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L’ABC DELL’EQUILIBRIO ACIDO-BASE “UMANIZZATO” SENZA LOGARITMI. “L’ESSENZIALE”

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[H^+] = K \frac{PCO_2}{[HCO_3^-]} = \frac{Polmone}{Rene}
\]

Componente respiratoria
Componente metabolica

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Chapter 1: Acid-base equilibrium is not a difficult topic

Introduction (from person to chemistry and not vice versa)

“Man is eternally poised in the perennial search for equilibrium.”

Each of our vital functions is linked to four fundamental equilibriums:

1. the acid-base equilibrium,
2. the hydro-electrolytic (ionic) equilibrium,
3. the osmotic equilibrium,
4. the volemic equilibrium,

inseparable from each other and basic material for the medical-scientific culture and, therefore, for the understanding of the fundamental responsible mechanisms, for the conservation of life.

The acid-base equilibrium (EAB) can be defined as the \textit{equilibrium of equilibria} because, at the end of all metabolic activities, it is the one that maintains the most vital and essential normal functions for survival.

Still, it is one of the most overlooked topics in our university and professional education. Every time the clinical discussion focuses on the acid-base equilibrium, a sense of respectful, if not genuine awe, emerges.

Everyone admits its fundamental importance in human physiology and pathology, but many carefully avoid studying this chapter further.

In fact, doctors behave towards EAB the way “Catholics behave towards the Bible: they have great respect for it and this respect shows it by being as far away as possible” (phrase used, on the subject of the Bible, by Paul Claudel, the French writer, quoted by Gianfranco Ravasi, the great scholar of sacred texts). This judgment also fits well with our topic discussed in this book.

The theme is not easy to approach but, in itself, it is not “difficult” nor should it be considered “reserved for a few experts”. It “was made difficult” when they introduced logarithms into Henderson’s simple equation. After many years of “crazy and desperate” study (at our wit’s end) it was pleasant to discover (albeit with a bit of anger given the time taken to understand it) that, for us as doctors, those logarithms were not indispensible and that we could learn the subject equally well without resorting to such a complicated route.

The purposes, therefore, of this book are:

- to make the acid-base equilibrium less odious
- to approach the topic with more sympathathy and with a practical clinical eye
- to assure that the topic can be studied easily, without stymieing under the “Caudine Forks” of the complex Henderson-Hasselbalch equation
- to apply Henderson’s simple equation in clinical practice (without Hasselbalch) and to assure that, in this way, nothing is lost in terms of scientificity.
The “fundamental” concepts

We doctors commonly take a long time of our professional life (university and post-university) to chase more and more cytokines with an increasingly indeterminate mechanism, prostaglandins with increasingly incomprehensible acronyms, lipoproteins with varying consistency that is less and less memorable, and we feel frustrated if we do not know the latest levogyrhic form of yet another new drug marketed. At the same time, because of the use of all the aforementioned time (which leaves no useful residual space), we are forced to neglect the more in-depth and more repetitive study of those elements (such as hydrogen ions, sodium, oxygen, bicarbonate, etc.) that are essential to the maintenance of life.

In the context of the acid-base equilibrium “the fundamentals” are represented by:

1. the hydrogen ions and the production of acid
2. the buffers and the rationale of the systems of control
3. the lung and kidney

The role of hydrogen ions and the production of acids

The human body, due to its metabolism, produces acids continuously and hydrogen is the emblem of the concept of acid.

The various metabolisms (protidic, glycidic, and lipidic), through the different metabolic stages, produce, as a final goal, three substances:

- ammonia (NH₃).
- water (H₂O)
- carbon dioxide (CO₂)

in addition to the generation of energy (ATP).

Every day 15,000-20,000 milliequivalents (mEq) of CO₂ are produced by our metabolic processes and tissue respiration (intracellular oxidative metabolism) following the transformation of carbonic acid (H₂CO₃) into water and carbon dioxide, which is then excreted from the lungs.

In fact, carbonic acid is nothing but CO₂ dissolved in water (CO₂ + H₂O = H₂CO₃) and therefore it is called a “volatile acid”.

