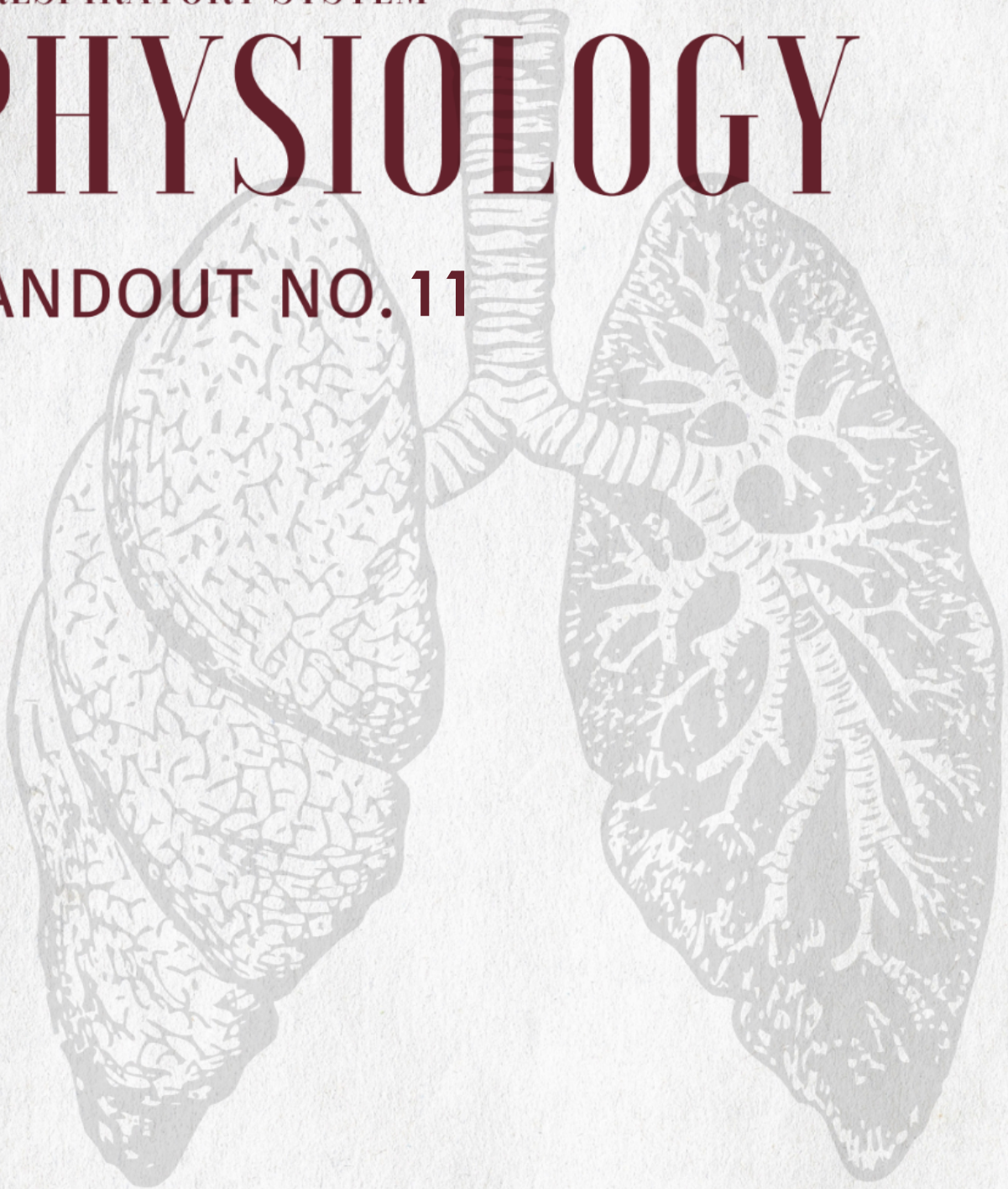
RESPIRATORY SYSTEM

PHYSIOLOGY

HANDOUT NO. 11



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Control of Breathing

Receptors (afferent) → Respiratory centers → increase or decrease ventilation (efferent)

TOPICS:

- Respiratory centers
- Chemoreceptors
- Hypo vs hyper ventilation
- O2 – CO2 potentiation effect
- Regulation in some cases:
  1- Emphysema and COPD
  2- High altitude (acclimatation)
  3- Anemia
  4- Voluntary apnea
  5- Exercise

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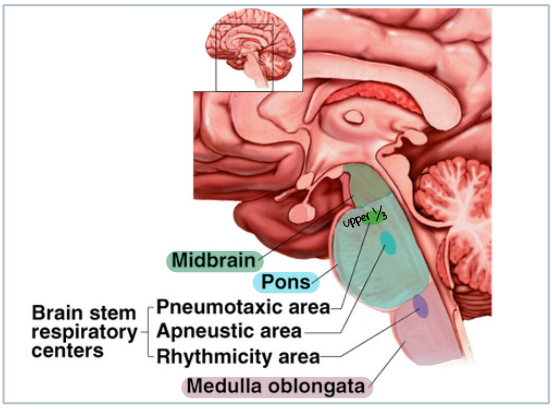
Respiratory centers:

- The brainstem consists of three main structures:
  1- Midbrain 2- Pons 3- Medulla oblongata



- The respiratory centers are organized into **three major groups of neurons**, located within **the pons and medulla oblongata**.

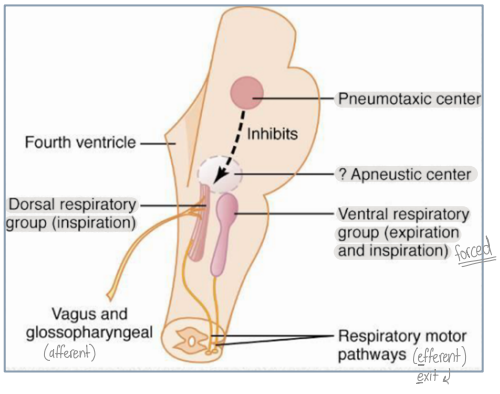
Two of these groups: in the medulla:

1- The dorsal respiratory group (DRG)
2- The ventral respiratory group (VRG)

The third group: in the pons

3- The pontine respiratory group, is located in the pons and includes two functional areas: the **pneumotaxic** center and the **apneustic** center, both of them are considered accessory respiratory centers

