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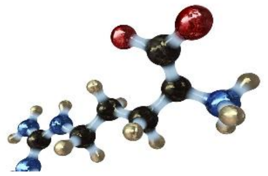


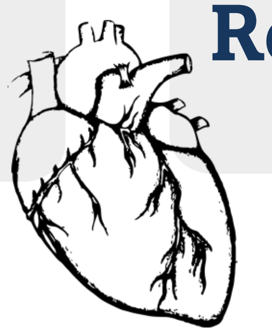
BioChemistry

﴿ وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ ﴾

MID | Lecture #5

pH and Buffers pt.3

Written by : Yamen Aljarrah
Alyaman Khalil



Reviewed by : Mohannad Barhoom

Color coding used in the modified:

- *Black: the original slides*
- *Navy Blue: the doctor’s explanation/words*
- *Gray: additional information and explanation*
- *Red: important information*

Biological buffers in human body

These buffers are very important in our body because they determine the protonation state of molecules (negatively or positively charged or neutral), for example (this example is important because these groups are present in the structure of proteins):

A. The carboxylic group would be neutral if protonated, and negatively charged if unprotonated.
B. The amine group would be positively charged if protonated, and neutral if unprotonated.

NOTES the prof mentioned in the lecture:

- A small movement in a hemoglobin molecule (less than 1nm) controls the structure and function of hemoglobin, and this small movement happens because of the protonation and unprotonation of carboxyl and amino groups in molecules (buffers are important here because they will regulate the protonation of these molecules).

- Lysosomes work in (5.00-5.50)Ph which is acidic and relatively low. This low Ph helps in changing the protonation state of the molecule that the lysosomes are going to break down, so the molecule loses its structure and becomes more accessible for lysosomes to break down and degrade the molecule.

- In the stomach, pepsin enzyme works in very low Ph(2.00), the enzyme would not be functional if the Ph is raised in the stomach. If someone has hyper acidity in the stomach(hurtburn) they would take antacids to neutralize the acid to relieve the pain but at the same time they would have indigestion (difficulties in digesting food) because the Ph is raised in the stomach.