Furthermore, a normal dietary intake and cellular catabolism cause the formation of 50-100 mEq of acid products in 24 hours, in the form of so-called fixed anions (the so-called “non-volatile fixed acids”).

The sources of H⁺ are essentially represented by dietary intake, cellular catabolism, and tissue respiration.

Just think, in fact, simple drinking water, coming from the tap, does not have a pH of 7 (as we would expect), but a pH of 5 (only pure water has a pH of 7); milk also has a pH of 6.6; coca cola has a pH of 2.8, just to name a few of the most common foods, which are almost all more acidic than the normal physiological pH of blood, 7.40.
If you enjoy practicing gas analysis on common IV drips used in the ward, you encounter special surprises.

Normal “Physiological” Saline Solution, commonly used in clinical practice, does not have a pH of 7.40 (as would be expected) but has a pH of 7.04 (or around 7.0 or lower), (Fig. 1) while Glucose Solution has a pH oscillating between 4.5 and 5.0. (Fig. 2)

![Image](image.png)

Fig. 1. Analysis of “Physiological” solution.

The question marks on the reports of the two gas analyses only indicate that the results are peculiar, but the gas-analyzer apparatus is calibrated well and functioning well.

The main concern of the human body, therefore, is to defend itself against acidity, because it normally produces hydrogen ions (H⁺, acids) and not hydroxyl ions (OH⁻, bases), so that acidosis is much more frequent than alkalosis.

The production of hydrogen ions also takes place in normal (physiological) conditions, while alkalinity is created only in a pathological situation; in this regard, it should not be forgotten that the hydrogen is the atom present in greater abundance in cells and that the greater share of hydrogen is in the form of water (2 hydrogen ions per molecule of H₂O).

The normal physiological state of the acid-base equilibrium ensures:
- an equilibrium between the production and excretion of hydrogen ions
- the regular activity of enzymes
- the optimal distribution of electrolytes
- effective myocardial contractility
- the optimal saturation of hemoglobin with oxygen

Hydrogen is the emblem of the concept of acid, because, according to Brønsted’s definition (commonly accepted), a substance is considered acidic when it is capable of releasing hydrogen ions, while it acts as a base when it is capable of accepting hydrogen ions. (4)
In the definition of Arrhenius (5) (slightly different and with less consensus than the previous one), an acid corresponds to any substance capable of producing an increased concentration of hydrogen ions, when it is dissolved in water.

In any case, whatever the preferred definition, hydrogen ions are the main actors, whose production also takes place in normal (physiological) conditions, because they are produced as a consequence of normal tissue respiration.

Ultimately, therefore, it is not so much the electric charge that determines the acid or base character, but only the tendency to dissociate or associate hydrogen (H⁺).

The role of buffers and the rationale of control systems

The acids normally produced by the body, as a direct consequence of our diet and our metabolism (and even more in fasting conditions), before reaching the excretory organs, pass into the blood and this passage, from production to elimination, must take place without changing the normal hydrogen ion concentration.

And this is the most surprising quality of our homeostatic systems, as expressed by L. J. Henderson (1878-1942) as early as 1908: “The most obvious and most important property of blood is its extraordinary ability to neutralize large quantities of acids or bases without losing its neutral reaction.” (6,7) (Fig. 3)

The “normal” concentration of hydrogen ions in the blood must oscillate around 40
nEq/liter (corresponding to a pH of 7.40) and variations in these numbers can alter all metabolic processes.

Søren Peter Lauritz Sørensen (1868-1939), Danish director from 1901 to 1938 at the Chemistry Department of the laboratory of the Carlsberg company of Copenhagen brewing beer, showed, in 1909, that “the normal concentration of the hydrogen ion it is an essential factor in all biological processes” and introduced and defined the concept of pH (which, under normal conditions, corresponds to a value of 7.40 units pH). (8) (Fig. 4)

![Fig. 3 Lawrence J. Henderson (1878-1942)](image)

Sørensen created the pH scale, using logarithms, because he was forced to work with very complicated numbers. In fact, at the time of Sørensen, the normal value of the hydrogen ion was expressed with the unit of measurement of equivalent grams/liter whereby the number 0.00000004 was obtained, with seven zeros after the comma followed by the number 4.