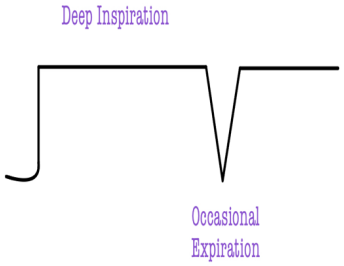
- Neurons in the reticular formation of the medulla oblongata form the rhythmicity center:
  a) Control autonomic breathing
  b) Consist of interacting neurons that fire either during inspiration (I neurons) or expiration (E neurons)



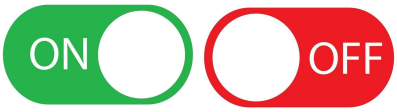
- The pons is divided into three sections: The inferior third, located closest to the medulla oblongata, contains the (apneustic center). The superior third, situated at the topmost portion of the pons, houses the (pneumotaxic center). These centers are interconnected and also send signals to the solitary nucleus (nucleus tractus solitarius)

- **The pneumotaxic center:** plays a crucial role in limiting inspiration by acting as an antagonist to both the apneustic center and the dorsal respiratory group (DRG). Its primary functions include regulating the respiratory rate and reducing tidal volume (the depth of inspiration).

☹ If the pneumotaxic center is damaged—such as by a lesion below the upper third of the pons—apneustic respiration (also known as Apneusis) may occur. This condition is characterized by prolonged inspiration with occasional expiration due to the loss of inhibitory control from the pneumotaxic center



In summary, the apneustic center stimulates (or "switches on") inspiration by the stimulation of Inspiratory ("I") Neurons in the medulla, while the pneumotaxic center inhibits (or "switches off") inspiration (DRG) and thus increases the Respiratory Rate (RR) because it shortens the duration of inspiration, allowing more cycles to occur per minute, so you can conclude that the pneumotaxic center is highly activated during exercise



By: Apneustic (inspiration)

By: Pneumotaxic (expiration)

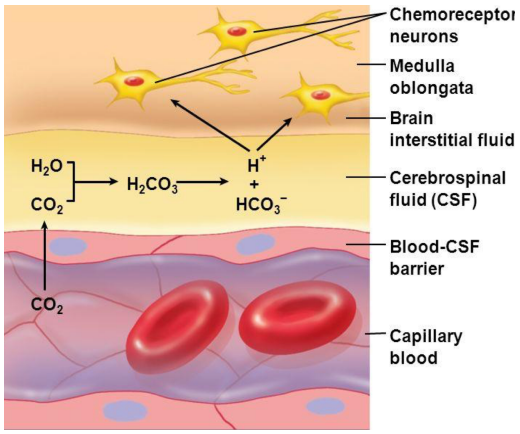
Chemoreceptors:

	Central Control (Chemoreceptors)	Peripheral Control (Chemoreceptors)
Location	Medulla (ventral surface), chemosensitive area	Carotid and aortic bodies
Primary Stimulus	**CO2 (via H+, which is produced when CO2 combines with Water)** H+ stimulates the chemosensitive area which in turn stimulates the neighboring neurons in the dorsal respiratory group (DRN), which subsequently sends impulses through the phrenic nerve to cause the contraction of the diaphragm, causing the initiation of respiration) $H_2O + CO_2 \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$	Mainly **O2 (hypoxia),** also sensitive to CO2 and H^+
Effect of CO2	Strong stimulation (via H^+ production in CSF)	Weak stimulation ($1/7^{TH}$ of central)
Effect of H^+	Potent effect due to H^+ increase in CSF	Weaker effect, less sensitive
Effect of O2	No direct effect	Strong stimulation when PO2 drops below 60 mm Hg
Response Speed	Slower, after a few days of adaptation (renal compensation)	Faster, important for immediate adjustments (e.g., exercise) بنحتاج إجابة سريعة عبين ما يصير تاقلم
Primary Role	Control CO2 levels and pH in the body	Detect and respond to low O2 levels (hypoxia)

⚡ The table is a summary of the ideas related to these receptors. Study the details first, and then refer back to it

✪ The **MAJOR CONTROLLER** of respiratory center activity is **CO_2**, through the production of **H^+ ions.**

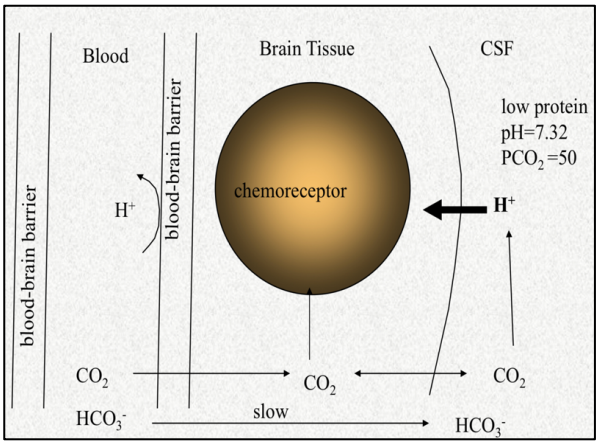
Any small change in the pH in the CSF due to rising CO_2 levels can be reflected in the body's respiratory control in the CSF because CO_2 diffuses across the BBB → reacts with water (carbonic acid) → (H^+) and bicarbonate + (HCO_3^-). This increase in H^+ concentration lowers the pH in the cerebrospinal fluid (CSF), directly stimulating the respiratory center in the brainstem. Even a small shift in CO_2 levels causes a significant change in H^+ concentration, which is highly sensitive to the respiratory control system. As a result, the body increases ventilation to expel excess CO_2 and restore normal pH, making CO_2 the primary driver of respiratory regulation through its effect on H^+ concentration (H^+ itself can't pass the BBB)



Now, why CO2 is the **major controller**?

