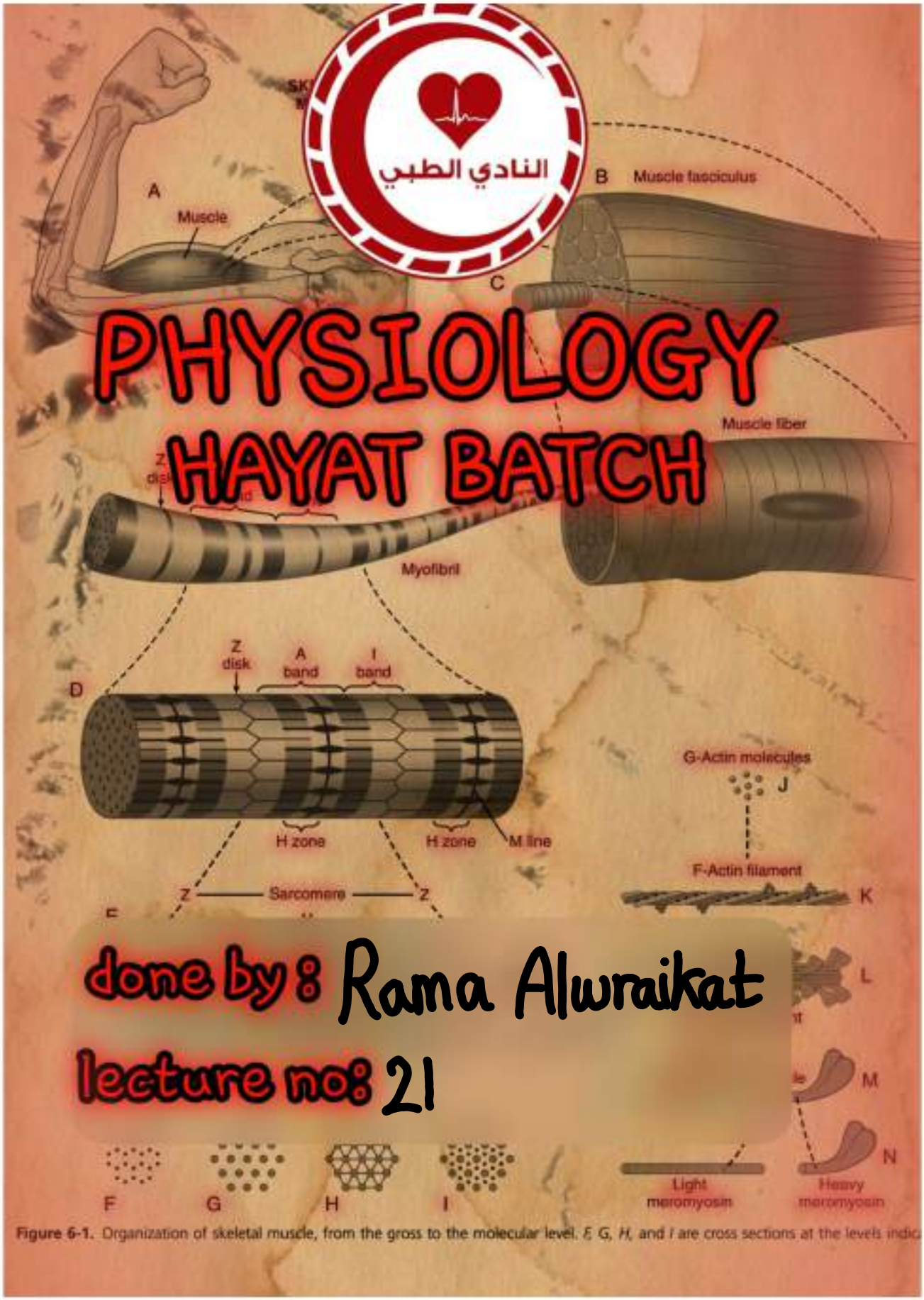


Figure 6-1. Organization of skeletal muscle, from the gross to the molecular level. *E*, *G*, *H*, and *I* are cross sections at the levels indic

Acid-Base balance I

Overview of the Respiratory regulation of acid-base balance

Physiology Lecture 21

Dr. Waleed R. Ezzat

Lecture Objectives:

- Define the meaning of buffer systems.
- Recognize the chemical acid-base buffer systems of the body fluids. Intra and extracellular buffers.
- Understand the overview of the respiratory regulation of acid-base balance

Homeostasis ← تحافظ على الأمور في الجسم

PH = H^+ Concentration of extracellular fluid ← من الأمثلة على ذلك

بحيث تعتمد عليه عمل الأنزيمات في الجسم وإذا تغير PH في الجسم ماراح تشتغل الأنزيمات بشكل طبيعي

