Co2 transport and the respiratory control

Co2 is transported in 3 forms in the blood: 1-dissolved form .2-bound to Hb (carbaminohemoglobin) .3-*__major form__* is as bicarbonate ion (HCO3-).

now for each 100ml (1dl) of blood at the capillaries around the alveoli, blood takes 5 ml of O2, and gives the alveoli 4 ml of CO2. This is since CO=5liters/min (equal to 50 dl/min) so O2 consumption =5*50=250ml/min and Co2 production=4*50=200ml/min → ***__Respiratory exchange ratio (resp.Q)=Co2production/O2consumption__*** =200/250=**0.8**

The CO2 given to the alveoli is transported in two forms:

1-Dissolved form: (0.4[difference]/4ml[total])=10% of CO2

2-Major form: CO2 produced here released into interstitium

To enter the plasma and crosses the membrane by simple diffusion according to this equation :

Co2+H2O → H2Co3, which further dissociates to H+ and HCO3-

[Mediated by carbonic anhydrase]

Henrys law: [Co2]=Pco2*solubility

40*0.06(more by 20 times than o2)

=2.4ml in arterial blood

But in the venous blood =45*0.06

~2.8ml

So the difference is =0.4 ml

H+ binds to Hb and HCO3 exits the cell in exchange with chloride (not by diffusion rather by special carriers, negative for negative exchange- elctroneutral)

__Therefore, Biacrabonate in the venous blood represent the Co2__ (it's carried in that form).

Cells need to get rid of CO2, if this is only done through the dissolved form, ***__the blood stays in the capillaries for 0.8 sec__*** which is not enough to remove the co2, the solution is to take this CO2 and **.convert it to another form very fast** which is **bicarbonate** by carbonic anhydrase.

** THE ADVANTAGES OF HAVING HB INSIDE RBCS (INSTEAD OF FREE IN PLASMA):*

1. The presence of 2,3BPG (mentioned previously)
2. The presence of reductase (converts ferric to ferrous)
3. Carbonic anhydrase present
4. To prevent filtration of Hb by the kidneys , since its molecular weight is relatively small
5. To prevent it from degradation by plasma enzymes
6. If it's free in the plasma it will increase viscosity which increases the resistance to blood flow

The Third Form of Transport is Carbinohemoglobin (CO2 binds with Hb in RBC)

The Forms of CO2 Transport				
	Arterial	**Venous**	**Difference**	**%**
HCo3	**43.2ml**	**45.6ml**	**2.4**	**60**
HbCO2	**2.4ml**	**3.6ml**	**1.2**	**30**
dissolved	**2.4ml**	**2.8ml;**	**0.4**	**10**
total			**4 ml**	**100%**

- **Question asked in the lecture:** O2 equilibrates with the plasma in the first third, CO2 equilibrates before that. If CO2 or O2 are carried as dissolved only, only little amounts of O2 can be delivered to cells. Therefore it's a big advantage to have Hb to carry the O2 and to convert the CO2 to bicarbonate since there is limited time to carry the 4 ml.
- **Don't forget:** that the Co2 dissociation curve is linear, that depicts the dependence of total blood carbon in all its forms on Pco2 (as CO2 increases PCO2 does as well).
- Venous blood contains <u>less</u> chloride than the arterial blood (Chloride Shift), but venous blood contains MORE chloride in the RBCs than the arterial.

Co2 transport and the respiratory control

RESPIRATORY CONTROL

*The object o*f the respiratory controller system is to maintain normal homeostasis of the ABGs (O_2, CO_2, H^+), may include pH.