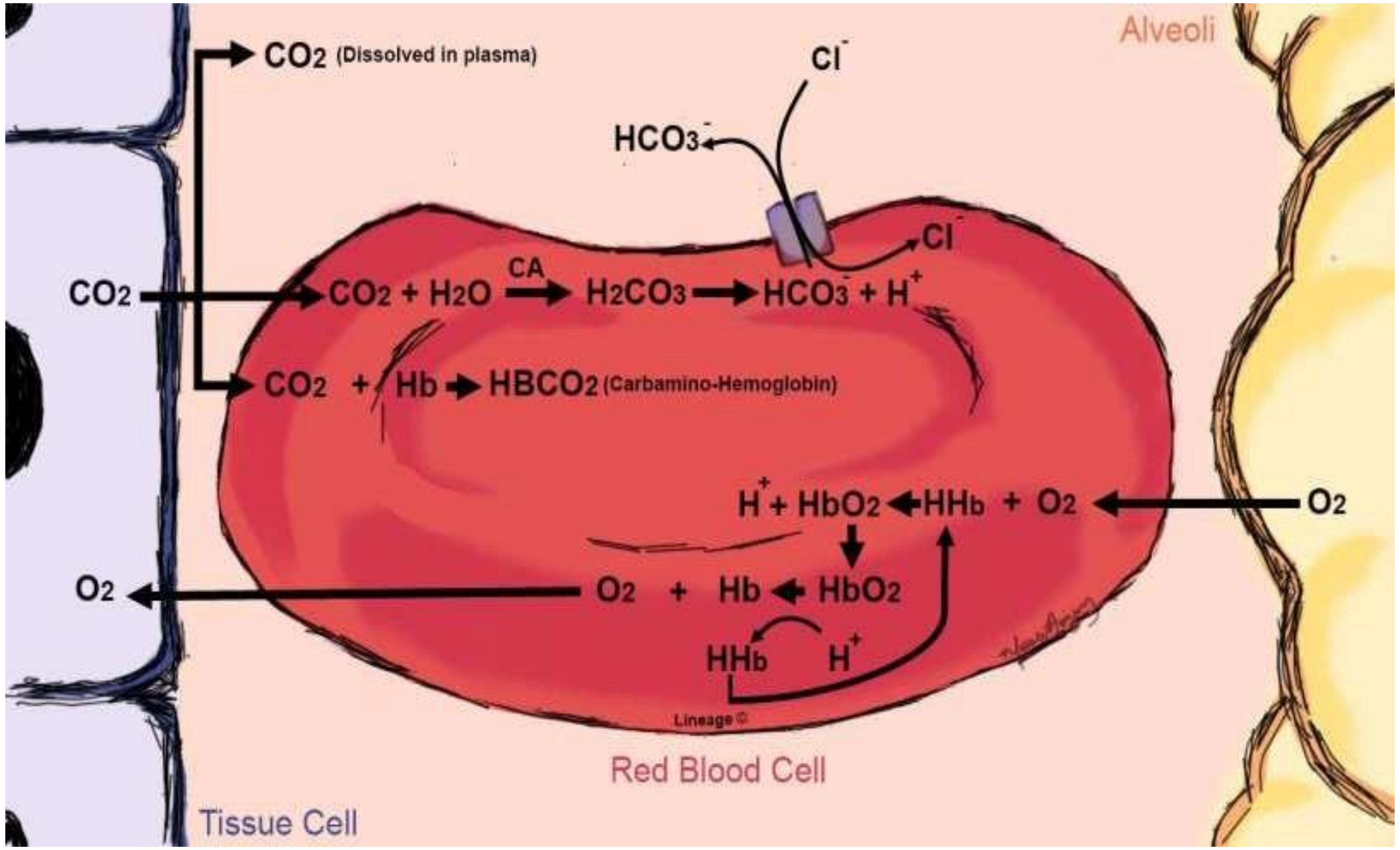
Biological buffers in human body

- Carbonic acid-bicarbonate system (blood) (most important buffer in blood)
- Dihydrogen phosphate-monohydrogen phosphate system (intracellular) (it's Pka value is near neutral (7.2) which helps keeping the cytosol pH neutral which is optimal for enzymes in the cytosol to work at high efficiency)
  - Metabolites: ATP, glucose-6-phosphate, bisphsphoglycerate (RBC) (these have a phosphate group which is negatively charged which makes the molecule acidic (low pKa))

    Metabolites are the small molecules, intermediates, and end products created during metabolism

- Proteins (they have carboxylic and amino groups and these affect the pH when protonation or deprotonation happens so they act as buffers by regulating the pH inside cells)
  - Hemoglobin in blood
  - Other proteins in blood and cells

Bicarbonate buffer in the human system



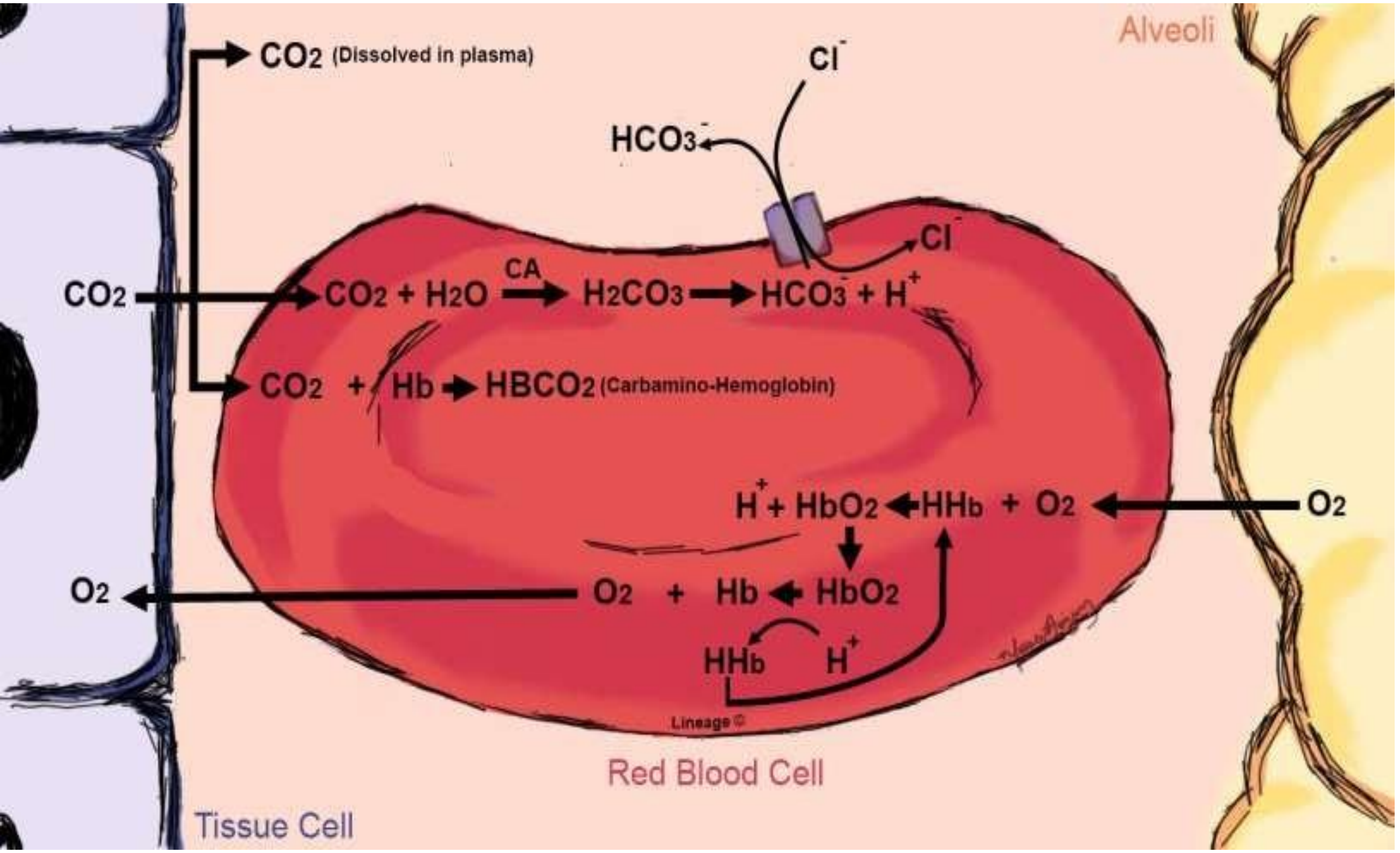
Note : lipophilic or hydrophobic gases like O2 and CO2 are not soluble in plasma , whereas hydrophilic molecule like HCO_3^- is soluble in plasma.

