any increase in P_aO_2 over 100 will not cause more saturation of hemoglobin because it is already 100% saturated. So, **↑PaO_2 over 100 has no effect on the controller system.**

❖ **When P_aO_2 decreases:**

When P_aO_2 decreases to less than 100, the control system also does nothing until P_aO_2 is below 60. As P_aO_2 is decreased to less than 60, firing increases. (This will be explained more in a bit)

2. CO

When P_aCO_2 increases → hyperventilation to return it back to normal
When P_aCO_2 decreases → hypoventilation to retain CO_2.

So, both ↓ $PaCO_2$ and ↑$PaCO_2$ causes a response (unlike O_2).

$$\mathbf{P_aCO_2 = (VCO2/VA)*K}$$

*K is a constant and it equals 0.863mmhg.lit/ml

*If ventilation is doubled then P_aCO_2 decreases to half.

*If ventilation is halved then P_aCO_2 is doubled keeping CO2 production constant.

Inspiration need contraction of muscles mainly the diaphragm. The diaphragm is a skeletal muscle. This means that it needs neurons and lacks automaticity; it cannot reach the threshold and generate an action potential by itself. It needs an external stimulus from motor neurons.

A motor neuron has a body, an axon and dendrites. The body is in the spinal cord. These are called **phrenic neurons**. They generate impulses and cause contraction of the diaphragm. These cells also lack automaticity so they must be stimulated in order to stimulate the diaphragm. They receive impulses from higher centers which contain another type of cells called **respiratory neurons** in the medulla.

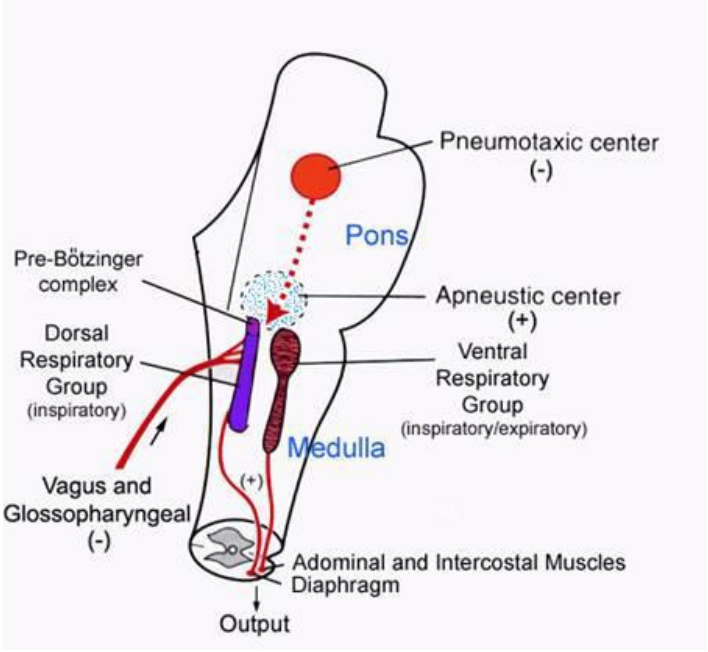
The CNS is composed of **three parts**:
- **The brain**
- **The spinal cord**
- **The brain stem** which is the bridge between the brain and the spinal cord

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

In the medulla, there is a collection of neurons. Any collection of neurons in the CNS which have *related* (related *not* the same) functions is called a center. So we have a ***respiratory center*** in the medulla. We actually have **two groups** of neurons:

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

2. **Ventral respiratory group:** located ventrally. These are <u>inspiratory and expiratory neurons</u>.



→During <u>quiet breathing</u>, there are no expiratory muscles working (expiration is passive). So during quiet breathing, the **dorsal group** is responsible for stimulation of phrenic neurons which then stimulate the diaphragm.

→While during <u>forced inspiration</u>, **ventral neurons** come to action.

In addition to the respiratory center in the medulla, we have an ***accessory respiratory center*** 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.

So, the dorsal center is not its own boss; the accessory enter 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).

Recap: What we said for now:

- 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: ↓ P_aCO_2, ↑P_aCO_2, ↓ P_aO_2 (below 60 mmHg), ↓ H+, and ↑H+. These three elements will *feedback* to the respiratory center, which will stimulate

To understand how the feedback system affects the respiratory center, we must first talk about chemoreceptors.

Chemoreceptors:

1) Central* chemoreceptors:

There are cells in the medulla which are sensitive to chemicals <u>mainly H+</u>. We call them chemosensitive cells.