- PO_2 must fall below 60 mmHg, any higher value doesn't stimulate the firing of the respiratory system. Moreover, changes in PO_2 affect peripheral chemoreceptors, while CO_2 directly affects the central chemoreceptors (through changes in the pH of the CSF)
- Peripheral chemoreceptors are located in the **CAROTID BODIES** (innervated by the Glossopharyngeal nerve , cranial nerve IX) and the **AORTIC BODIES** (innervated by the Vagus nerve, cranial nerve X).
- CAROTID BODIES are **MORE SENSITIVE** to changes in **O2**, **but they also respond to** CO2 **and** H^+ **to a lesser extent. They are 5 times faster in their response compared to the central chemoreceptors.**

(THIS IS THE DR'S EXPLANATION – MENTIONED DURING THE LECTURE)

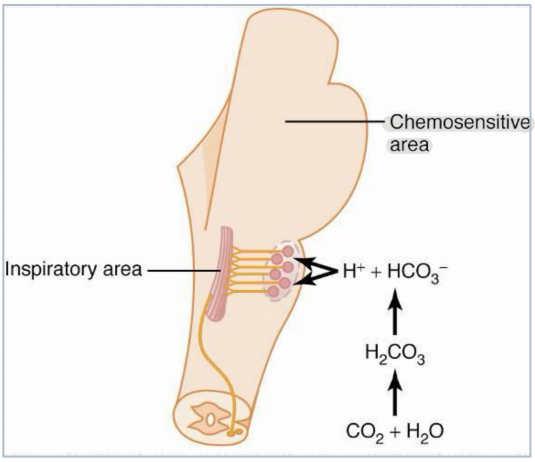


	CSF	***BLOOD***
HCO_3^-	24	28
protein	<45 mg%	6-8 g%
pH	7.32	7.4

CSF have less buffering capacity…and thus pH is shifted faster

- Hydrogen ions (H^+) and bicarbonate (HCO_3^-) cannot pass through the blood-brain barrier easily due to their charged nature, while carbon dioxide (CO_2), being uncharged, can cross the barrier freely. Even small increases in hydrogen ion concentration can significantly affect the pH, making the chemoreceptors highly sensitive to changes in CO_2, as CO_2 is the source of the hydrogen ions when it reacts with water to form carbonic acid, which dissociates into H^+

- Also, the cerebrospinal fluid (CSF) is a low-protein environment with very low levels of hydrogen ions and the (PCO_2) doesn't exceed 50 mmHg.

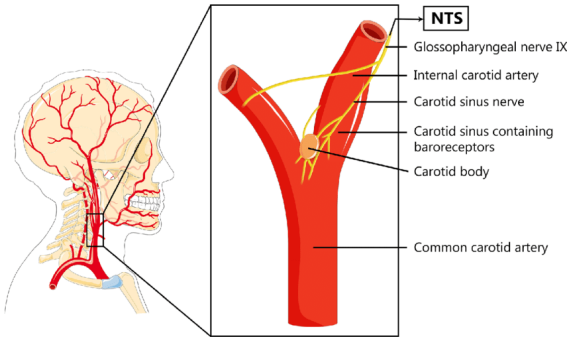


- The low buffering capacity of the CSF is attributed to being a low protein environment, as proteins help to buffer changes in pH, thus being highly sensitive for changes in (H^+) and pH.

  The doctor mentioned that the levels of (HCO3-) are usually lower, being 22 in the CSF and between 24-26 in blood. But it's not a big deal!

Chemosensitive Area: (beneath the medulla, between the 9th & 10th cranial nerves) is sensitive to **H^+** (acidic pH), even though **H^+** can't cross the **BBB** or **CSF barrier** easily. When **CO_2 ↑**, **pH ↓** in both **blood** and **CSF**, but **CSF** responds faster. **CSF pH** normalizes in **24-48 hrs**, while **blood** takes **days**. In **COPD**, **CO_2 ↑** but **CSF pH** stays normal → no increased ventilation. **CO_2** has a strong **acute effect** (hrs) → rapid pH ↓ → ↑ ventilation, but a weak **chronic effect**(days) as kidneys compensate and restore pH balance.

Carotid bodies blood flow (mL/g/min):



- The carotid bodies are specialized **PERIPHERAL CHEMORECEPTORS**, which are nerve cells located outside the brain (so called peripheral) and are crucial for detecting changes in blood oxygen levels, thus crucial in hypoxic conditions
- Like all cells, they have an **ARTERIAL END**, **CAPILLARIES**, **INTERSTITIAL SPACE**, and **VENOUS END**. The **ARTERIAL PO2** in the carotid bodies is typically around **100 MMHG**, while in the **INTERSTITIAL SPACE**, it is slightly lower at **95 MMHG**. (arterial ~ interstitial)
- What's special about them?

  These chemoreceptors are the only chemoreceptors that are primarily **exposed to arterial blood**, which makes them essential to monitor systemic changes!
- WHY?

  Because they receive an **EXTREMELY HIGH BLOOD FLOW**, about 20 times the weight of the bodies themselves each minute. This large blood flow ensures that the chemoreceptors are exposed predominantly to **ARTERIAL BLOOD** with high oxygen.

Blood Flow: Extremely high (20 ml/g/min), ensuring exposure to arterial blood with high PO_2.

A-V Difference: Minimal (0.5%), indicating low oxygen extraction despite high blood flow.

O_2 Consumption: Very low, reflecting their role in monitoring blood gases rather than meeting metabolic demands.

Tissue	Blood flow (ml/g/min)	A-V difference (Vol %)	Flow ml/min	O_2 consumption ml/min
Heart	0.8	11	250	27
Brain	0.5	6.2 (25-30% Extraction)	750-900	
Skeletal Muscle	0.03	6	1200	70
Liver	0.6	3.4 Reconditioner organ		
SKIN	0.1			
Kidney	4.2	1.4	1250	18
Carotid bodies	20	0.5	0.6	

Hyperventilation and Hypoventilation:

- **HYPER-VENTILATION**: This is when alveolar ventilation (VA) exceeds CO_2 production (VCO_2). This leads to a **decrease in P_ACO_2**. However, we do not refer to it as hyperventilation during exercise unless there is acidosis, which occurs in severe exercise.