1. When you inhale, O2 diffuses out of the alveoli into the RBC because it is lipophilic, then it binds with the hemoglobin molecule.

2. O2 is released from the hemoglobin and it diffuses out from the rbc into the peripheral tissues.

3. CO2 is released from these tissues and it diffuses out into the RBC because it's lipophilic and hydrophobic. Inside the RBC , CO2 combines with H2O forming carbonic acid H2CO3 (this is an enzymatic reaction). In addition, some CO2 might bind with hemoglobin BUT most of it is converted to Bicarbonate ion and a proton.

Bicarbonate buffer in the human system



4. H2CO3 dissociates instantly into a bicarbonate ion HCO_3^- and a proton .

5. HCO_3^- Is kicked out of the RBC into the blood plasma "and Cl- enters the rbc instead" (it's hydrophilic because it's charged so it's soluble in plasma).

6. When the RBC reaches the lungs, HCO_3^- will enter the RBC again, and the reverse reaction takes place:

$(H^+ + HCO_3^- \longrightarrow H_2CO_3 \longrightarrow CO_2 + H_2O)$

Then CO_2 is exhaled out of the lungs.

Note: CO2 and the bicarbonate ion are both factors that buffers the blood pH

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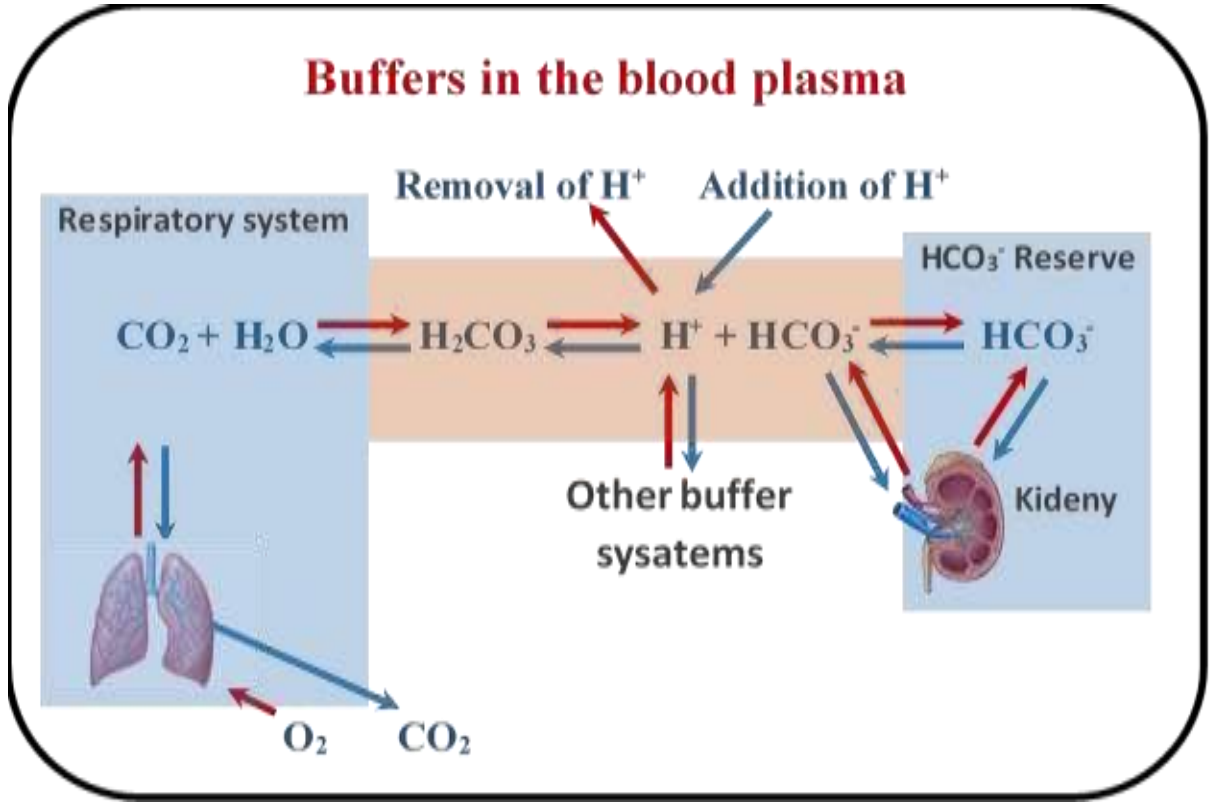
Bicarbonate buffer

These reactions happen with enzymes.



$$CO_2\,(d) + H_2O \underset{}{\overset{K_h}{\rightleftharpoons}} H_2CO_3$$

$$H_2CO_3 \overset{K_a}{\rightleftharpoons} H^+ + HCO_3^-$$

- Blood (instantaneously)

$$CO_2 + H_20 \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

Lungs

(within minutes)

Excretion via kidneys (hours to days)

Notes :

- CO_2 levels are controlled by the lungs by exhalation, while HCO_3^- levels are controlled by kidneys by urination.