* الحوامض الموجودة في الجسم من نوع (weak acids) وبشكل رئيسي (H_2CO_3 - Carbonic Acid) وهو لد يتأين بشكل كامل بل يتأين إلى CO_3/H_2 ويبقى جزء غير متأين على شكل H_2CO_3

* H^+ يتكون في الخلية من metabolism يكون في Intracellular fluid ومن يخرج إلى Extracellular fluid إذاً أعلى تركيز H^+ يكون في ECF ثم Interstitial fluid ويكون تركيزه أيضاً أعلى من Venous Blood (الدم في الوريد) وهو more acidic مقارنة بالدم في الشريان Arterial إذاً Body fluids or ECF هي تميل Acidic or Alkaline ؟ هي تميل Alkaline (قاعدية) لأنها لحتيمة موجبة ± الذي يعتبر neutral (متعادل)

Introduction:

- Precise H^+ regulation is essential because the **activities of almost all enzyme** systems in the body are influenced by H^+ concentration.(PH)
- Most acids and bases in the extracellular fluid involved in normal acid-base regulation are **weak acids and bases**, such as (H_2CO_3) acid and (HCO_3^-) base. ← الدم في الشريان
- The normal arterial blood [H^+] is **40 nEq/L** which is equivalent to pH of **7.4**, whereas the pH of venous blood and interstitial fluids is about **7.35**. ← الدم في الوريد
- Intracellular pH is slightly lower than plasma pH because cell metabolism produces acid.

	H^+ Concentration (mEq/L)	pH
Extracellular Fluid		
• Arterial blood	• 4.0×10^{-5}	• 7.40
• Venous blood	• 4.5×10^{-5}	• 7.35
• Interstitial fluid	• 4.5×10^{-5}	• 7.35
Intracellular fluid	1×10^{-3} to 4×10^{-5}	6.0–7.4

metabolism ← تختلف قيمته حسب

تكلمت خطوط دفاعية

3 Systems that regulate the $[H^+]$ in the body fluids to prevent *acidosis* or *alkalosis*:

1. Chemical acid-base buffer systems (acts **immediately** to combine with an acid or a base to prevent excessive changes in $[H^+]$). Chemical buffer systems do not eliminate or add H^+ to the body but only keep them tied up until balance can be re-established.
2. The respiratory center which regulate the removal of extracellular fluid CO_2 (the second line of defense)
3. The kidneys which can excrete either acidic or alkaline urine (the **most powerful** of the acid-base regulatory systems)

Buffer إما ← Weak Acid + it's salt (ملح) ← الهدف منه المحافظة على PH من التغير الكبير
Weak Base + it's salt

- **Two types of acids** are produced in the body; volatile and nonvolatile acids

1. **Volatile acids** is CO_2 which combines with H_2O to form the weak acid H_2CO_3 which dissociates into H^+ and HCO_3^-. The enzyme **carbonic anhydrase** is present in most cells and catalyzes the reversible reaction between CO_2 and H_2O.

HCO_3^- ← Bicarbonate

هو عبارة عن Acid يتحول إلى غاز و يخرج خارج الجسم

في البداية CO_2 يتحول إلى حامض ضعيف (Buffer) وبنفس الوقت رح يكون وسيلة لنقل CO_2 من الخلايا إلى الرئتين

عندنا غازين الأكسجين وثاني أكسيد الكربون و أحلامهم خوبان في الماء هو غاز CO_2 وصار أنقل (وزنه أكثر)

والاكسجين لأنه قليل الذوبان في الماء خله carrier ينقله في plasma وهو Hemoglobin أما CO_2 يذوب في الماء ويذوب في البلازما

ويتحد مع الماء H_2O ليكون Buffer $CO_2 + H_2O \rightarrow H_2CO_3$ ويوجد إنزيم في جميع خلايا الجسم يساعد على اتحاد CO_2 مع H_2O وإنتاج H_2CO_3

Carbonic Anhydrase ← الذي يتأين إلى H^+ / HCO_3^- حتى وصولهم إلى lungs يتحدوا و يكونوا CO_2 ويخرج خارج الجسم

2. Nonvolatile acids are also called **fixed acids** such as *H_2SO_4 (from protein catabolism) and *phosphoric acid (from phospholipids catabolism).

Other fixed acids as ***ketoacids**, ***lactic acid**, and ***salicylic acid** may be produced in incomplete fatty acid oxidation as in uncontrolled diabetes mellitus, starvation, and alcoholism.