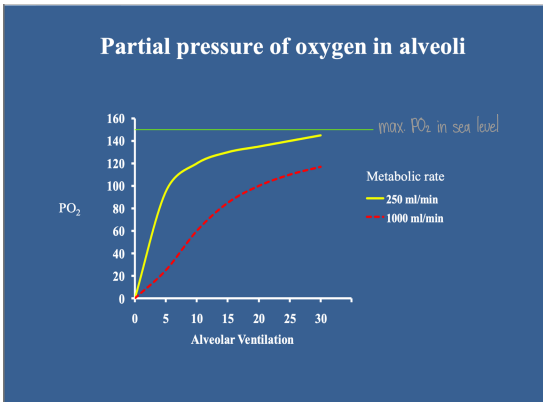
Physiology of Deep-Sea Diving

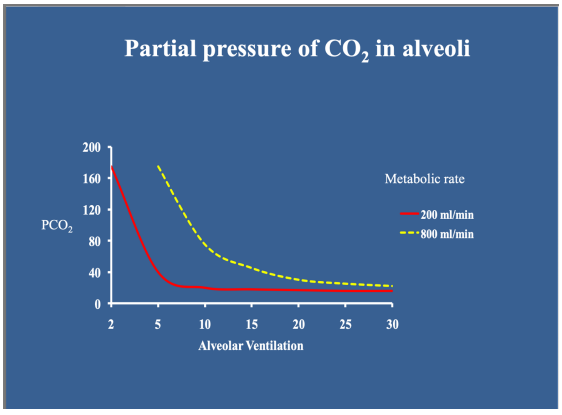
This is seen in divers before diving, they often engage in rapid breathing (hyperventilation) to increase their ventilation rate. This hyperventilation increases the arterial and alveolar PaO_2, more importantly, this reduces the alveolar, thus the arterial $PaCO_2$ by expelling and washing out more CO_2 from the body. As a result, when they submerge and can no longer exhale CO_2, their $PaCO_2$ is significantly lower than the normal baseline of 40 mmHg, often dropping to around 20 mmHg or less!! This reduced initial CO_2 concentration delays the accumulation of CO_2 to critical levels, allowing the diver to remain underwater for a longer duration without experiencing the urge to breathe.

⚠ This hyperventilation technique should not be repeated more than four times, as excessive repetition (e.g., performing it 10 times) can significantly decrease the arterial partial pressure of oxygen (PaO_2). If the PaO_2 falls below 60 mmHg, it can trigger hypoxia, which stimulates the respiratory centers (through peripheral chemoreceptors) in the brainstem to initiate a response. This hypoxic state can lead to dangerous physiological effects, such as coma and death.

- **HYPO-VENTILATION**: This occurs when alveolar ventilation is less than CO_2 production. This results in an increase in **P_ACO_2**, as less CO_2 is expelled from the body.

HOW ALVEOLAR VENTILATION AFFECTS P_AO2 ANA P_ACO2?





ASPECT	OXYGEN (O_2)	CARBON DIOXIDE (CO_2)
Metabolic rate	O_2 consumption: ~250 ml/min (at rest)	CO_2 production: ~200 ml/min (at rest)
Equation	$P_AO2 \propto \frac{VA}{VO2\ (cons.)}$	$P_ACO2 \propto \frac{VC02\ (prod.)}{VA}$
Normal value	PaO_2: ~100 mmHg	$PaCO_2$: ~40 mmHg
During exercise (increased metabolic rate)	**O_2 CONSUMPTION INCREASES** and **VENTILATION INCREASES** to match this increased demand, maintaining **P_AO_2** constant	**CO_2 PRODUCTION INCREASES** and **VENTILATION INCREASES** proportionally to remove the excess CO_2, maintaining **P_ACO_2** constant
Effect of unchanged ventilation but increased metabolic rate	PaO_2 decreases due to insufficient oxygen delivery (because ventilation doesn't increase enough to meet the higher O_2 consumption)	$PaCO_2$ increases as CO_2 accumulates in the blood due to the lack of ventilation increase
Effect of unchanged metabolic rate but increased ventilation	PaO_2 increases slightly due to enhanced oxygenation (because more air is reaching the alveoli).	$PaCO_2$ decreases as excess CO_2 is removed through increased ventilation.

- At sea level, atmospheric pressure is 760 mmHg, and oxygen makes up 21% of the air. After accounting for water vapor pressure in the lungs (47 mmHg), the inspired oxygen partial pressure (PO_2) is calculated as:

  $PO_2 = (760 - 47) \times 0.21 = 150$ mmHg

- In a normal resting state, with alveolar ventilation at 4 L/min, the alveolar PO_2 stabilizes at ~100 mmHg. This provides sufficient oxygen to meet the body's resting oxygen consumption (VO_2) of 250 ml/min

- **Maximum Alveolar PO_2** (Plateau Level): When ventilation increases significantly, alveolar PO_2 rises but reaches a maximum of ~150 mmHg. Beyond this point, increasing ventilation does not increase oxygen availability further, as the system is limited by the concentration of oxygen in room air. (This value may vary at different altitudes, such as mountains or the Jordan Valley (Ghor al-Ordān), and should be adjusted if specified in the question)
- Assuming perfusion is adequate, hyperventilation makes alveolar air like atmospheric air and hypoventilation makes alveolar air like mixed venous blood.

O2 and CO2 Potentiation effect:

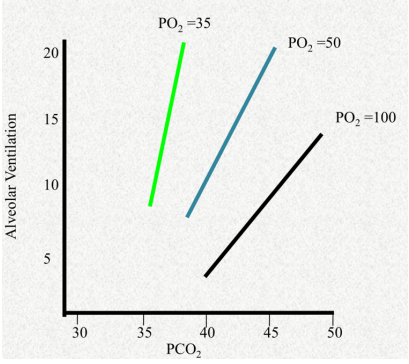
- When oxygen levels in the blood are low (hypoxia) and there is an increase in hydrogen ion concentration (acidosis), their effects on respiratory stimulation are **additive**. For example, if a decrease in oxygen stimulates respiration by a factor of 3 and an increase in H^+ stimulates by a factor of 4, the combined effect will be additive, resulting in a total stimulation of 7. [3 (by O_2) + 4 (by H^+) = 7 times]

- However, when hypoxia is combined with hypercapnia (elevated CO_2 levels), the interaction is not an additive but **synergistic** 🔥, leading to a **potentiation effect**. In this case, if low oxygen stimulates respiration by 3 and increased CO_2 stimulates by 4, the combined effect is significantly greater—closer to 11—due to their synergistic impact on the respiratory centers. [3 (by O_2) + 4 (by CO_2) = 11 times]

  ➔ This occurs because low (PO_2) enhances the **sensitivity of chemoreceptors to changes in the (PCO_2)**, potentiating the respiratory response. Similarly, high (PCO_2) increases the sensitivity of the carotid bodies to a drop in (PO_2), further potentiating the stimulation of respiration.