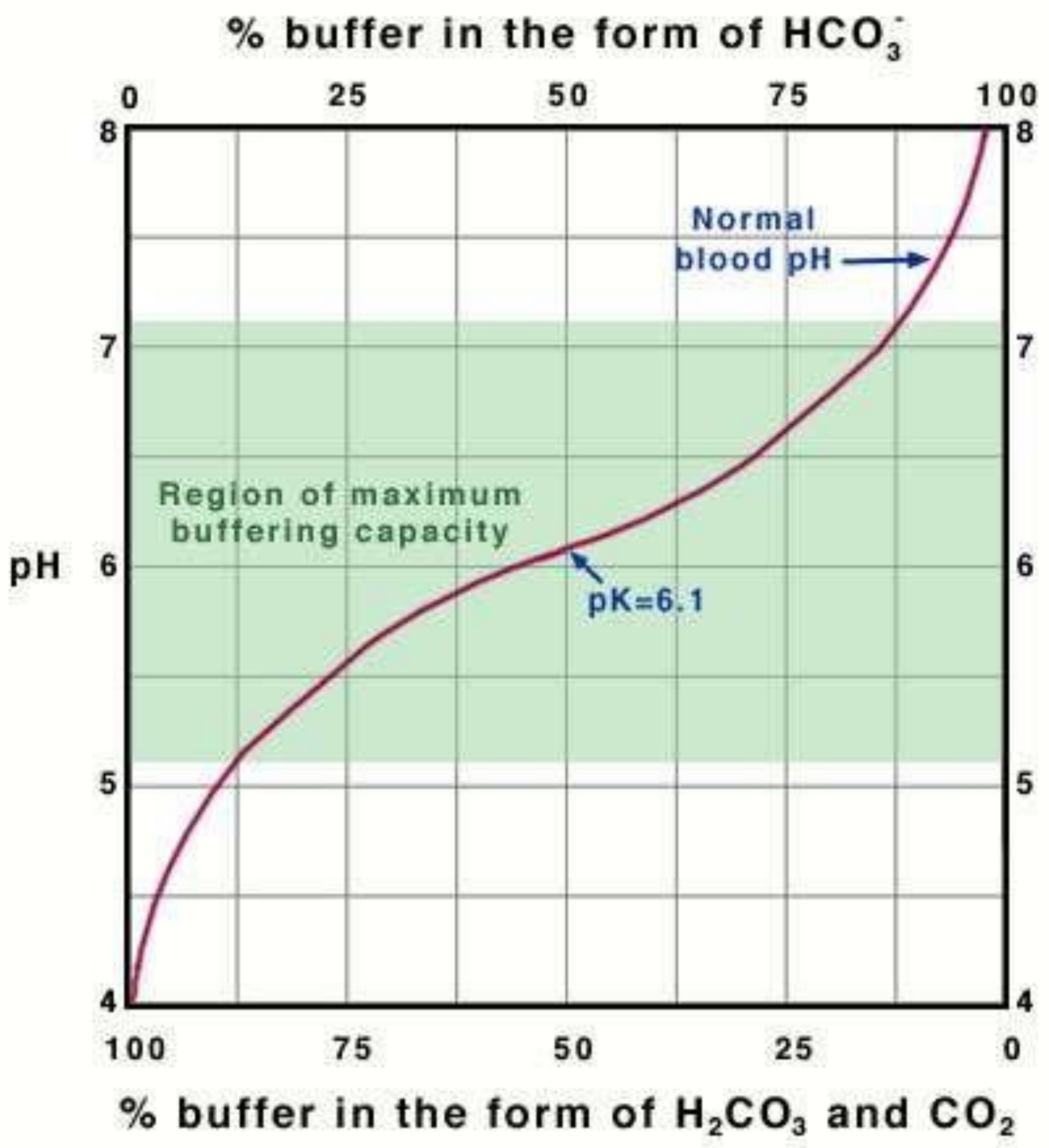
- When you try to breath and exhale very quickly you will feel dizzy because the blood pH has changed.

- People who have panic attacks breath very quickly, so they might lose consciousness because their nervous system is trying to control their breathing rates in order to regulate the blood pH and get it back to 7.4 . When someone gets a panic attack , they are usually given a plastic bag to breath with, so they inhale CO2 and its levels stay in the normal range in the blood.

- Aspirin is an acidic drug, so taking it in large quantities will drop the blood pH which will cause disfunction of a lot of body systems and could lead to death.

Titration curve of bicarbonate buffer

Note pKa



Buffering range :
(5.1-7.1)pH
The normal blood pH is OUTSIDE the bicarbonate buffer range.

Why is this buffer effective?

- Even though the normal blood pH of 7.4 is outside the optimal buffering range of the bicarbonate buffer, which is 6.1, this buffer pair is important due to three properties:
  - Bicarbonate is present in a relatively high concentration in the ECF (24mmol/L).
  - The components of the buffer system are effectively under physiological control: the CO_2 by the lungs, and the bicarbonate by the kidneys.
  - It is an open system (not a closed system like in laboratory).
    - An open system is a system that continuously interacts with its environment.

    All these reasons work together in order to make this buffer effective for buffering the blood, for example, if we put the bicarbonate ion buffer in a beaker in the lab and in high concentration, it still wouldn’t be effective and won’t buffer the blood pH because this is a closed system.

Acidosis and alkalosis

In case the pH of the blood goes outside the normal range, we have a pathological condition (acidosis or alkalosis)

- Both pathological conditions can be either metabolic or respiratory.