الجوع ← → إدمان الكحول

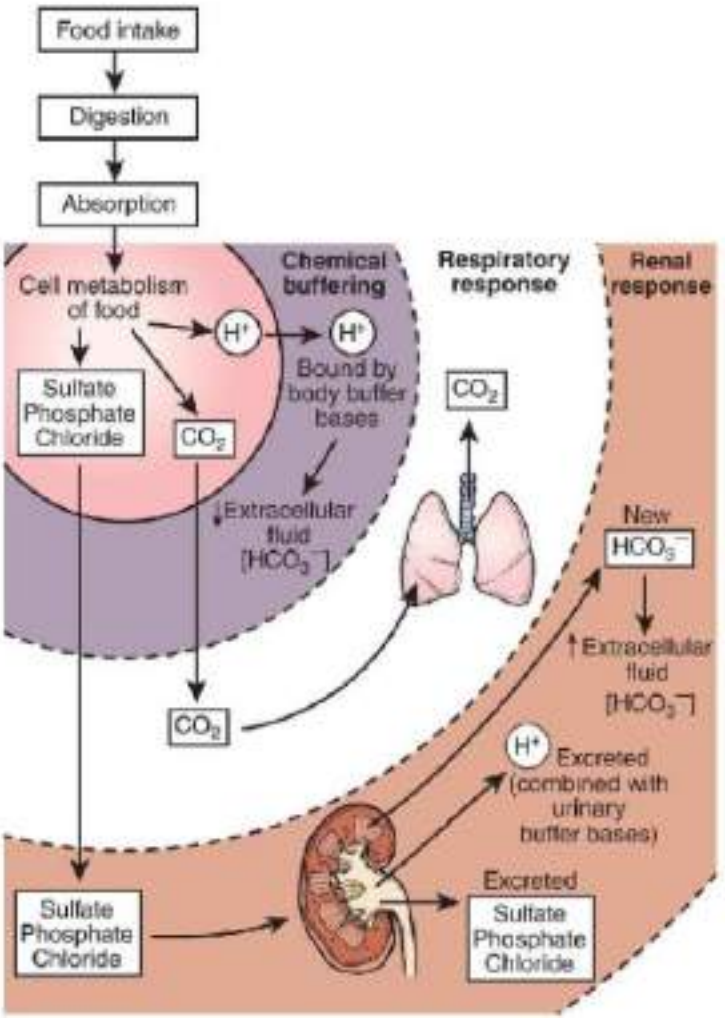
Nonvolatile acids are buffered in the body and are then excreted by the kidneys.

Nonvolatile Acids → fixed Acids → لا تتحول إلى غاز

H_2SO_4 = Sulfuric Acid

Salicylic Acid = Aspirin

*مريض السكري يحدث عنده زيادة في ketoacids مما يؤدي إلى PH يهبط on acidic side ← تسمى ketoacidosis



- The chemical acid-base buffer system is composed of extra and intracellular buffers

1. **Extracellular buffers**
   - CO_2/HCO_3^- (the major)

     $CO_2 + H_2O \leftrightarrows H_2CO_3 \leftrightarrows H^+ + HCO_3^-$

     $$pH = 6.1 + \log \frac{HCO_3^-}{0.03 \times PCO_2}$$ Henderson-Hasselbalch eq.

     HCO_3^- → concentration of HCO_3^-

     PCO_2 → Partial Pressure الضغط الجزيئي
   - Phosphate [$H_2PO_4^-/HPO_4^{-2}$] (the minor). However, it is most important as a urinary buffer

     (the minor) ← أقل أهمية

     $H_2PO_4^- \leftrightarrows H^+ + HPO_4^{-2}$
2. **Intracellular buffers**
   - Organic phosphates (such as AMP, ADP, ATP, and DPG)
   - Proteins (such as the **hemoglobin** which is the major protein buffer)

Phosphate → Urinary Buffer → كان في البداية تركيزه قليل لكن ما كله ينزل في kidneys ↓ Renal tubule وينسحب HCO_3^- / CO_2 يصبح تركيزه عالي

سحنة البروتينات سالبة فممكن تستقبل H^+ وأكبر بروتين في RBCs هو Hemoglobin كذلك Organic Phosphate يعتبر يستقبل H^+

كيف يكون خط دفاع فعّال ضد Respiratory System ؟ acidity

التخلص من جزيء CO_2 واحد يعادل التخلص من أيون H^+ واحد

الأن إذا زاد $\uparrow H^+$ رح يتحرك التفاعل بهذا الاتجاه $H_2CO_3 \longleftarrow HCO_3^- + H^+$ سوف يسبب زيادة H_2CO_3 مع نقصان HCO_3^-

ثم $H_2CO_3 \longleftarrow H_2O + CO_2$ lungs تطرح CO_2 فكأنها تخلصنا من H^+ فزيادة الحموضة يصاحبها زيادة في التنفس (Hyper ventilation)

فإذا كان في مشكلة في kidneys وإنها لا تستطيع طرح fixed acids هنا يسبب زيادة الحموضة التي تسمى Acidosis

