

**Author Reply to: Whither the Bicarbonate Era**

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To the Editor:

We thank Dr. Swenson for the interest in our experimental study, in which we employed electro dialysis to reduce the plasma chloride concentration and correct acidemia in healthy piglets with either metabolic or respiratory acidosis (1). By selectively removing chloride, the main extracellular negatively charged ion, we were able to increase plasma Strong Ion Difference (SID), thus effectively correcting the experimentally induced acidemia. Of note, removing chloride to increase SID is exactly what healthy kidneys do during acidemia, especially of respiratory origin (2, 3). This occurs, among other mechanisms, through the downregulation of pendrin, the renal  $\text{Cl}^-/\text{HCO}_3^-$  exchanger (4). Electro dialysis, despite its complexity, has the advantage of being faster and independent from renal function. Furthermore, as correctly pointed out, chloride removal has the straightforward advantage of correcting acidemia without changing natremia nor osmolarity, as opposed to what happens with the administration of sodium-bicarbonate.

Acid-base balance is undoubtedly a complex topic that has polarized opinions also in the past, with the well-known trans-Atlantic debate between the Boston and Copenhagen schools (5). It is therefore not surprising that this is somehow happening again, although the current clash is between enthusiasts of the physico-chemical approach, i.e. the Stewart's approach, and the rest of the world.

The Stewart's approach has the advantage of combining two very important aspects of medicine: the acid-base and the hydro-electrolyte equilibrium (6).

It is based on the principle that the pH of a biological solution can be varied *independently* by 3 variables: i) the partial pressure of carbon dioxide ( $\text{PCO}_2$ ), ii) SID and ii) the total amount of non-carbonic weak acids ( $\text{ATOT}$ ), which in the extracellular space are mainly constituted by albumin and phosphates. The claim made by Dr. Swenson that only the strong ions determine pH and bicarbonate of a biological solution is, therefore, partially incorrect since it does not take into account  $\text{PCO}_2$  and  $\text{ATOT}$ . Furthermore, it is important underlining that these variables are not

completely independent from each other. Indeed, a certain degree of interdependence is certainly present (7).

Technology is improving quickly and modern blood gas analyzers provide reliable measurements of blood gases and pH, requiring only *microliters* of whole blood. In addition, they reliably measure, through direct ion-selective electrodes, also the concentration of the major extracellular electrolytes, namely sodium, potassium, ionized calcium, chloride and also lactate. Currently, blood gas analyzers do not measure albumin and phosphate concentration. However, these variables can be at first guessed and, in case of complex acid-base disorders, easily measured. We therefore think that Dr. Swenson overstates the economic and biological costs (anemia and transfusion) related to a single blood gas analysis.

In conclusion, we respectfully do not believe that teaching and understanding the physico-chemical approach to acid-base equilibrium is difficult. What matters is to comprehend that the physico-chemical approach is the base to integrate electrolytes and acid-base balance rationally. Stewart's and Van Slyke's approaches are two faces of the same medal: as such, trying to demonstrate the superiority of one over the other may not be worth the effort. The medal is always the same. Similarly to what happens during language learning, it is on the one hand difficult to learn a new language (approach) if one has spoken (applied) another one for decades. On the other, children (trainees) learn the language (approach) they grow in, without even noticing. Of note, if more languages are spoken together, both can be learned with a reasonable effort. Given the reasonable advantages of bilingualism, one wonders why both methods cannot be applied in the near future, without necessarily trying to demonstrate the superiority of one over the other.

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