- What is the feedback system for controlling respiration: also the **ABGs** which drive ventilation when they are abnormal.
- What are the tools used by this system to maintain homeostasis: **receptors**, either **hyperventilating** OR **hypoventilating**

- The diaphragm is a skeletal muscle which receives motor input from the ventral horn of the spinal cord (C3-C5) though the **phrenic nerves.** These lack automaticity and must receive impulses from higher centers in the medulla → two groups of neurons: the **respiratory center**

- The two groups are

1. **Dorsal respiratory neurons (DRN)**: Inspiratory neurons (I.N), control the diaphragm
2. **Ventral respiratory neurons (VRN)**: Inspiratory and expiratory neurons (I and E.N), the inspiratory neurons stimulate the contraction *of the external intercostals muscles and the inspiratory accessory muscles* (neck muscles), but the expiratory stimulate the contraction of the expiratory muscles such as the *internal intercostal muscles and the abdominal muscles.*

- During normal breathing ONLY the **dorsal neurons work**; the ventral are silent.
- During forced respiration or exercise **BOTH** will work.

- The **brain stem** consists of 4 areas; the lowest one which is connected to the spinal cord is the medulla which is 3 cm long. Above the medulla we have the **PONs** ,which have ***2 respiratory accessory centers***:

1. In the upper third of the pons called **PNEUMOTAXIC CENTER**, which switches **OFF** the **DRN**
2. In the lower third of the pons called **APNEUSTIC CENTER**, which switches **ON** the **DRN**

- *Inside the medulla* we have **pacemaker cells** *close to the VRN* which give impulses for 2 sec, and then stop beating for 3 sec → those cause *inspiration and expiration* period respectively and therefore the **respiratory cycle** is **5** sec and the **respiratory rate** =**12** breaths /min.

- Also *in the medulla* we have a **CHEMOSENSITIVE AREA** (anatomically different than the respiratory center) which contains cells sensitive to chemicals especially (H^+). Follow this:

- **Hypoxia suppresses** these cells (DRN). Hypercapnia: an **increase in CO_2 also suppresses** them. BUT **H^+ stimulates** these cells and hence stimulating the DRN and this drives ventilation.

- The medulla receive input coming through the 9th cranial nerve (glossopharyngeal nerve) and the 10th (vagus nerve) which carry information from **peripheral chemoreceptors**. These peripheral chemoreceptors carry information regarding the condition of the ABGs to the respiratory center. They are located in the major arteries such as the Aorta – Aortic bodies, and Carotid bodies, NOT sinuses.
- These carotid bodies are cells that send information, BUT how can these cells know about the ABGs in the arterial blood DESPITE that there is significant distance (20 micrometers) between them and the capillaries, therefore the cells **can only report and analyze interstitial gases.**
- There are **2 hypotheses** to explain this fact:

CO_2 transport and the respiratory control

1. We bring arterial blood, for example 20ml/dl, and if you assume these cells are metabolically inactive, the PO2 arterial and interstitial will be =100mmHg. But it cannot work because these cells are the most active cells in the body.
2. We deliver too much blood to this region beyond the consumption of these cells, by this way we find that the [A-V] arterio-venous O2 difference =**0.5** (arterial=20 and venous=19.5).

[A-V] in the heart = 11

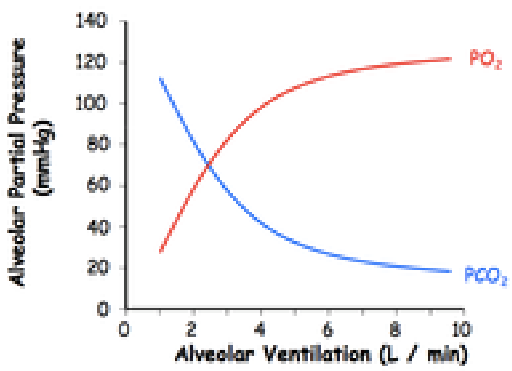
In skeletal muscles = 5

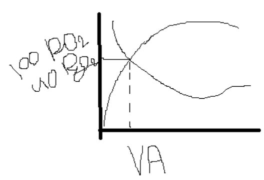
- In the heart the [A-V] O2 difference is 11, so the heart extracts most of the O2, in the skeletal muscles it is 5 and in the kidneys 1.4 → Whenever the [a-v] O2 **difference is small**, it indicates that blood goes to this organ not only to nourish it but also for other purposes, such organs are called **RECONDITIONAL ORGANS**. For example, the kidneys change the composition of the blood and the blood goes to it not only to supply it but also for filtration, it reconditioned the renal artery blood so its composition is different from the renal vein.
- The **difference is large** in **ESSENTIAL ORGANS** (receives as they need)