* أما في حال وجود مشكلة في lungs فهنا أيضًا يحدث Acidosis بسبب زيادة acidity بسبب Volatile Acids وهنا مطلوب من kidneys تصلح الوضع إن أمكن، زيادة CO_2 سيحرك التفاعل $H_2CO_3 \longleftarrow H_2O + CO_2$ وبالتالي تزداد الحموضة $HCO_3^- + H^+$

The Respiratory System

الزفير الرئوي

- Pulmonary expiration of CO_2 **balances** intracellular metabolic formation of CO_2 and the PCO_2 of the extracellular fluid.
- Whenever $[H^+]$ increases above normal, the respiratory system is stimulated, and alveolar ventilation increases. This mechanism decreases the PCO_2 in extracellular fluid and reduces $[H^+]$ back toward normal.

$$\uparrow[H^+] \rightarrow \uparrow \text{alveolar ventilation} \rightarrow \downarrow PCO_2$$

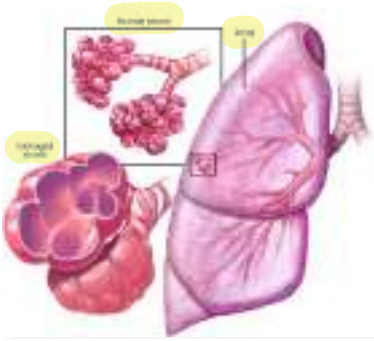
- Respiratory system acts as such as a typical **negative feedback controller** of hydrogen ion concentration. The gain is about -1 to -3 (50 to 75% effectiveness).
- The buffering power of the respiratory system is **1-2 times** as great as the buffering power of all other chemical buffers.

خلل

- Impairment of lung function such as in **emphysema** can cause **respiratory acidosis**. Here the kidneys become the sole remaining physiological mechanism for returning pH toward normal.

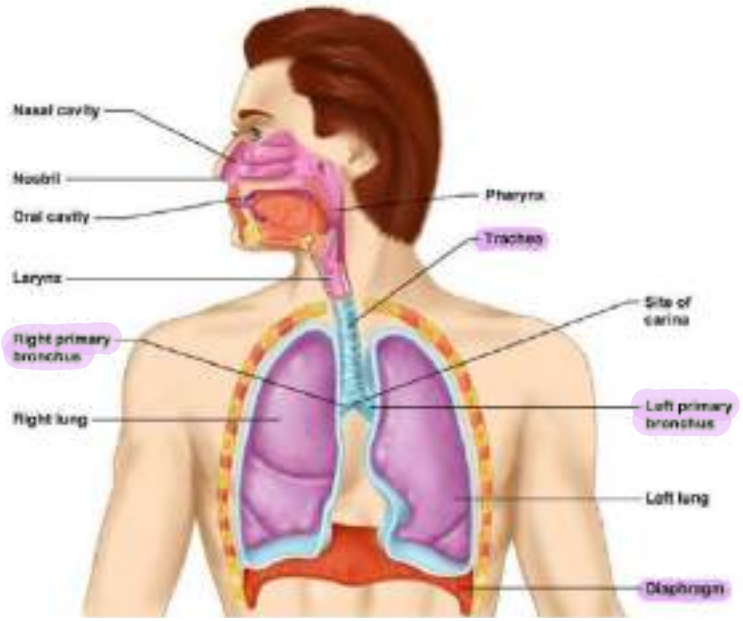
الأن زيادة CO_2 بسبب التدخين تبدأ الرئتين بالتكيف وتتمزق الجدران بين الحويصلات الهوائية ومساحة السطح لتبادل الغازات والرئتين فيها elastic tissue يبدأ يتمزق ← مرض Emphysema يكون شكل chest مثل البرميل Barrel shaped