Even with the unit of measurement of mEq/liter, the normal value is represented by a complex number (0.00004) with four zeros after the comma followed by the number 4.

One can guess, therefore, why, at that time with those complex numbers, the need was felt to “invent” the new unit of measurement of the pH scale, with which the “normal” value of 7.40 arose (a much more handy number, during calculations).

Sørensen was certainly brilliant but, if he had taken one further spurt of genius, we could have avoided many difficulties in understanding this crucial topic.

In fact, if he had invented a new unit of measurement, the nanoequivalent, which did not exist at his time, we would have had a normal value of hydrogen ions equal to 40 nEq, an even more manageable number of the same 7.40 and without using to logarithms. (Fig. 5)
Fig. 4 Soren P. L. Sørensen (1868 1939)

Valori Normali

\[
[H^+] = 0,00000004 \text{ gEq/L} \\
[H^+] = 0,00004 \text{ mEq/L} \\
pH = 7.40
\]

\[
[H^+] = 40 \text{ nanoEq/L}
\]

Fig. 5 Different units of measurement and pH
It can be deduced that free $H^+$, in conditions of physiological normality, are present in extremely low concentrations (just 40 nEq) and their stability in a narrow range (from 16 to 160 nEq) is crucial to still maintain compatibility with the life.

To get a clear idea of the order of magnitude, just think that the concentration of normal sodium is 140 mEq/L, that is 3.5 million times larger than the hydrogen, and this remarkable difference is even more evident if you look at the image of the “twin towers” of Gamble’s ionogram, where the dimensional values of the cations and anions are visually represented (9, 10). (Figure 6)

![Fig. 6 - The vital “twin columns”](image)

According to the principle of ionic electroneutrality, in every instant, the number of positive charges must always be equal to the number of negative charges and therefore, to be precise, 154 cations and 154 anions in each liter.

In the cation column on the left, sodium, potassium, calcium, and magnesium are very evident, while, at first glance, hydrogen ions are not traceable, although they are cations.
If you look more carefully, however, you can see at the bottom of the same column of cations, on the bottom left, the presence of the item “Others 1” [“Altri 1”] whose value 1 mEq (compared to the value 140 of Sodium) is inclusive of hydrogen ions and also lithium ions and positively charged paraproteins. (Tab. 1)

![Image of a table showing the concentration of cations and anions in mEq/L](image)

Tab. 1. Numerical values of Gamble’s ionogram.

*Fig. 6 certainly represents one of the slides to save from a library fire.* The body therefore has the vital need to maintain this concentration of hydrogen ions in the normal range (35-45 nEq) and nature has prepared numerous self-control systems.

The defenses against changes in normal hydrogen ion concentration are mainly based on three different systems:

- the buffers,
- the lungs
- the kidneys

with different times of intervention. (Fig. 7)
The role of buffers

It was ever the same Sørensen who also introduced the concept of buffer referring to the bumpers (shock-absorbers) of the railway carriages that serve to cushion the immediate impacts and, in fact, the body buffer systems (Fig. 8) come react within a fraction of a second, rendering inactive “free” acids (circulating and non-circulating, extracellular and intracellular).

The buffer is a substance that has the ability to donate or accept hydrogen ions, if the addition of a base or an acid in the buffer solution is capable of changing the acid-base state of the solution itself.