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

The cerebral cortex, 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).

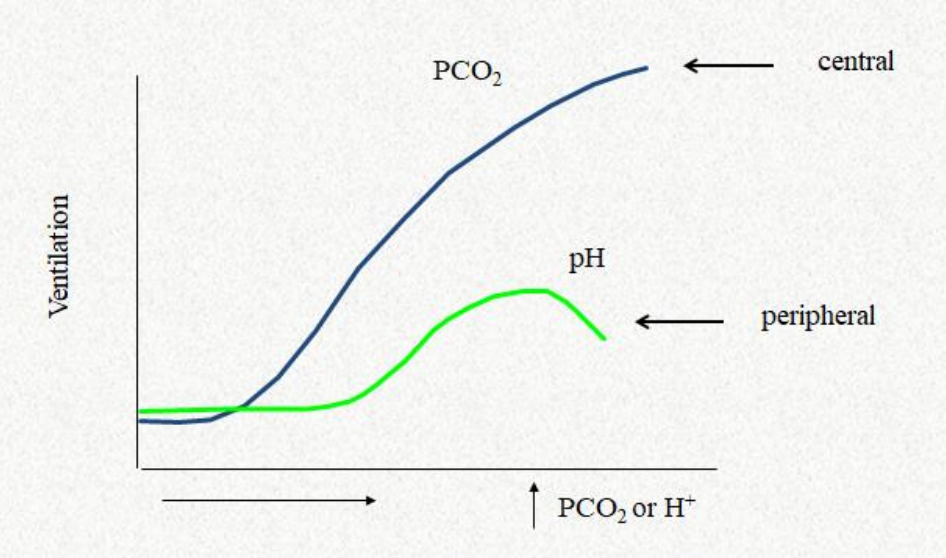
There is no barrier to CO_2 (it crosses any membrane), so CO_2 in the <u>blood can cross the blood-brain barrier</u>. In the CSF, it combines with H_2O forming H_2CO_3 → H_2CO_3 dissociates into HCO_3^- and H+.
When H+ in the CSF (cerebrospinal fluid) **increases**, it will stimulate the chemosensitive 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.

So we concluded that the major controller of the respiratory system is CO_2 but **indirectly** (through H+).

If someone took a whole pack of aspirin (salicylic *acid*), H+ will also increase in blood (acidosis). But H+ cannot cross BBB as easy as CO_2. So it takes much more time before it can stimulate the respiratory center.

*anything inside bones is considered central and anything outside bones is considered peripheral. So we have a central and a peripheral nervous system.



Notice:
When CO_2 increases centrally (H+ increases) → ventilation increases

The feedback system as we said involves CO_2, H+ *and* O_2. Now, **what about O_2?**

2) Peripheral chemoreceptors

To maintain normal ABGs, I need to "see" what is going on inside peripheral arterial blood. 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). These are **carotid and aortic bodies**, respectively. They are called chemoreceptors because they detect chemicals (H+, CO_2, O_2).

Don't confuse carotid and aortic *bodies* with carotid and aortic *sinuses* which contain baroreceptors that sense the blood pressure.

These bodies are most <u>sensitive for oxygen</u>, and start firing at PO_2 less than 60mmHg.

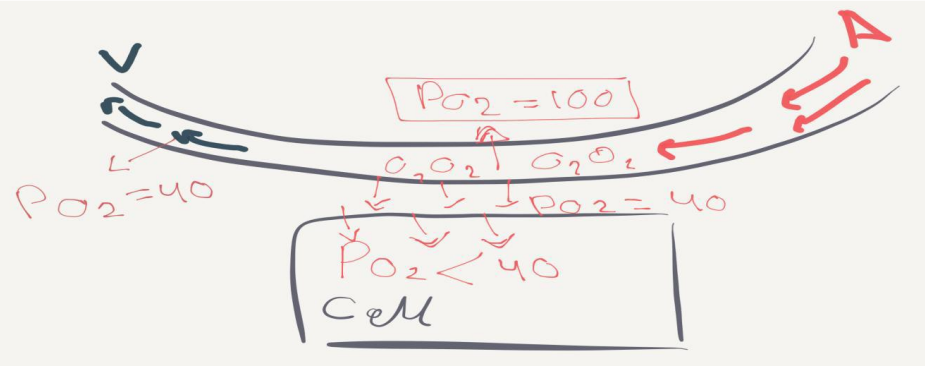
Remember:
Receptors for CO_2 and H+ are in the medulla

<u>How do they work?</u>

Recall what we said in the first lectures:

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. This cell cannot see arterial PO_2; it can only see what is around it (the interstitial). *<u>If</u>* this was the case in carotid bodies (i.e. interstitial PO_2 is 40), they will always tell the respiratory center that PO_2 is low where it is actually not (arterial PO_2 is 100-normal)!