- Acidosis (pH< 7.35)
  - Metabolic: production of ketone bodies (starvation and diabetes)
    Because of — Uncontrolled diabetes
    Ketone bodies are metabolites that decreases the pH.
  - Respiratory: pulmonary (asthma; emphysema)
    Causes an increase in PCO2 (lowering the pH)

- Alkalosis (pH > 7.45)
  - Metabolic: excessive administration of salts
    Alkaline salts (antacids)
  - Respiratory: hyperventilation (anxiety)
    Panic attack

PO2 and PCO2 means the partial pressure (in mmHg or torr)

Normal Arterial Blood Gases (memorize these numbers)

Normal ABG Figures	
PH	7.35-7.45
PO2	80-100
PC02	35-45
HC03	22-28 mmol/L or mEq/L

Usually, veins are used for blood withdrawing. But for ABG testing, arteries are used.

The normal range is 7.35-7.45. However, our blood pH normally is approximately 7.4 (not near to the ends of the interval)
- When the pH is normal but near to 7.35, it is an indicator of a compensated acidosis.
- When the pH is normal but near to 7.45, it is an indicator of a compensated alkalosis.

Acidosis and alkalosis

- Lungs and kidneys are the organs that controls the blood pH (by changing PCO_2 for lungs and $[HCO_3^-]$ for kidneys).

- If the problem is with the lungs, it is called respiratory (acidosis or alkalosis). The body fixes it via the kidneys.

- If the problem is with the kidney or about metabolism (like taking a high dose of aspirin), the it is called metabolic (acidosis or alkalosis) . The body fixes it via the lungs.

- If both PCO_2 and $[HCO_3^-]$ are outside their normal ranges, there is compensation (if the pH is in its normal range, it is full otherwise it is partial).

- If they are in their normal ranges (one or both) and the pH is outside its normal range, there is no compensation.

According to Le Chatelier's principle

Respiratory conditions

Related to PCO2 (PCO2 reflects the concentration of CO2)

Respiratory Acidosis

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow \mathbf{CO_2} + H_2O$$

CO2 increases -- H+ increases-- pH decreases

Respiratory Alkalosis

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow {\scriptstyle CO_2} + H_2O$$

CO2 decreases -- H+ decreases -- pH increases

Metabolic conditions

Related to [H+]