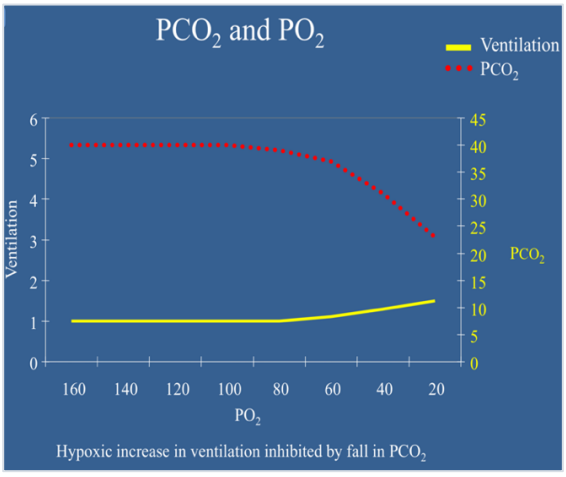
In essence, while oxygen depletion adds to the effects of hypoxia, it potentiates the effects of hypercapnia through mutual enhancement of chemoreceptor sensitivity, resulting in a stronger respiratory drive. This explains why hypoxia and hypercapnia together evoke a far greater respiratory response than either stimulus alone.

➔ This diagram illustrates the potentiation effect observed when oxygen levels are low and carbon dioxide levels are high:



- **Black Line (PO_2 = 100)**: When oxygen is at normal levels (PO_2 = 100), alveolar ventilation increases as PCO_2 rises.
- **Blue Line (PO_2 = 50)**: When the partial pressure of oxygen (PO_2) decreases to 50, the slope of the relationship between ventilation and PCO_2 increases compared to the black line (PO_2 = 100). This indicates the potentiation effect, where a drop in oxygen levels enhances the response to rising carbon dioxide levels.
- **Green Line (PO_2 = 35)**: As oxygen levels drop further to PO_2 = 35, the slopeof the curve becomes even high. This demonstrates a greater degree of potentiation, with low oxygen levels significantly amplifying the response to increases in PCO_2.

Now kindly Observe the following diagram and read the paragraph:



Red Dotted Line (PCO₂): This line represents the partial pressure of carbon dioxide (PCO_2) in the blood as it decreases progressively with increased ventilation. Initially, PCO_2 remains steady but starts to decline significantly as PO_2 decreases and ventilation increases due to hypoxic drive.

Yellow Line (Ventilation): This line shows ventilation as an effect of PO_2. As PO_2 decreases, ventilation initially increases due to the hypoxic response. However, the fall in PCO_2 caused by hyperventilation leads to a feedback inhibition of ventilation. This explains the leveling-off or reduced slope in ventilation even when PO_2 continues to decrease.

TO SUM UP:

- Carbon dioxide is the major stimulus for increased respiration
- CO_2 acts as the primary drive for respiration by influencing the chemosensitive areas in the medulla.
- Acts on chemosensitive areas through H^+
- CO_2 crosses the blood-brain barrier and reacts with water to form H^+, which stimulates the chemosensitive neurons
- CO_2, in CSF is **more effective** than in medullary interstitial fluid because CSF has less protein (acid-base buffers).
- CO_2, has strong acute effect (hrs) but weak chronic effect (days) because it is compensated by the kidney.
- If PaCO2 is high, while peripheral chemoreceptors are denervated, ventilation will still be high to almost the same extent (80-90%), indicating the importance of the central chemosensitive area
- Peripheral chemoreceptors are mainly affected by low PO_2
- Low oxygen levels (PO_2) primarily stimulate peripheral chemoreceptors, such as those in the carotid and aortic bodies.
- If PCO_2 is constant, low oxygen can be important
- When PO_2 drops below 60 mmHg, hypoxic stimulation activates respiratory centers, increasing ventilation

Why is oxygen's effect on respiration blunted?

Because the primary drive for ventilation is carbon dioxide (CO_2), not oxygen. The central chemoreceptors are highly sensitive to changes in CO_2 and pH, whereas peripheral chemoreceptors respond to oxygen only when its partial pressure drops significantly (below 60 mmHg). At normal oxygen levels, the influence of oxygen on respiration is minimal compared to the dominant effect of CO_2

😂 HYPOXIA IN EMPHYSEMA AND COPD:

- In patients with **emphysema**, where ↑**PCO_2** is high (hypercapnia) and ↓**PO_2** is low (hypoxemia) (around 50 mmHg), this condition generally develops over several years, not overnight. In this scenario, the primary factor that drives the respiratory response IS CO_2 via **HYDROGEN IONS (H^+)**. (While CO_2 on its own has an inhibitory effect on breathing, H^+ IONS are the actual stimulatory agents that trigger ventilation).

- When both the concentration of HCO_3^- (bicarbonate) and CO_2 are elevated, the **pH** in the cerebrospinal fluid (CSF) stays **normal** = primary drive (low pH) is lost. In such cases, **HYPOXIA** (low PO_2) becomes the dominant factor driving ventilation as the body senses the low oxygen levels (PO_2 of about 50 mmHg).

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

- If the patient with emphysema or COPD was given oxygen (pure oxygen), the **PO_2** would rise (for example, reaching 80 mmHg), and this would effectively **DAMPEN** the ventilatory drive because the body would sense that there is enough oxygen, thereby reducing the urge to breathe. As a result of this reduced ventilation, **CO_2** will accumulate in the blood. If the P**CO_2** level rises to **70 mmHg**, it can cause deleterious effects on the body and if it increases to **100 mmHg** , it can lead to death. The reason is that high CO_2 can suppress the **respiratory centers**, particularly the Dorsal Respiratory Nucleus **(DRN)**, and this leads to respiratory failure.

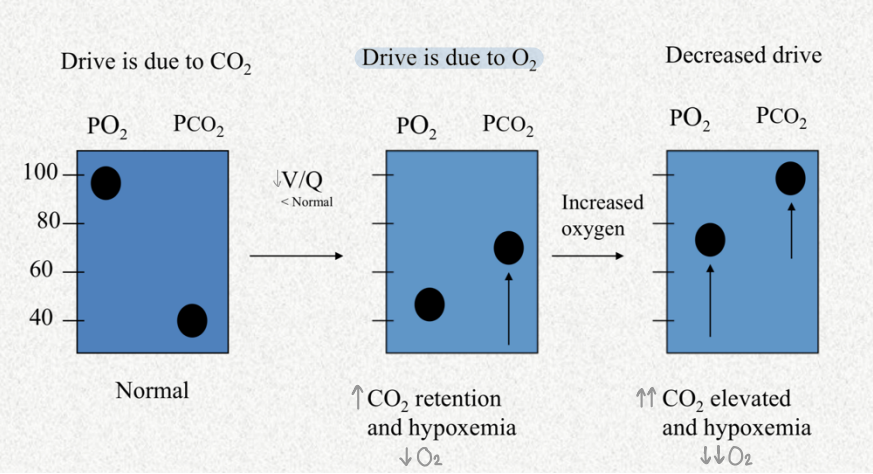
Alright, the take-home message from this delightful lecture is :

In patients with emphysema or COPD, it's crucial **TO NOT GIVE PURE OXYGEN** all at once !!!! Instead, oxygen should be administered **gradually** to avoid eliminating the hypoxic drive. For instance, it's safer to provide **42% O_2** rather than 100% oxygen, as this approach prevents excessive CO_2 buildup and reduces the risk of respiratory suppression.