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

There is something different about carotid bodies that is not found anywhere else. That is, <u>the interstitial PO_2 in carotid bodies is equal to arterial PO_2</u> so they can send the brain a massage about *arterial* PO_2. 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 method won't work with carotid bodies, which takes us to the second point.

2. Bringing an extremely <u>high blood flow</u> (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 <u>the highest</u> 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

As a result, these cells are surrounded by arterial PO_2. They sense arterial PO_2; whenever it decreases they can see this and tell respiratory centers.

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

<u>The effect of high altitudes on ventilation</u>

If somebody ascended to high altitudes, what will happen?

①At the level of the Dead Sea (-350m):

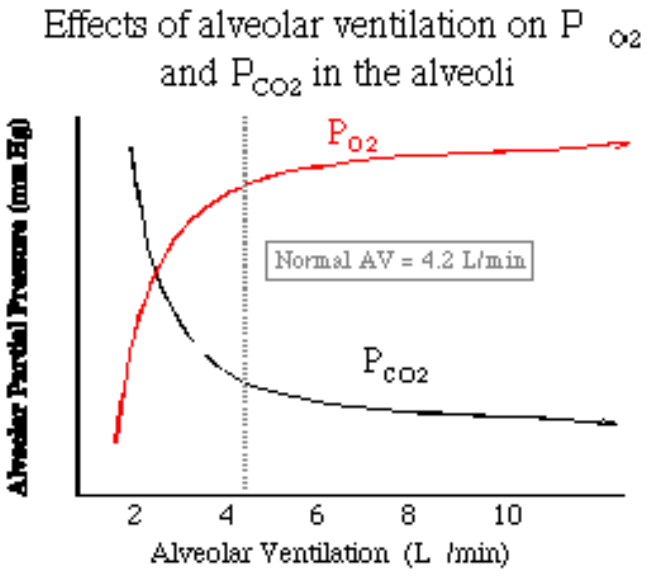
Ventilation will not be affected because as we said if PO_2 increases above 100, there will be no suppression.

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 PO_2 is higher than 60.

③At higher altitudes

PO_2 is lower than 60 → <u>hyperventilation</u>.
Hyperventilation affects ABGs as follows:
↑ PO_2, ↓ PCO_2, ↓H+ (↑pH)
So, hypoxia stimulated ventilation.



But at the same time, he now developed hypocapnia (decreased PCO_2) because of increased ventilation. Hypocapnia should decrease ventilation.

According to Henderson Hasselbalch equation, at high altitudes →↓ PCO_2 → ↑pH → alkalosis → <u>alkalosis suppresses ventilation</u>
[You should memorize this equation]

Henderson Hasselbalch equation

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

So, now there are **<u>2 antagonizing effects</u>**:
One drives ventilation (hypoxia), and another that decreases ventilation (hypocapnia).

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 HCO_3^- in urine. **After 5-10 days**, HCO_3^- decreases. So, ↓HCO_3^- → <u>↓CO_2</u> → <u>pH is back to normal</u>. Remember: We said that H+ is what affects respiratory centers, so as long as it is normal (even if CO_2 is low), things are OK.

So, after 5-10 days, CO_2 is low but H+ is normal and this person has tolerated CO_2 drop (***acclimatization*** تأقلم). The kidney brought pH back to normal and removed the effect of low CO_2. Now O_2 alone can exert its effects and increase ventilation (even with low CO_2) until it reaches the expected level (3x).

When **someone is hyperventilating → ↓CO_2 → ↑pH → alkalosis**
Normally, 50% of our Ca is bound and 50% is free. When there is alkalosis, free Ca gets bound (only 30 or 40% free). Low free Ca → hypocalcemia. Hypocalcemia stimulates motor neurons and causes carpopedal spasms (spasms in the muscles of the hands), this is followed by spasm of muscles of the face. If this is left untreated, it can affect the diaphragm and death.

You can give him/her a bag to breathe in. By doing this, you are bringing CO_2 and thus H+ back to normal. This will increase free Ca. ***THE END***

THE END……. GOOD LUCK.