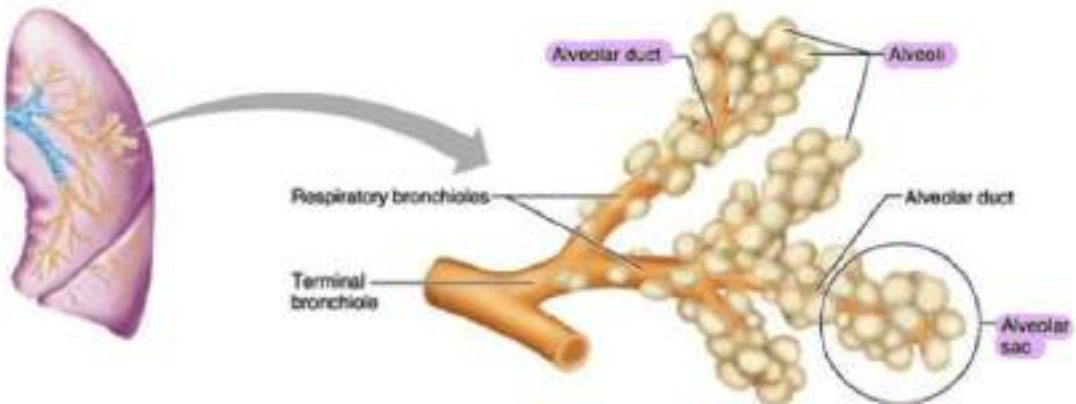
Respiratory Acidosis



هذا الدكتور ما شرحه بس حكا اقرأوه

- Air passages; trachea → bronchi → (branching) → respiratory bronchioles = end branches of "bronchial tree"
- Thoracic cavity; lungs are surrounded by pleural membrane (double membrane with lubricating fluid in between), situated inside rib cage and above diaphragm
- Sites of gas exchange; alveoli are the sites of gas exchange = outpouchings of wall of respiratory bronchioles (alveolar sac looks like a bunch of grapes). Alveoli have large total surface area (about the size of a tennis court); each alveolus is surrounded by a web of capillaries





كيف بتتنفس و كيف بيدخل الهواء للرئتين ؟

في الجهاز التنفسي يوجد شيئين متعاكسين في اتجاه الحركة وأولهما lungs تحب تكش لأنه يحيط بها elastic tissue بينما chest العكس يحب يكبر وعظام القفص الصدري يبعد للاعلى

الآن عملية الشهيق Respiration ترفع عظام القفص الصدري للاعلى وحجم chest يزيد عن طبيعته عهلات وهذا يزيد الفراغ بين الرئتين و القفص الصدري فيصبح الضغط more negative فالرئتين تشفط الهواء ⟸ Respiration is an active process because we are using our muscles to increase vertical & transverse & anteroposterior diameters so that increases negativity & decreases pressure inside lungs less than Atmospheric pressure (الضغط الجوي)

رح ينتقل الهواء من الضغط العالي للأقل فيدخل داخل القصبة الهوائية للحويصلات

أما الزفير chest ينزل يضغط على lungs و يضغط الحويصلات فيزداد الضغط فيها و يصير أعلى من الضغط الجوي فالهواء الذي داخلها يخرج

- Increase size of thoracic (chest) cavity → **negative pressure** so that air is "pulled" into the lungs when we inhale (air pressure inside lungs is lower than atmospheric pressure) ← عند الشهيق
- To increase chest cavity size:
  1. Use "**intercostal**" (rib) muscles to pull ribs up and out (expanding rib cage; mainly occurs only during deep breathing)
  2. Contract **diaphragm muscle** to "flatten" dome (this is the major means of inhaling when at rest)
- To decrease chest cavity size: relax diaphragm and rib muscles
- Inhaling involves muscle *contraction*; exhaling is normally *passive* (muscles relax) ← عند الزفير

* Hemoglobin فيه → Heme group (iron + O_2 مكان ارتباط)

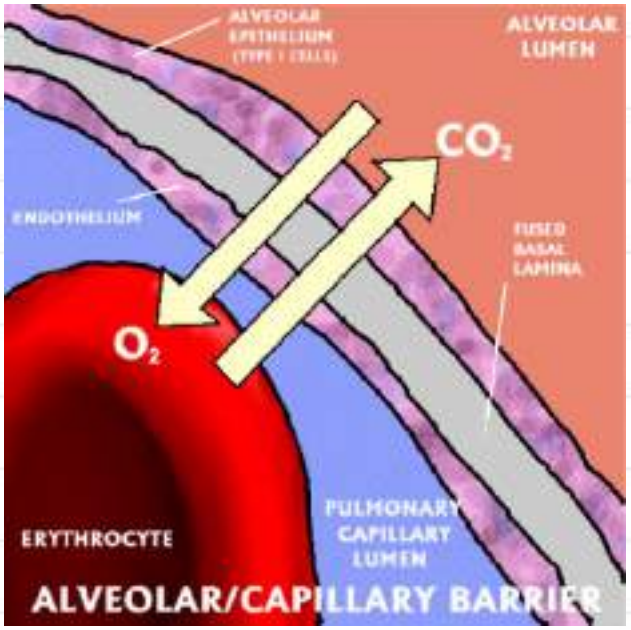
23% of → Carbon dioxide (CO_2)