PCO_2, can reach a value of 100 mmHg. This level is narcotic and can suppress ventilation totally. Hence too much O_2, can kill the patient: "too much of a good thing can kill you" !!!

The doctor also mentioned that we will have questions about the changes in measurements of patients with emphysema, like:

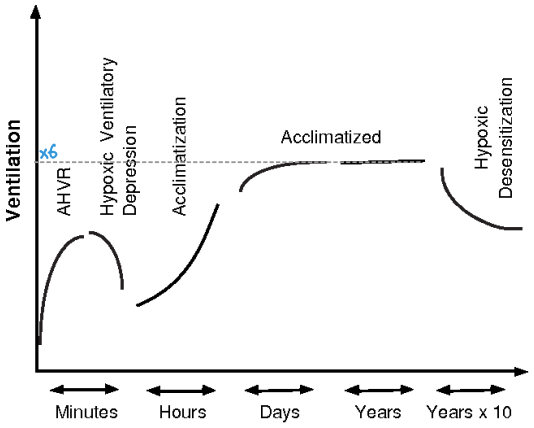
Parameter	Answer
1. PaO_2	Decreased due to impaired gas exchange caused by the destruction of alveolar walls.
2. $PaCO_2$	Often normal or slightly increased. In severe cases, CO_2 retention may occur due to hypoventilation.
3. Total Lung Capacity (TLC)	Increased because of hyperinflation and air trapping caused by the loss of elastic recoil.
4. Functional Residual Capacity (FRC)	Increased due to air trapping and hyperinflation.
5. DLCO	Decreased because the destruction of alveolar walls reduces the surface area available for gas exchange.
6. Pulmonary Vascular Resistance (PVR)	Increased due to capillary bed destruction and hypoxic vasoconstriction, which can lead to pulmonary hypertension in advanced cases.
7. Drive for Ventilation	In emphysema, ventilation is driven by CO_2 in the early stages, but in chronic stages, due to CO_2 retention and hypercapnia, the central chemoreceptors become desensitized, and low O_2 levels (PO_2) take over as the primary drive for ventilation.



In normal individuals, ventilation is driven by CO_2 levels, with oxygen levels remaining adequate. However, in patients with emphysema, there are low oxygen levels (hypoxemia) and high CO_2 levels (hypercapnia). If supplemental oxygen is provided to increase oxygen levels, ventilation may be suppressed due to the loss of hypoxic drive. This suppression leads to further CO_2 accumulation, creating a **feedback loop** that inhibits the dorsal respiratory group, potentially causing apnea and death.

ACCLIMATIZATION TO HIGH ALTITUDES:

- When a person ascends from sea level to higher altitudes, alveolar ventilation increases, initially and immediately from 1 to 2 (1 indicates a ventilation rate of 4.2 L/min, so it can get doubled to 8.4 L/min). After few days, ventilation rate continues to rise and can reach 5 to 6 times the sea level's rate (acclimatized level, their new NORMAL levels), a process called **acclimatization**. This increase in ventilation is a response to the drop in PO2 below 60 mmHg (hypoxia).

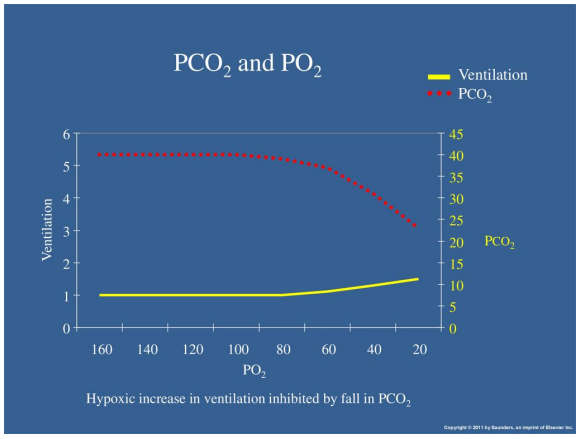


(The carotid bodies, which are sensitive to hypoxia, are also sensitive to increased PCO2, but their sensitivity to CO2 (also via the increase in H+) is weaker, around 1/7th of the central chemoreceptors' sensitivity but 5x faster. The carotid bodies respond quickly to changes in PO2 and PCO2, but their response is less powerful and effective, although it's faster (كأنّه أول واحد جاوب، بس جوابه مش كامل). If we removed the afferent nerves supplying the carotid and aortic bodies, the body would still respond similarly to changes in ABGs and pH, but after a longer duration)

- As **ventilation increases**, it leads to two changes: a **rise in PO2** and a **decrease in PCO2**, especially in the alveoli.

- Now, in the first day, there is a peripheral stimulation of the carotid bodies mainly due to hypoxiemia (reduced arterial PO2) and. With the increased ventilation, lower CO2, thus lower hydrogen ions, will suppresses the respiratory drive.