- The size of the **carotid bodies** =2 mm. and their weight is =25-29 mg,
  Despite that they have their OWN artery (the carotid bodies artery)
  So the **blood flow to them in terms of ml/g is the HIGHEST blood flow** in our body =**20 ml/g**.
  So they are exposed to arterial blood not to venous blood (the oxygen surrounding them is almost arterial)

Blood Flow:
Brain:
=0.5ml/g (weight 1400g and 750 ml of blood)
Skeletal muscles:
=1200ml/28000g=0.04
Kidneys:
=1200ml/300g=4ml

Control of Breathing





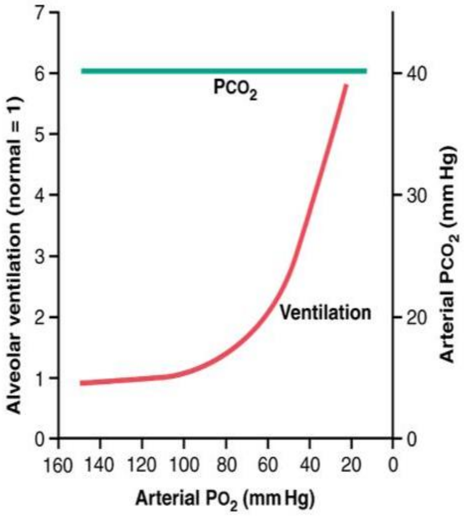
We mentioned that the purpose of the controller system is to maintain normal ABGs and H+, the feedback system utilizes these elements by either hyper or hypo-ventilating.

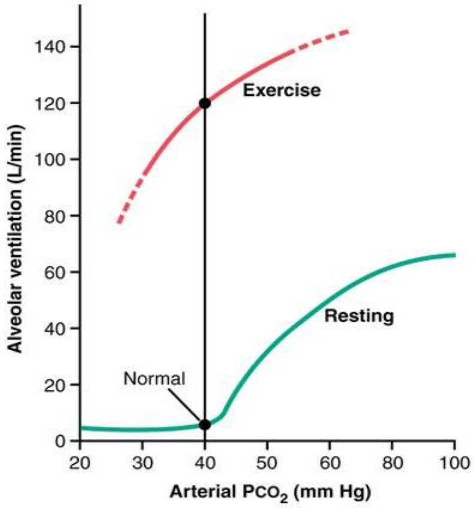
- **Hyperventilation**: increase in O2 and decrease in CO2, this way we can return them to normal levels.

Now, by looking at the graph, the ventilation point is one unit (100%) =6liters /min and we can notice how increased ventilation will increase O2 and decrease CO2.

Another graph, look below:

Co2 transport and the respiratory control





- Here the graph is reversed. We placed the PO2 on the x-axis and the ventilation on the y-axis. For example: let's assume that if the PO2 = 100, ventilation =1. And when PO2 = 200, ventilation is still 1 unit. We can see that whenever the **PO2** is **above 60** →the ventilation is **normal**, but **below 60**, **hyperventilation** occurs.

- Also in the next graph (right), PCO2 x Ventilation, is not like the previous one, it's rather linear. More **PCO2** means **more ventilation** to wash it out. During exercise the curve is *shifted upward* but has the *same slope*, which means *increased ventilation but PCO2 is the same.*

- SO during exercise it's **NOT** CO2 which drives ventilation (may reach up to 16), it's the **protons H+**

- We said that in the medulla oblongata there is a **chemosensetive area**, the central cells there are sensitive to H+, BUT these protons cannot cross the CSF barrier which surrounds the medulla, so if you have acidosis in your blood this H takes too much effort to pass this barrier to the CFS and to the centers to drive ventilation (to wash CO2, leads to less H and more pH).
- If you want to know if someone has a hypoglycemic coma or diabetic ketoacidosis; for example if a child has type 1 diabetes with acidosis → drives ventilation, hyperventilating patient.