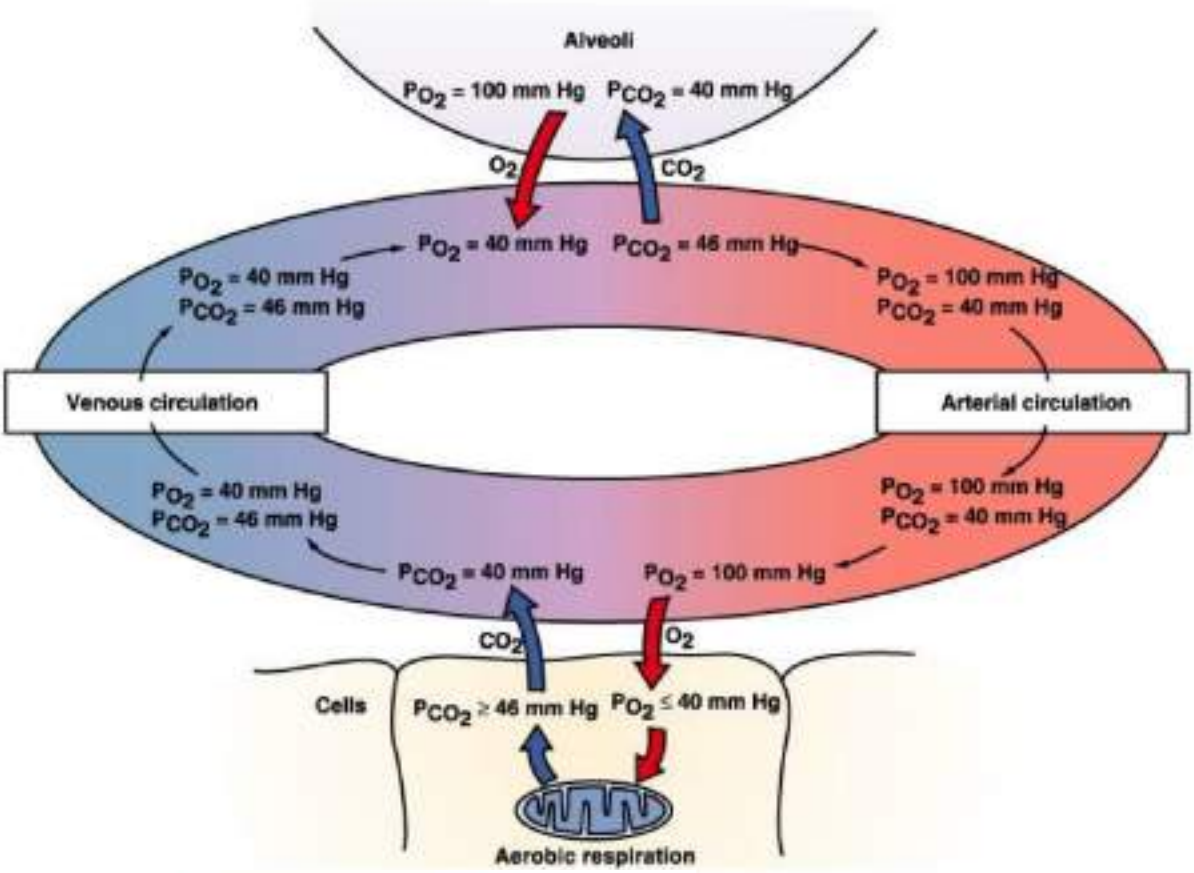
O_2 بتتعلق في Heme group مكان تكون ليس

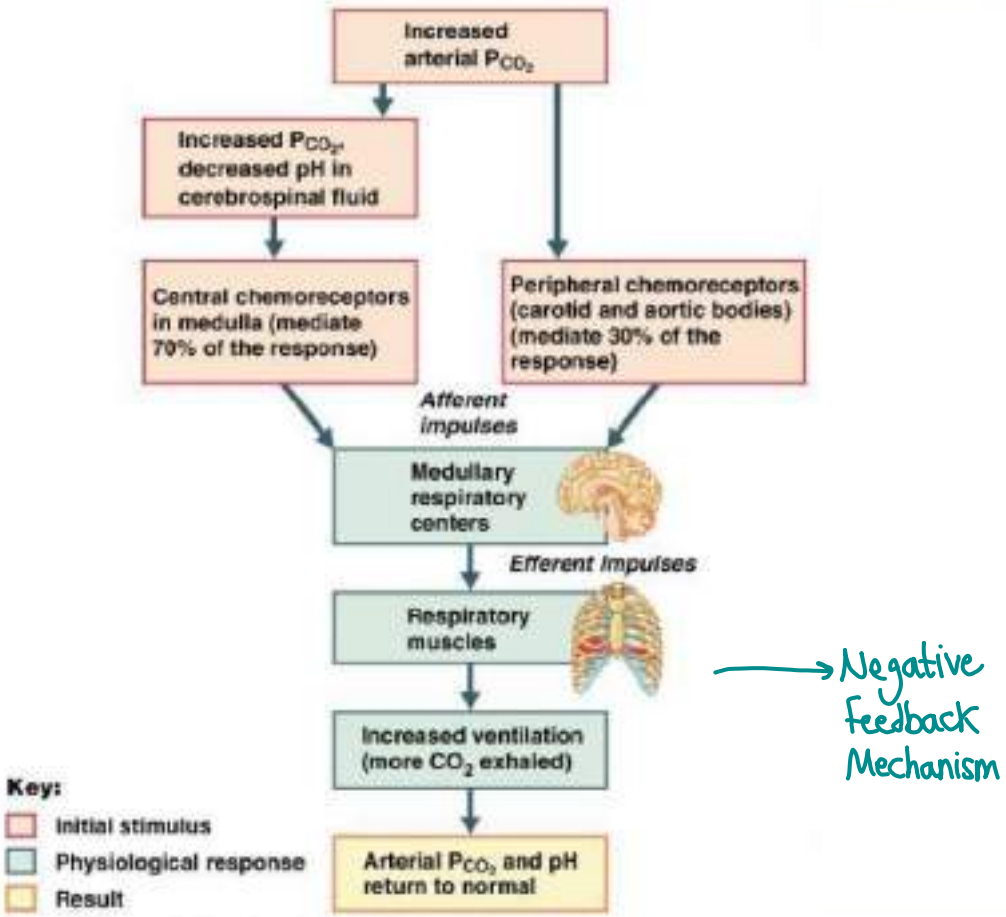
Gas exchange and transport

- Diffusion is rapid between alveoli and lung capillaries; gases diffuse down their concentration gradients
- Note: "concentration" refers to the amount of gas that is actually dissolved in the blood = "partial pressure". This does not include gases complexed with Hb or carried in the form of carbonic acid. → H_2CO_3 — Hb → Hemoglobin
- Partial pressure of oxygen (PO_2) is high in alveoli, low in pulmonary arteries → oxygen diffuses into blood; partial pressure in body capillaries is higher than in tissue fluid → oxygen diffuses out of body capillaries
