[Foreword]

Luciano Gattinoni

When I first heard a lecture on the physicochemical approach to acid-base equilibrium based on Stewart's work my first reaction was: "another useless and complicating addition to an already difficult topic". After studying it, however, I realized that the Stewart approach is the best way to understand and remember acid-base equilibrium per se, and, more importantly, its relationship with another key equilibrium of living organisms, the electrolytes.

Medical students bump into the acid-base equilibrium several times throughout their course of study, in chemistry, biochemistry, pathology, clinics and during the post-graduate courses, particularly when the acute stage of illness is the main topic. Unfortunately the acid-base equilibrium is usually forgotten as many times as it is taught. Usually, the knowledge of this topic is limited to the realization that pH may indicate alkalosis or acidosis, that Base Excess may assess the metabolic acidosis/alkalosis and that PCO_2 changes may be associated with respiratory changes. In different chapters of their physiology textbooks, these students study electrolyte equilibrium, learning about concepts such as hyper- or hypo- natremia, -chloremia, -kalemia and their clinical consequences. Acid-base equilibrium and electrolyte equilibrium are then taught, analyzed, learned and forgotten as part of two different worlds.

The great merit of Stewart's physical-chemical approach is to show that acid-base and electrolytes are part of the same picture. In a painting the details may be beautiful, but if the details are considered only by themselves one cannot appreciate the whole scene. In analogy, looking at Leonardo's famous painting "The Last Supper", the discussion between the three Apostles on the right or on the left corners does not give us the whole picture. I believe that Stewart's approach gives us the complete painting, while other approaches give us only the details. While these other approaches describe the same reality and are true, only the Stewart one provides a tool for fully understanding of the problem.

What is important in the "beautiful mind" of the physicochemical approach is, first, the distinction between independent and dependent variables, second the embedding of the acid-base equilibrium in the general equilibrium of water and electrolytes. Stewart identified three independent variables which may change the hydrogen concentration in water (i.e. the acid-base

equilibrium): the strong ion difference (SID), the total weak acid concentration (A_{TOT}) and the PCO_2 (which is nothing else than a different expression of another weak acid, the carbonic acid). The strong ion difference is regulated by the kidney, weak acid concentration primarily by liver, PCO_2 by the lung. All the independent variables are present in concentrations on the order of millimoles or milliequivalents and their interaction with water dictates the amount of free hydrogen ions, the concentration of which is in the order of nanomoles.

The best way to understand the architecture of the Stewart's model is to visualize a histogram with two columns: one including all the strong ions with positive charge, and the other one with all the strong ions with negative charge. The difference in electrical charge between these two columns is called strong ion difference. In normal plasma this amounts to about 42 mEq/L. Indeed, to reach the electroneutrality, 42 mEq of negative charged ions, different from strong ions, are required. These are basically the bicarbonate (HCO_3^-) and the negative charged form of the weak acids (A^-), primarily albumin plus an extremely small amount of hydroxyl (OH^-). The sum of $[HCO_3^-] + [A^-]$ which equals the strong ion difference was called "Buffer Base" by Singer and Hastings, and later by Siggaard-Andersen. Indeed the big difference between the Siggaard-Andersen's approach and the Stewart's approach is that the first considers what happens inside the buffer base domain. As an example, in the Siggaard-Andersen's model the normal buffer base (42 mEq/L as the normal [SID]) may decrease by 10 mEq/L if the $[A^-]$ and $[HCO_3^-]$ are consumed by adding 10 mEq of H^+. In this case the actual buffer base is 32 mEq/L and the difference between the actual buffer base and the ideal buffer base is equal to –10 mEq/L, this difference being called base excess. In the Stewart model the same problem is considered from another point of view. If a strong ion is added to the system the difference between the two columns changes. As an example, adding 10 mEq/L of lactate the strong ion difference decreases from 42 mEq/L to 32 mEq/L. The "space" available for A^- and HCO_3^- and OH^- decreases, indeed part of A^- will become AH, part of HCO_3^- will become H_2CO_3 and part of OH^- will become H_2O. As the product of H^+ and OH^- is constant, a decrease of OH^- will correspond to an increase of H^+, i.e. acidosis.

The disadvantage of Siggaard-Andersen's approach is that it implies adding or subtracting H^+ to the solution, which is impossible. The more general Stewart's approach explains the acid-base variations on a more valuable physical basis. As an example adding pure water to a solution in which the strong ion difference is 42 mEq/L will decrease [SID], while subtracting pure water will increase [SID]. In the first case acidosis develops, in the second case alkalosis. The Stewart's approach basically allows one to understand the acid-base equilibrium considering what enters the system, as an example lactate or other dietary strong ions assumed with food or infused in solution and what is eliminated from the system primarily with urine. This mass balance approach is not fully appreciated to date, but it is impossible using the Siggaard-Andersen or Henderson-Hasselbalch models.

This book includes the original chapters of Stewart's classic treatise and many other contributions relative to the acid-base disturbances in different clinical conditions. It will be clear to the reader how the physicochemical approach can be helpful in understanding mechanisms

barely understandable using the traditional approaches. Clinical acid-base equilibrium has been studied for more than 100 years. Nothing is definitive; however the physicochemical approach represents a further step in this rather complicated field -not just to compute the pH but to better understand the pathophysiology of the system.