- If you were asked to hold your breath, this decreases O2 –for example- from 100 to 80 (20%) and CO2 will accumulate maximally to 50. CO2 in the blood diffuses freely to the CSF without a barrier, in the CFS CO2 will bind to H2O and is converted to H+. This H+ stimulates the chemosensitive area

Conclusion: **CO2 does drive ventilation here but INDIRECTLY through H+**

- CO2 at partial pressure = 75 has a suppressive effect on the brain (used for anesthesia long ago)

- CO2 at partial pressure =100 has a suppressive effect on ventilation RATHER than increasing it, although it is converted to H+ but the CO2 itself has a suppressive effect.

Comparison between the blood and the CSF:

Blood: pH=7.4. Protein concentration =6-8**g**/dl. The proteins act as a buffer system in the blood for H+

CSF: pH=7.32. Protein concentration =45**mg**/dl, therefore there is NO buffer system here; any increase or decrease in H+ will be immediately reflected as PH changes.

Co2 transport and the respiratory control

The pH according to the Henderson–Hasselbalch equation:

= 6.1+ log [HCO3-]/ (PCO2*0.03)

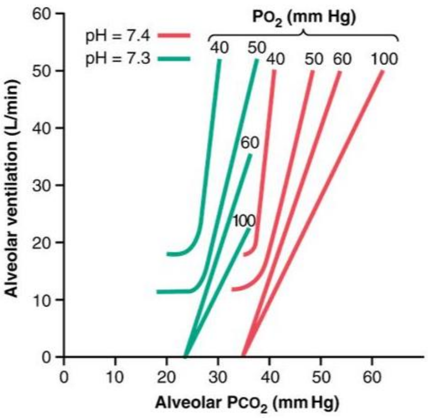
= 6.1+ log 24millimolar / (40mmHg*0.03)

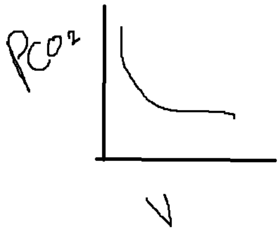
= 6.1 + log (24/1.2)

= 7.4

- The 6.1 is the dissociation constant of carbonic acid. For the CO2 we multiply by 0.03 (conversion factor) to convert mmHg to millimoles.
- From the past equation we conclude that when CO2 increases, pH decreases.
- Any disturbance in the CO2 concentration → Respiratory disturbance, if the disturbance is in the bicarbonate concentration then it's metabolic.

Types of Disturbances	
Respiratory acidosis	Increase CO2
Metabolic acidosis	Decrease HCo3-
Respiratory alkalosis	Decrease CO2
Metabolic alkalosis	Increase HCo3-

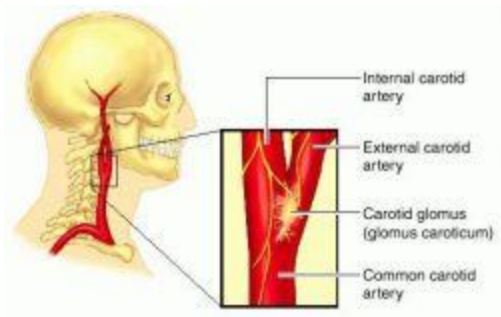




From the last graphs: more ventilation → less CO2 → less H+→ higher PH

Finally, keep in mind:

- **Carotid bodies** have the HIGHEST blood flow per gram in our body, and the oxygen surrounding them is almost arterial; they have their own artery.



تجري الرياح كما تجري سفينتنا   نحن الرياح ونحن البحر والسفن

ا ن الذي يرتجي شيئا بهمته   يلقاه لو حاربته الانس والجن

فاقصد الى قمم الاشياء تدركها   تجري الرياح كما رادت لها سفن

#اصنعوا واقعكم كما تريدون

Done by: Hadeel Alyazori