- Hb can pickup four molecules of oxygen = **oxyhemoglobin (HbO_2)**; strength of binding is fairly weak, depends on partial pressure of oxygen. Hb releases oxygen rapidly where oxygen pressure is low as in the tissues
- **70%** of carbon dioxide is carried in blood as **carbonic acid**; 23% is carried bound to Hb (**carbaminohemoglobin**)

70% → تذوب كذوبان السكر في الماء







→ Negative Feedback Mechanism

Respiratory Center ← هو المتحكم في عملية التنفس حيث يبعث impulses تعمل تقلصات في العضلات الهيكلي ويحدث التنفس وهو موجود في الدماغ

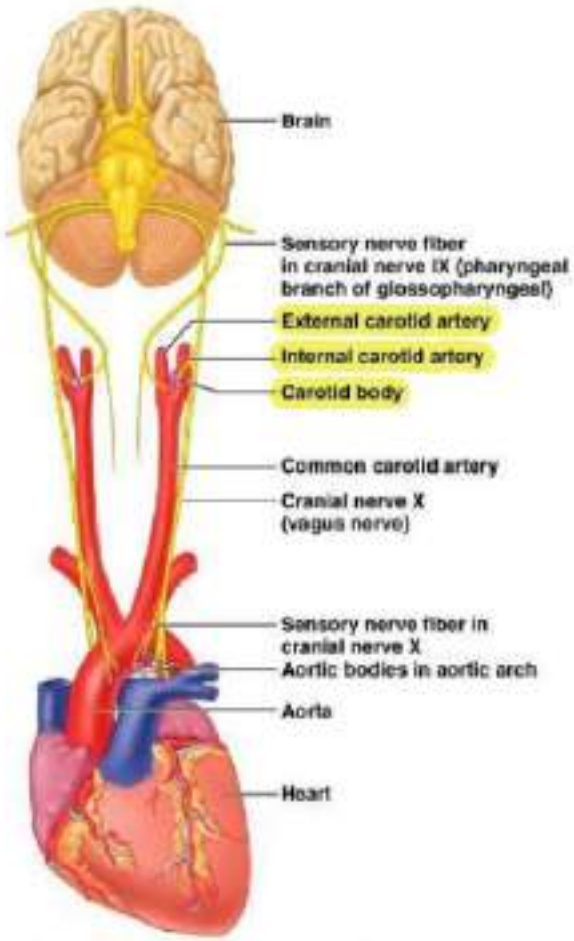
Medulla Oblongata ← الجزء الأول منه اسمه foramen magnum ← الحبل الشوكي يمتد من العمود الفقري ويدخل للدماغ عن طريقه
↳ here respiratory center located