- Therefore, the body has two **antagonizing signals:** the main one is **hypoxia stimulating ventilation**, and **the decreased PCO2 (hypocapnia)** that works against it 🥷



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

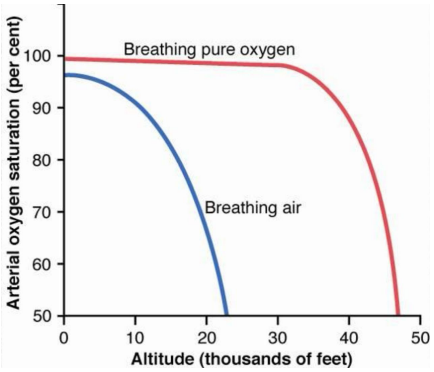
- Because of this, initially, hypoxia may not cause its full effect on increasing the alveolar ventilation (like the hypoxia can't fully express itself 😔). The ventilation might increase by only 1-2 times instead of the expected 6 folds increase. To reach the full expected adaptation , the **kidneys** must compensate for the respiratory alkalosis (high HCO3-) that has happened, how will that happen?! Over 3-5 days, the kidneys excrete more bicarbonate in the urine and reabsorb less, which helps to bring the blood's pH back to normal and allows the respiratory system to respond more effectively to hypoxia.

$$\leftrightarrow PH = 6.1 + LOG \frac{\downarrow[HCO_3^-]}{\downarrow[CO_2]}$$

TO SUM UP :

High altitude → hypoxia → peripheral chemoreceptor stimulation → increased ventilation → higher CO_2 loss in exhalation → lower H+ levels → higher pH → respiratory alkalosis → inhibition of respiratory center (high pH antagonizes the increased ventilation)→ kidney excretion of bicarbonate → decreased CSF bicarbonate → full respiratory center activation (restoring respiratory drive after renal compensation 💪)→ ventilation increases to 5-6x normal (after acclimatization)

Physiological Acclimatization (adjustments to high altitudes):

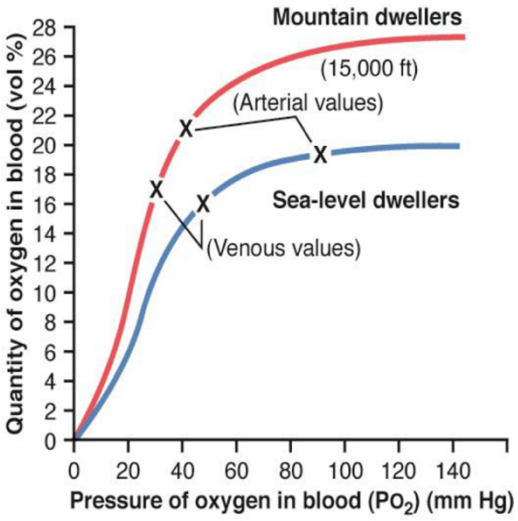


1. Increased ventilation: (as we discussed now)
   a. Due to decreased PO_2
   b. The increase is slowed by decreased PCO_2
   c. Ventilation increases by 70% in the first day and 400-500% in the coming few days

(Initially, the increased ventilation lowers PCO_2, causing respiratory alkalosis, which slows further ventilation. However, over a few days, the kidneys compensate by excreting bicarbonate (HCO_3^-), restoring pH balance and removing the inhibitory effect of alkalosis, allowing ventilation to increase further)

2. Increased hematocrit (content)
3. Increased diffusing capacity
4. Increased capillarity

This diagram compares the relationship between the partial pressure of oxygen (PO_2) and the oxygen-carrying capacity in the blood of mountain dwellers (red curve) and sea-level dwellers (blue curve)



- Key Difference: **Mountain dwellers**, living at high altitudes, have adapted to low oxygen environments (e.g., 15,000 ft) by increasing their hematocrit (PCV), which enhances their oxygen-carrying capacity lower oxygen availability in the atmosphere. So, at a PO_2 of around 40 mmHg (venous values), the oxygen content in mountain dwellers is significantly higher than that of sea-level dwellers. This difference is due to the elevated red blood cell count and hemoglobin levels in mountain dwellers.

❓ What is the atmospheric PO_2 at 10,000 ft (barometric pressure = 508 mmHg)?

The person has normal alveolar ventilation.

A. 95 mmHg

B. 106 mmHg

C. 149 mmHg

D. 159 mmHg

Answer:

Percentage of Oxygen is constant, 21%, so you just multiply it with the total pressure, which is 508 mmHg, getting an atmospheric pressure of Oxygen with **106 mmHg.**

🩸 ANEMIA:

- In patients with anemia (e.g., from bleeding), where the H**emoglobin** level drops from 15 g/dL to 9 g/dL, the **PO_2**, **PCO_2** remains normal and **Saturation** remains at 100%. However, **the overall Oxygen carrying capacity of the blood** (mL/dL) decreases because there is less hemoglobin available to carry oxygen. Although oxygen saturation is 100%, the **Volume of $O_{2\ (mL)}$ that can be carried** in the blood (dL) is reduced which results in low **venous PO_2** and **low venous O_2 saturation**. Sooo 👇
  - Arterial PO_2: Normal in anemia
  - Venous PO_2: Reduced due to increased oxygen extraction by tissues
    This reflects the body's effort to maintain adequate oxygen supply to tissues despite reduced oxygen-carrying capacity

❓ What is the effect of anemia on ventilation? no effect (neither increase nor decrease)

❓ Blood transfusion to anemic pts effect: just the O2 concentration increase (no effects on po2 and poco2)

❓ A patient with **HEMOGLOBIN = 10 G/DL**, calculate the oxygen carrying capacity:

- **OXYGEN CARRYING CAPACITY PER 1 GRAM OF HEMOGLOBIN** = 1.34 mL
- **10 G/DL × 1.34 ML/G × 100% (SATURATION LEVEL)** = **13.4 ML/DL OF OXYGEN** carried by hemoglobin at 100% saturation.

❓ If the saturation is 90%, calculate the oxygen carrying capacity:

- **90% SATURATION = 13.4 × 0.9** = **12.06 ML/DL OF OXYGEN** carried at 90% saturation.

❓ Following the previous question: If the oxygen extraction ratio is 33%, this means the tissues have extracted one-third of the oxygen, and only two-thirds of the oxygen remains in the venous blood:

- **33% EXTRACTION** of 12.06 mL = **4 ML** of oxygen extracted.
- Therefore, the **VENOUS OXYGEN CONCENTRATION** would be: **12 ML/DL - 4 ML/DL** = **8 ML/DL of oxygen** remaining in the venous blood.

