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L'ABC
dell'Equilibrio Acido-Base
“umanizzato”
Senza Logaritmi.
“l’Essenziale”

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

2019

English Edition (2020)
Translated by Michael J. Braus, Ph.D.
Chapter 2: *Henderson’s “fundamental” (but less famous) equation

Lawrence Joseph Henderson, creator of the crucial formula, but overshadowed by Hasselbalch

Lawrence J. Henderson (1878-1942), born in Lynn and died in Cambridge, Massachusetts, United States, Professor of Physiology at Harvard University (United States) (Fig. 3 of Chapter 1) studying the biological systems from a mathematical and physicochemical point of view, was fascinated by the properties of the blood to buffer large quantities of acids or bases.

He was the first to understand and quantitatively describe the buffering effect of the carbonic acid-bicarbonate system interacting with hydrogen ions in the blood.

He also described the blood buffer systems, mathematically characterized them, and elaborated (1908) his ingenious and “fundamental” formula, known (even if only by a few) as “Henderson’s equation”. (6) (Formula 1 and Fig. 1)

\[
[H^+] = K \frac{[H_2CO_3]}{[HCO_3^-]}
\]

1,2 mEq / Litro

\[
[H^+] = \frac{800}{24} \text{ mEq / Litro}
\]

Formula 1 - Henderson’s equation with numerical values.

In this formula the problem of the acid-base equilibrium had already been summarized very well, namely that the concentration of hydrogen ions (and therefore the acidity or basicity of a solution) is given by the quantitative relationship existing between the concentration of carbonic acid \([H_2CO_3]\) to the numerator, and the concentration of bicarbonates \([HCO_3^-]\) to the denominator, according to a constant \(K\), which, in the specific case, is numerically 800.

Carbon dioxide \((H_2CO_3)\), then, is nothing more than carbon dioxide \((CO_2)\) dissolved in water \((CO_2 + H_2O = H_2CO_3)\) and between the two substances (carbon dioxide and carbon acid) there is a perfectly linear correlation on the basis to Henry’s law, which says verbatim: “The amount of a physically dissolved gas in a solution is directly proportional to its partial pressure” (12, 13) that is “the higher the pressure of \(CO_2\) \((PCO_2)\) the more it dissolves in the water itself and forms carbonic acid”, therefore, knowing the value of \(PCO_2\), it is easy to trace the \(H_2CO_3\) value and vice versa. (Fig. 2)
CONCERNING THE RELATIONSHIP BETWEEN THE
STRENGTH OF ACIDS AND THEIR CAPACITY TO
PREERVE NEUTRALITY.

BY LAWRENCE J. HENDERSON.

[From the Laboratory of Biological Chemistry in the Harvard Medical School.]

In the light of relationships already discussed concerning the
mechanism for the preservation of neutrality in the animal organ-
ism, it is interesting to consider what the principles underlying
the regulation of the reaction of a simple solution may be, for in
this way it may be possible to discover how closely the physiological
mechanism approaches to ideal conditions.

According to the mass law, in the pure solution of a weak acid,
HA, the relationship holds, —

\[ k \cdot (HA) = (H) \cdot (A), \]

where \( k \) is the ionization constant of the acid and the enclosed
quantities represent the concentrations of the respective substances.
This equation may be more conveniently written

\[ (H) = k \cdot \frac{(HA)}{(A)}. \]

If now the sodium salt, or other salt with a strong base, of the acid
be introduced into such a solution as is above considered, it is evi-
dent that we shall have the following condition. The concentration
of unionized molecules of acid will be almost precisely equal to the
total amount of acid present, while the concentration of the ions
(A), much increased because of the presence of the salt, will be
equal to the concentration of the salt multiplied by its degree of
dissociation. This latter factor, varying with the strength of the
acid and the concentration of the salt, will usually not be less than 0.6.

We may therefore write the equation, —

\[ (H) = K \cdot \frac{HA}{MA} \]

where \( K \) is the ionization constant of the acid divided by the degree
of ionization of the salt, and HA and MA represent the amounts
of acid and salt present in the solution.

Fig. 1. Henderson’s original work with the presentation of his equation (6).
The Henderson-Campbell equation

Based on the correlation of Henry’s law, the numerator of Henderson’s equation can also be expressed as $\text{PCO}_2$ (instead of $\text{H}_2\text{CO}_3$), and this simplifies things a lot because, in laboratory practice, $\text{PCO}_2$ can be much more easily measured compared to $\text{H}_2\text{CO}_3$, whose level is very low in plasma and extracellular liquids.

Henderson's equation can therefore also be expressed in this alternative way of Formula 3.

$$[H^+] = K \frac{\text{PCO}_2}{[\text{HC}O_3^-]}$$

Formula 3. The Henderson-Campbell equation.

This variation was proposed by E. J. M. Campbell in 1962 (14) (Fig. 3), giving rise to the definitive Henderson-Campbell equation that is the simplest and most practical to use (14, 15).

In fact, it allows us to switch from chemistry (often unpleasant) to the clinic (more congenial to us). Considering, in fact, that the lung is mainly responsible for regulating the pressure of carbon dioxide and the kidney is mainly responsible for regulating the concentration of bicarbonate, we can conclude that the concentration of hydrogen ions is the result of the relationship between the function of the lung and the function of the kidney, i.e. between the respiratory and metabolic components.

It may seem reductive or trivial, but just this small variation of the formula allows us to better understand relationships in the clinic and leads us to a “more humane” equation, summarized in the next image, which represents well another slide to save in a library fire. (Fig. 4) This image simplifies the memorization of the formula, and it is simple to recall it to mind (even in moments of memory vacuum) because the lung is above the diaphragm (fraction line) and the kidney is below it.

Under pathological conditions this balance can be broken and acid-base alterations, isolated or mixed, can be easily diagnosed if one always keeps this Henderson-Campbell equation in mind. For example, in case of a lung disease, if $\text{PCO}_2$ increases (pulmonary
Fig. 3. Moran Campbell (1925-2004).

Fig. 4. Henderson Campbell’s “humanized” equation.
heart, pneumonia, asthma, COPD, etc.) there will be an increase in hydrogenations and therefore an *acidosis* of *respiratory* origin; if, on the other hand, PCO₂ decreases (for example, due to hyperventilation in the course of an anxiety crisis), hydrogenations decrease and there will be *respiratory alkalosis*.

If, on the other hand, the kidneys do not work (as happens, for example, during kidney failure in which the kidneys lose the function of reabsorbing bicarbonates), the latter decreases (in the denominator) and consequently there will be an increase in free hydrogen, an *acidosis*, in this case of *metabolic* origin.

If the bicarbonates increase in the denominator of the formula (for example, for their incorrect intravenous administration or for a gastric acid vomiting, in which many hydrogen ions and many chlorine ions are lost), consequently, the free hydrogen ions decrease and there will be a *metabolic alkalosis*.

These are the classic conditions that label the 4 “simple” acid-base equilibrium disorders (respiratory acidosis, metabolic acidosis, respiratory alkalosis, metabolic alkalosis), and it does not take long to identify them well.