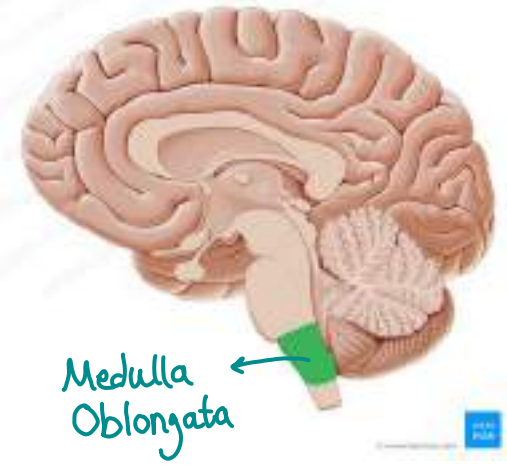
There are two chemoreceptors → Central Chemoreceptors → in → Medulla Oblongata → monitor → CO_2
→ Peripheral Chemoreceptors → in → Aortic arch
→ Carotid Sinuses (Carotid Bodies)
monitor → O_2 / CO_2 / PH (H^+)

* ما يرتفع CO_2 في الجسم يروح إلى Respiratory Center بإشارتين واحدة من Central Cemoreceptor وواحدة Peripheral Chemoreceptor فهنا Respiratory Center يزيد Respiratory Rate و يعمل Hyper Ventilation لكن إذا الأكسجين نقص أيضاً يروح معه Hyper Ventilation وإذا ارتفع H^+ في الجسم نفس الشيء يروح Hyper Ventilation ← من هذه الاثنين يستشعر Peripheral Chemoreceptor

Cerebrospinal fluid → fluid in the hollow spaces in the brain
↳ central cemoreceptor monitor CO_2 in cerebrospinal fluid
↳ CO_2 uses simple diffusion to enter cerebrospinal fluid from plasma (lipid soluble)

نسبة CO_2 في cerebrospinal fluid = نسبته في الدم لا فرق بينهما





The Respiratory System (cont.)
Control of respiration

- Nervous system controls rate and depth of breathing; the respiratory center is located in the **medulla oblongata**. It sends periodic signals to the diaphragm causing it to contract (10 -14 times per minute at rest)
- Respiratory center monitors blood PCO_2, PO_2, and blood pH by **chemoreceptors**: when blood carbon dioxide goes up, rate and depth of breathing increase
- Breathing faster and deeper causes the lung to get rid of more carbon dioxide → slow breathing (= negative feedback)
- * **Peripheral chemoreceptors** are found primarily in the carotid sinuses (**carotid bodies**) and the aortic arch. * **Central chemoreceptors** are found on the medulla oblongata
- The peripheral chemoreceptors monitor plasma PCO_2, pH, and PO_2
- Central chemoreceptors primarily monitor pH of cerebrospinal fluid. These receptors are the **major control** of respiration

The Respiratory System (cont.)
Control of plasma pH

- Changes in respiratory rate and depth can result in changes in plasma pH
- The respiratory system can correct and regulate the plasma pH. This occurs when there is a change in plasma pH that is not initially caused by the respiratory system itself
- **Metabolic acidosis** is typically caused by ingestion of too much alcohol (alcohol is metabolized to acetic acid), excessive loss of HCO_3^- in diarrhea, accumulation of excess lactic acid during exercise or shock, and the production of acidic ketone bodies as a result of starvation or in diabetic crisis $H^+ \uparrow / PH \downarrow$
- In response to metabolic acidosis, the respiratory rate and depth will rise as the body attempts to "blow off" CO_2. Ridding the body of CO_2 will help raise the plasma pH ← يحدث Hyper Ventilation
- **Metabolic alkalosis** is typically caused by excessive vomiting, excessive ingestion of antacids, or constipation $H^+ \downarrow$ ← إمساك
- In response to metabolic alkalosis, respiratory rate and depth will be slow and shallow. This will enhance retention of CO_2 and production of H^+ and thus will lower pH

* Antiacids ↓ مثل أدوية التي تخفف الحموضة من المعدة

Test Question:

Q. A patient with paralysis (شلل أو عجز) of the respiratory muscles suffered from an increase in $PaCO_2$ from 40 to 60 mmHg and an increase in the concentration of hydrogen ion in arterial blood from 40 mEq/L (pH 7.4) to 50 mEq/L (pH 7.3). As a result, which of the following would happen?

(CO_2↑ H↑ PH↓)

A. The plasma HCO_3^- would decrease. X
B. The pH of the urine would increase. decrease
C. The buffering capacity of plasma proteins is diminished. X
D. The central chemoreceptors would be stimulated.
E. The peripheral chemoreceptors would be inhibited. X
stimulated

قليلًا مِن التفاؤلِ يَصنعُ ألف طريق نَحو السَّعادةِ..

بالتوفيق

#النادي_الطبي

#معكم_خطوة_بخطوة