

[AFTERWORD]

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“The truth is a beautiful and terrible thing..”

- Albus Dumbledore, Harry Potter and the Philosopher’s Stone

It is now more than a quarter of a century ago since Peter Stewart, the maverick Canadian working in the US, published his book and then his paper in the Canadian Journal of Physiology and Pharmacology. For over ten years, Stewart’s work remained largely ignored despite the enthusiastic editorial from Robert Blake Reeves that accompanied Stewart’s Canadian paper. One reason for Stewart’s work being ignored was also one of Stewart’s faults: his published works are inadequately referenced. In particular it is a pity that Stewart did not mention that clinical chemists such as Gamble and Van Slyke would have supported his ideas about strong ions. Further, Stewart’s definition of an acid is not something he invented, but relates to Arrhenius’s 19th Century definition that is more biologically useful (something that increases hydrogen ion concentration) than the later Bronsted-Lowry definition (hydrogen ion donor).

As we celebrate the Stewart paradigm shift with this book we need to recognize that in some ways it is a “Back to the Future” paradigm shift. In the 1950s some clinical chemists were arguing that clinicians needed to catch up with the modern view of acid-base chemistry. They argued that to view sodium as a base and chloride as an acid (as Gamble and Van Slyke did) was old-hat and that the future lay with bicarbonate. We can ask why there was this passion for bicarbonate in the mid 20th Century? In that BC (before calculators) era the Henderson-Hasselbalch equation was very attractive. If one assumed that the major players were bicarbonate and carbon dioxide, then, armed with that fairly simple equation one could, or so it appeared, describe all the variables for plasma acid-base chemistry. Further, to be really modern, carbonic acid is a real (ie Bronsted-Lowry) acid. Thus came the rise of bicarbonate. Therefore, bicarbonate, which Stewart (and Van Slyke) viewed as a dependent, but useful, marker of acid-base status became an independent central mechanism as well as marker. This is a trick of physical chemistry. Any weak acid and its conjugate base can be inserted into the Henderson-Hasselbalch equation and give the appearance of controlling the situation. The second dissociation of

phosphate is another example. It would be interesting to know how the last 50 years of clinical chemistry would have differed if bicarbonate had not usurped the strong ions.

Another reason Stewart's work has been slow to catch on is that his original work did not readily lend itself to clinical application. Over the last 15 years a growing number of clinical researchers have contributed to making the Stewart approach clinician friendly. Many of them are involved with this book. Of particular interest are those who initially set out to debunk Stewart but after test driving his Ferrari decided to trade-in the bicarbonate Ford Anglia. Some have become so passionate as to view Stewart as a modern day Galileo fighting the bicarbonate based forces of darkness. James Figge and the late Vladimir Fencel played an important role in bringing Stewart to the bedside. A great irony is that these physicians came from Boston, the home of the bicarbonate rules-of-thumb. Fencel was a driving force in marrying Stewart's ideas with the existing concept of base-excess. Figge has been instrumental in allowing us to quantify the albumin anion component of the weak acids. Even some of the bicarbonate diehards grudgingly admit that Figge's work on albumin has relevance to their view, particularly in quantifying the anion gap.

The most important word associated with Peter Stewart is "quantitative". The bicarbonate based approach to acid-base disorders is qualitative if the rules-of-thumb are used, or at best quantitative, but limited, if base-excess is used on its own. Another irony is that some of the leading advocates of base-excess are also some of the leading naysayers for Stewart's work. This is unfortunate because base-excess and Stewart's work compliment each other well. If the Stewart approach is used we can quantify the effects on base excess of many plasma ions including sodium, chloride, albumin, phosphate, lactate, and therefore, unmeasured ions.

Stewart has revolutionized our understanding of acid-base assessment and therapy. Stewart helps us tailor our fluid therapies to the chemical needs of our patients. We can drive home the error of their ways to our many colleagues who believe that normal saline is a physiological solution. Mind you, Dr Ringer and Dr Hartmann could have told them the same, more than 50 years ago. We can easily explain the alkalinizing effects of Ringer's/Hartmann's in terms of the strong ions and largely ignore bicarbonate. The role of albumin becomes obvious and quantifiable. The role of other administered weak acids such as polygeline remains more elusive but is part of the quantified strong-ion-gap. As discussed in this book, Stewart greatly assists in assessing renal replacement therapies and the effects of drugs such as diuretics, again allowing us to largely ignore bicarbonate. As for renal physiology itself, Stewart transforms it from a bicarbonate centred nightmare to a relatively straightforward proposition. It is all about sodium and chloride. Stewart supplies a unifying approach; sodium and chloride, the major players in tonicity also become the major players in acid-base regulation.

The bicarbonate advocates, particularly the rules-of-thumb crowd, are not necessarily Lord Voldemort style forces of darkness. Rather they can be viewed as clinical chemistry Neanderthals. They are tough and adapted to their current environment but will ultimately be replaced by a scientifically and practically superior group: clinical chemistry Homo sapiens; those applying the Stewart approach. Based on current evidence, albumin should become a routine vari-

able in basic clinical chemistry. Base-excess needs to be embraced, by all, as a stepping-stone to a quantitative clinical approach using Stewart's principles. We need to be able to measure, reliably, as many clinical chemistry variables as possible. This will allow us to quantify the role of different plasma constituents in different disease states. Further, as we measure more plasma constituents the strong-ion-gap will become smaller in a given situation; there will be fewer known unknowns and unknown unknowns.

The strong-ion-gap also needs a new name because neither the gap itself nor the measured ions are all strong ions; weak acids are also important. One suggestion, with a nod to indigenous groups, is to refer to the strong-ion-gap as the net-unmeasured-ions (NUI) and the measured strong-ion and weak acid effects as the sum-of-all-measured-ions (SAMI). We need reliable reference ranges for the strong-ion-difference, strong-ion-gap, and the ionic effects of common weak acids. An associated area is to have a greater understanding of the predictive value of all these diagnostic tools, alone and in combination, in different disease states. Because of these types of issues and Stewart's approach being used around the globe, we need an international Stewart consensus group that also acts as a collaborative research group. We should encourage our most antagonistic colleagues to test-drive Stewart, they may become converts. Unfortunately, the Stewart road trip is unlikely to lead any of us to Stockholm, but it is exciting to be in the swirl of a paradigm shift "Back to the Future".