Metabolic Acidosis

$$\mathbf{H^+} + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$$

H+ increases--pH decreases

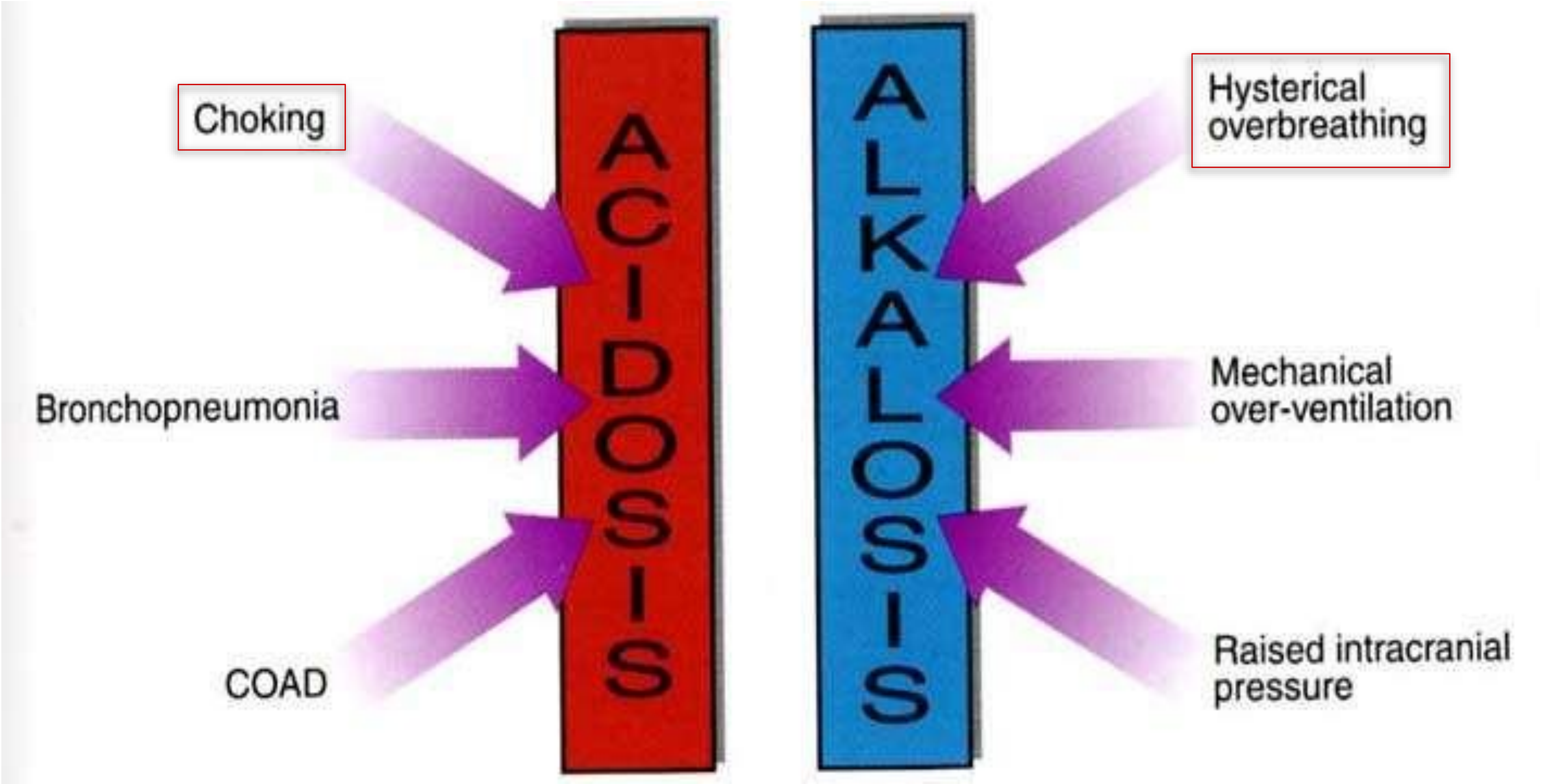
Metabolic Alkalosis

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

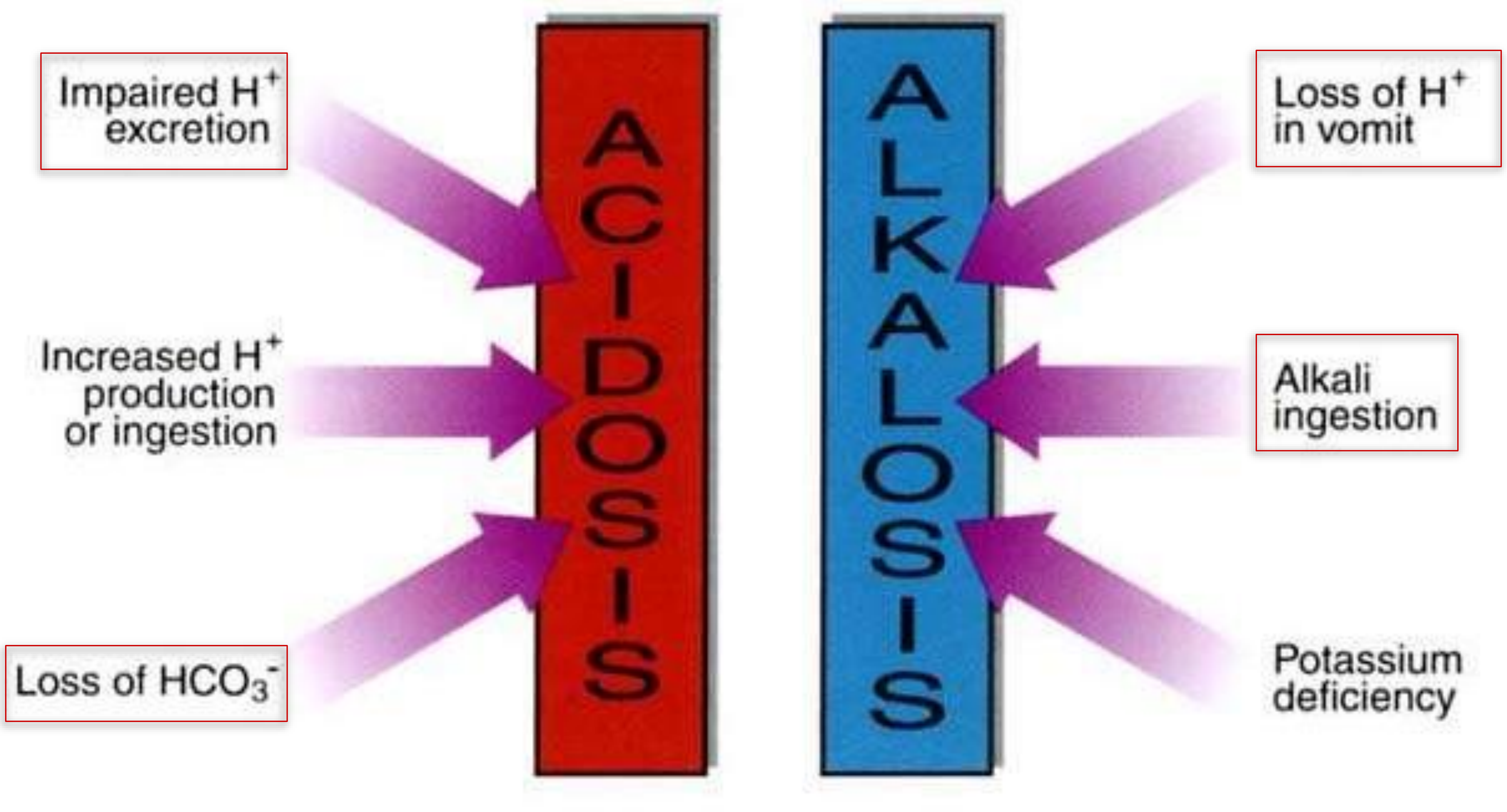
H+ decreases--pH increases

The ones in red boxes are important

Causes of respiratory acid-base disorders



Causes of metabolic acid-base disorders



Compensation

- Compensation: A change in HCO_3^- or pCO_2 as a result of the primary event in order to return the pH to normal levels.
- If the underlying problem is metabolic, hyperventilation or hypoventilation alters pCO_2; it is called respiratory compensation.
- If the problem is respiratory, renal mechanisms drives metabolic compensation via changing $[HCO_3^-]$.
- Complete compensation if brought back within normal limits
- Partial compensation if the pH is still outside norms.