To restore the original buffer condition it is necessary to do two things: remove the excess acid or restore the base eventually consumed.
“Total” bodily buffers are present in the order of 2,400 mEq throughout the body. The bicarbonate/carbonic acid buffer system is the system present in greater quantities than the others and plays a crucial role as it represents the crossroads of arrival and departure of those substances that can modify the normal hydrogen ion concentration of the blood. Of all the buffer systems, it is the most important for three fundamental reasons:

1. for its greater percentage (65%) (Fig. 8) “Carbon acid is produced by metabolic processes in quantities far greater than any other acid and is easily converted to the gaseous form (CO₂).” (11)
2. because it is the only ubiquitous substance. It is present in interstitial fluid, plasma, erythrocytes, cells and bones, while the rest are not ubiquitous, (Figure 9)
3. because it is the only system that has two escape routes: one, rapid, through the lungs transforming into CO₂ (which is immediately eliminated in a few minutes) and the other, transforming into bicarbonate and hydrogen ions, the latter of which are eliminated with the kidney, while the bicarbonates are reabsorbed and return to circulation (Fig. 10). This second type of compensation is slower to achieve because the kidneys can take 2-3 hours or even 1-2 days before they manage to work at full capacity.

![Table of Buffers Distribution](image)

Fig. 9. The distribution of buffers in the body.

Figure 10 is the “fundamental” image to understand the physiological mechanism of acid-base equilibrium and deserves to be memorized well. Practically, it is the first of those images that we catalog among the “slides to be saved in a library fire”.

The role of the lung and that of the kidney

Carbonic acid is the only substance that has an escape hatch, transforming itself into something volatile (CO₂), while residual water, from a practical point of view, is mainly eliminated through the urinary tract.
Fig. 10 - General scheme of acid-base equilibrium.
The lung is delegated to perform the delicate function of ensuring the gas-exchange of oxygen and carbon dioxide between living organisms and their surrounding environment, in such a way as to obtain normal values of the pressures of these two gases in the blood. When this physiological function fails, the blood cannot oxygenate sufficiently, causing "hypoxemia" and, with the worsening of conditions, there is also an accumulation of carbon dioxide ("hypercapnia") which leads to acidosis and to death.

Once the kidney compensation mechanism has been started, it remains stable and its contribution is crucial, because, if there were no bicarbonate recovery in the kidney, we would see its complete consumption within a few hours or days.

The “total” bodily buffer systems, as we have already said, are present in the order of 2,400 mEq throughout the body, while the acids produced in 24 hours (volatile and non-volatile) are 15,000-20,000 mEq (Fig. 11 and 12).

![ACIDI PRODOTTI NELLE 24 ORE](image)

Fig. 11 Acids produced in 24 hours and total bodily buffers.

This discrepancy between acids produced in 24 hours (15-20,000 mEq) and the total body buffer systems (2,400 mEq) suggests the need for swabs to be continuously renewed throughout the day, on pain of running out of available stocks, and this function is responsible for the kidney with its regeneration and reabsorption of bicarbonates.

One of the most important tasks of the kidney, in fact, in addition to that of providing for the formation and elimination of urine, is to recover the bicarbonates.

After glomerular filtration, the bicarbonates are reabsorbed at the tubular level in the order of 85-90% already in the first portion of the proximal tubule (Figure 13).

The kidney then contributes to acid-base homeostasis through its corrective activity that
Sistemi tampone

La discrepanza, fra acidi prodotti nelle 24 h (15 - 20.000 mEq) e il totale dei sistemi tampone del corpo (2.400 mEq), fa intuire la necessità che i tamponi siano continuamente rinnovati nel corso della giornata.

Fig. 12 Obvious discrepancy between the acids produced and the total bicarbonates available.

Fig. 13 - The nephron and its absorption sites.
also consists of eliminating, through the urine, the fixed acids and hydrogen ions in the form of water (two hydrogenations per molecule) and in the form of ammonium and phosphates.

If there were only buffers, our survival could last only a few hours due to the rapid exhaustion of the bicarbonates, which are no longer reabsorbed and regenerated.

If there were only lungs, then, we would all die immediately already in the acute phases, because they are slow to take action and, before their effective intervention, we would have already died due to excess of acids that could no longer be buffered.

To summarize, therefore, the organic buffers (bases) are entrusted with the role of emergency and instantaneous intervention, the lung has the task of eliminating volatile acids (CO₂), and the kidney is responsible for eliminating fixed acids and to recover bicarbonates.