- Co poisoning: Oxygen Saturation Curve shifts to the left, low O_2 sat, low [O2] concentration, normal PO2 and PCO2. So, Breathing CO acutely will ____ respiration? A. Increase B. Decrease C. No change
  Answer is: No change (because PO2 and PCO2 are normal, so no stimulation of chemoreceptors)

Remember: $PO_{2(50\%)}$ = **26 MMHG** (which means 50% of hemoglobin is saturated with Oxygen, its partial pressure is 26 mmHg

- let's say you have a skeletal muscle, and we know that it extracts around 5 mL of oxygen per 100 mL of blood, which is about 25%. Now, if I increase the blood flow while keeping the metabolism constant—or if I keep the blood flow constant and increase the metabolism—you need to check what happens to PO_2 and PCO_2? Go back to Lecture 8

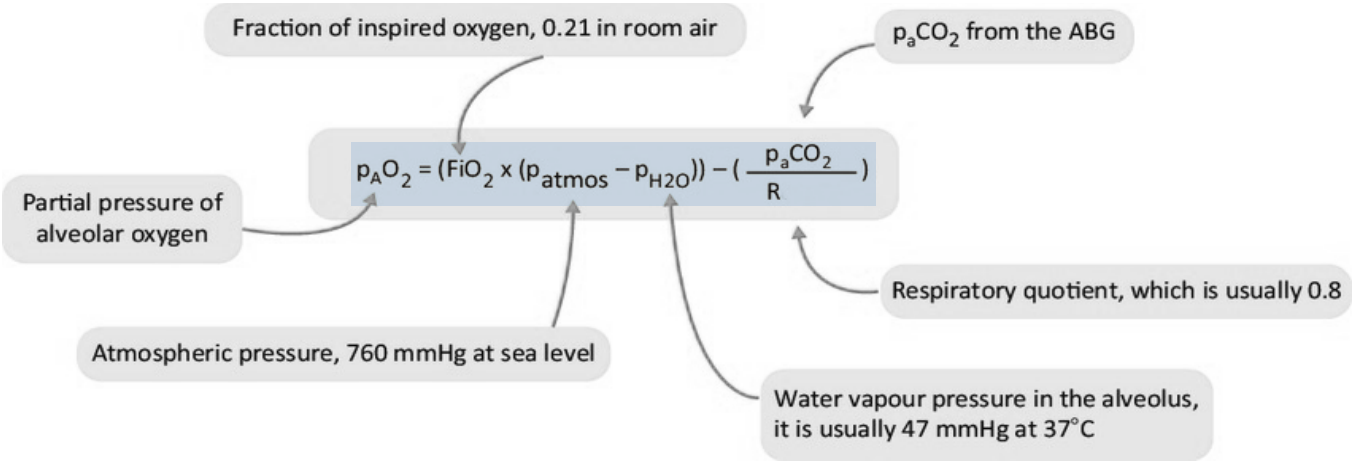
Voluntary Apnea and CO_2 Buildup:

- When someone stops breathing voluntarily (voluntary apnea) for a minute, the primary drive to resume ventilation is the buildup of carbon dioxide (CO_2) in the blood, which increases the arterial partial pressure of CO_2 ($PaCO_2$). This rise in CO_2 leads to an increase in hydrogen ion (H^+) concentration due to the formation of carbonic acid, which stimulates the central chemoreceptors in the medulla. While low oxygen (hypoxia) can also contribute to the drive to breathe, the primary and most immediate trigger is the accumulation of CO_2 and the resulting **acidosis**.

⚠ **WARNING!** The doctor mentioned this question that may pop up in the exam:

- A patient with acute respiratory distress syndrome (ARDS) is connected to mechanical ventilation with an oxygen concentration of 70% (FiO_2 = 0.7) instead of the normal atmospheric oxygen concentration of 21% (FiO_2 = 0.21). The patient has an arterial partial pressure of oxygen (PaO_2) of 90 mmHg. Calculate the alveolar-arterial (A-a) gradient for oxygen using the alveolar gas equation.

To calculate the **A-a gradient**, we use the alveolar gas equation to find the alveolar PO2:



Apply our inputs to the equation, with FiO2 being 0.7, PaCO2 is assumed to be at normal levels: 40 mmHg then find PO2, which will be 449.1 mmHg. Then find the difference between alveolar and arterial PO2, which will be 359.1 mmHg.

🏋️ RESPIRATION DURING EXERCISE:

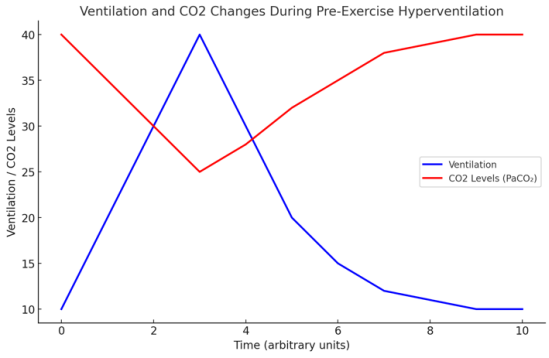
- Linear increase in ventilation with increasing oxygen consumption. Ventilation increases linearly until it reaches VO_2max.
- O_2 consumption at rest is 250 ml/min. In exercise, it increases 20-fold (5,000 ml/min).
- Arterial PO_2, PCO_2, and pH do not change during exercise.
- In contrast, $PaCO_2$ may decrease slightly

❓ What drives ventilation during exercise?

1) Ventilation increases immediately (instantaneously) with the onset of exercise, then it gradually increases to a final value, which is determined by **the severity of the exercise**. The more strenuous the exercise, the greater the initial rise at the onset and the higher the final level of ventilation. Following exercise, there is an immediate decrease in ventilation, followed by a more gradual return to the resting level.
2) Because of the initial increase in ventilation (before muscle movement), the $PaCO_2$ would decrease slightly. Then, **exercising muscles produce ↑CO_2,** which brings $PaCO_2$ back to normal levels, where it remains until the end of exercise. **When muscles stop exercising (end of exercise), ventilation decreases instantly**, causing an increase in $PaCO_2$, which **stimulates the respiratory center**. This increases ventilation slightly, and then it decreases gradually but remains higher than resting levels due to the oxygen debt.
3) Overflow of signals from the cortex (more impulses are transmitted through the phrenic nerve to increase the rate of contraction of diaphragm, thus inspiration)
4) Body movements (Afferent fibers from the highly active muscles may also stimulate the DRG to increase the rate of impulses)
5) Increased body temperature
6) Designed to control PCO_2
7) Learned response

Conclusion: We are not sure regarding the exact mechanism responsible for increased ventilation during exercise.

Before starting a marathon 🏃, some individuals engage in hyperventilation, increasing their ventilation rate even though they are not yet producing extra carbon dioxide (CO_2) from physical activity (muscles). This leads to a reduction in the ($PaCO_2$) in the blood since the CO_2 being exhaled exceeds the amount being produced. As CO_2 levels decrease, the drive for ventilation diminishes, resulting in a subsequent decrease in ventilation. Observe the extra diagram ➡️



The End of Respiratory Physiology 🤭