$$H^+(aq) + HCO_3^-(aq) \rightleftharpoons H_2CO_3(aq) \rightleftharpoons H_2O(l) + CO_2(g)$$

$$H^+_{(aq)} + HCO_3^-{}_{(aq)} \rightleftharpoons H_2CO_{3(aq)} \rightleftharpoons H_2O_{(l)} + CO_{2(g)}$$

You can memorize this table, but understanding the cases is easier and more fun

FULL COMPENSATION

	pH	pCO_2	HCO_3^-
Resp. acidosis	Normal But<7.40	↑	↑
Resp. alkalosis	Normal but>7.40	↓	↓
Met. Acidosis	Normal but<7.40	↓	↓
Met. alkalosis	Normal but>7.40	↑	↑

$$H^+(aq) + HCO_3^-(aq) \rightleftharpoons H_2CO_3(aq) \rightleftharpoons H_2O(l) + CO_2(g)$$

PARTIAL COMPENSATION

	pH	pCO_2	HCO_3^-
Res.Acidosis	↓	↑	↑
Res.Alkalosis	↑	↓	↓
Met. Acidosis	↓	↓	↓
Met.Alkalosis	↑	↑	↑

Example 1

You can know the type by reading the case, but you should also know it from numbers only (apply **Le Chatelier's principle**)

- Mrs. X is admitted with severe attack of asthma. Her arterial blood gas result is as follows:
  - pH : 7.22
  - pCO_2 : 55
  - HCO_3^- : 25

  - pH is low – acidosis
  - pCO_2 is high – in the opposite direction of the pH.
  - HCO_3^- is Normal
- Respiratory Acidosis Which means there is no compensation

Normal ABG Figures	
PH	7.35-7.45
PO2	80-100
PC02	35-45
HC03	22-28

$$H^+(aq) + HCO_3^-(aq) \rightleftharpoons H_2CO_3(aq) \rightleftharpoons H_2O(l) + CO_2(g)$$

Example 2

- Mr. D is admitted with recurring bowel obstruction and has been experiencing continuous vomiting for the last several hours. His ABG is:
  - pH: 7.5
  - pCO_2:42
  - HCO_3^-: 33

PH is abnormal, [HCO3−] is abnormal and pCO2 is in normal ranges, which means there is no compensation.

Normal ABG Figures	
PH	7.35-7.45
PO2	80-100
PC02	35-45
HC03	22-28

- Metabolic alkalosis

$$H^+ (aq) + HCO_3^- (aq) \rightleftharpoons H_2CO_3 (aq) \rightleftharpoons H_2O (l) + CO_2 (g)$$

Very important example

Example 3

- Mrs. H is a kidney dialysis patient who has missed his last 2 appointments at the dialysis center. His ABG results:
  - pH: 7.32
  - pCO_2: 32
  - HCO_3^-: 18

Normal ABG Figures	
PH	7.35-7.45
PO2	80-100
PC02	35-45
HC03	22-28

- Partially compensated metabolic Acidosis

The partial compensation here is by lowering PCO2 (hyperventilation)

$$H^+ (aq) + HCO_3^- (aq) \rightleftharpoons H_2CO_3 (aq) \rightleftharpoons H_2O (l) + CO_2 (g)$$

Try both types (respiratory and metabolic) by applying Le Chatelier's principle to this equation when partial compensation is present.

Example 4

- Mr. K with Chronic obstructive pulmonary disease (COPD). His ABG is:
  - pH: 7.35
  - pCO_2: 48
  - HCO_3^-:30

PCO2 and HCO3- are abnormal and PH is normal meaning there is full compensation

Normal ABG Figures	
PH	7.35-7.45
PO2	80-100
PC02	35-45
HC03	22-28

- Fully compensated Respiratory Acidosis

The compensation here is by increasing [HCO3-] via kidneys

$$H^+ (aq) + HCO_3^- (aq) \rightleftharpoons H_2CO_3 (aq) \rightleftharpoons H_2O (l) + CO_2 (g)$$

$$H^+_{(aq)} + HCO_3^-{}_{(aq)} \rightleftharpoons H_2CO_{3(aq)} \rightleftharpoons H_2O_{(l)} + CO_{2(g)}$$

- Mr. S is a 53-year-old man presented to ED with the following ABG.
  - pH: 7.51
  - pCO_2: 50
  - HCO_3^-: 40

- Metabolic alkalosis with partial compensation

Normal ABG Figures

PH	7.35-7.45
PO2	80-100
PC02	35-45
HC03	22-28

Practice ABG's

1.	pH 7.48	$PaCO_2$ 32	HCO_3^- 24
2.	pH 7.32	$PaCO_2$ 48	HCO_3^- 25
3.	pH 7.30	$PaCO_2$ 40	HCO_3^- 18
4.	pH 7.38	$PaCO_2$ 48	HCO_3^- 31
5.	pH 7.49	$PaCO_2$ 40	HCO_3^- 30
6.	pH 7.35	$PaCO_2$ 48	HCO_3^- 30
7.	pH 7.45	$PaCO_2$ 47	HCO_3^- 29
8.	pH 7.31	$PaCO_2$ 38	HCO_3^- 15
9.	pH 7.30	$PaCO_2$ 50	HCO_3^- 24
10.	pH 7.48	$PaCO_2$ 40	HCO_3^- 30

Normal ABG Figures	
PH	7.35-7.45
PO2	80-100
PC02	35-45
HC03	22-28

Answers to Practice ABG's

$$H^{+}_{(aq)} + HCO_3^{-}{}_{(aq)} \rightleftharpoons H_2CO_{3(aq)} \rightleftharpoons H_2O_{(l)} + CO_{2(g)}$$

1. Respiratory alkalosis
2. Respiratory acidosis
3. Metabolic acidosis
4. Compensated Respiratory acidosis (fully)
5. Metabolic alkalosis
6. Compensated Respiratory acidosis (fully)
7. Compensated Metabolic alkalosis (fully)
8. Metabolic acidosis
9. Respiratory acidosis
10. Metabolic alkalosis

Quiz!

Good luck!

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide 21	Partial compensation	No compensation
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

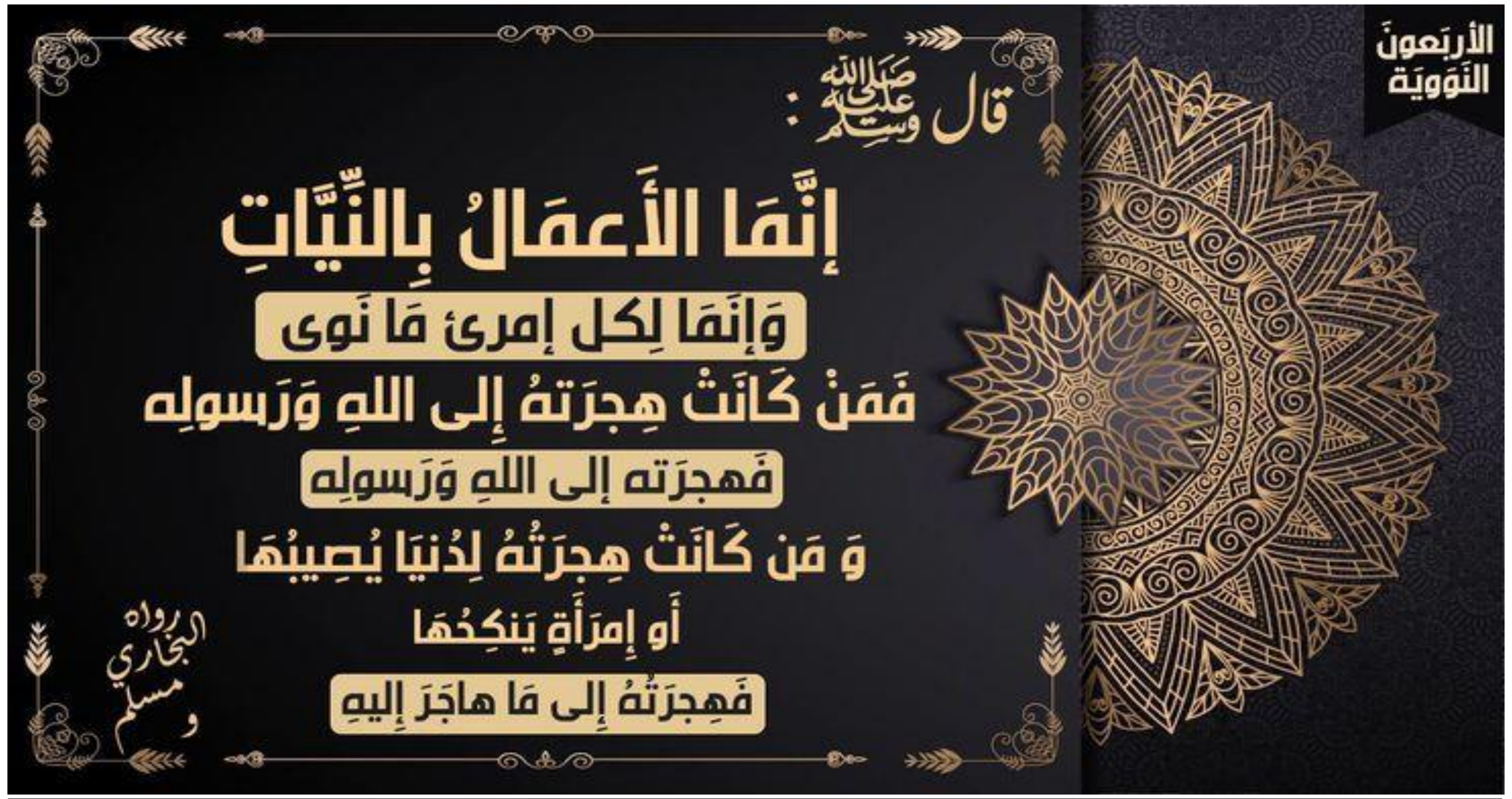
Reference Used:

Prof. Mamoun Ahram recorded lecture

[pH and buffers 3]

Extra References for the Reader to Use:

Marks' Basic Medical Biochemistry (6th edition)



فمَنْ قصَدَ بعَملِه مَنفعةً دُنيويَّةً لم يَنلْ إلَّا تلكَ المَنفعةَ ولو كان عِبادةً، فَلا ثَوابَ له عليها، ومَن قصَدَ بعَملِه التَّقرُّبَ إلى اللهِ تعالَى وابتغاءَ مَرضاتِه، نالَ مِن عَملِه المَثوبةَ والأجرَ ولو كان عمَلًا عاديًّا، كالأكلِ والشُّربِ