using hemodialysis with a low bicarbonate dialysate. *ASAIO J* 2019; 65:605–613.
3. Fencl V, Leith DE. Stewart's quantitative acid-base chemistry: applications in biology and medicine. *Respir Physiol* 1993;91:1–16.
4. Zanella A, Caironi P, Castagna L, Rezoagli E, Salerno D, Scotti E, *et al*. Extracorporeal chloride removal by electrodialysis: a novel approach to correct acidemia. *Am J Respir Crit Care Med* 2020;201:799–813.
5. Dubin A, Menises MM, Masevicius FD, Moseinco MC, Kutscherauer DO, Ventrice E, *et al*. Comparison of three different methods of evaluation of metabolic acid-base disorders. *Crit Care Med* 2007;35: 1264–1270.
6. Ring T, Kellum JA. Strong relationships in acid-base chemistry - modeling protons based on predictable concentrations of strong ions, total weak acid concentrations, and pCO2. *PLoS One* 2016;11: e0162872.
7. Story DA. Stewart acid-base: a simplified bedside approach. *Anesth Analg* 2016;123:511–515.

Reply by Zanella *et al.* to Swenson

From the Authors:

We thank Dr. Swenson for the interest in our experimental study, in which we employed electrodialysis 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 the plasma strong ion difference (SID), thus effectively correcting the experimentally induced acidemia. Of note, removing chloride to increase the SID is exactly what healthy kidneys do during acidemia, especially acidemia of respiratory origin (2, 3). This occurs, among other mechanisms, through the downregulation of pendrin, the renal Cl^-/HCO_3^- exchanger (4). Electrodialysis, 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 or osmolarity, as opposed to what happens with the administration of sodium bicarbonate.

Acid–base balance is undoubtedly a complex topic that has also had polarized opinions 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 physicochemical approach (i.e., the Stewart approach) and the rest of the world.

The Stewart approach has the advantage of combining the following two very important aspects of medicine: the acid–base and the hydroelectrolyte equilibrium (6).

It is based on the principle that the pH of a biological solution can be varied independently by three variables: *1*) P_{CO_2}, *2*) the SID, and *3*) the total amount of noncarbonic weak acids, 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 because it does not take into account P_{CO_2} and total amount of noncarbonic weak acids. Furthermore, it is important to underline 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, the concentration of the major extracellular electrolytes, namely, sodium, potassium, ionized calcium, chloride, and 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 believe 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 physicochemical approach to acid–base equilibrium is difficult. What matters is to comprehend that the physicochemical 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. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Alberto Zanella, M.D.*
University of Milan
Milan, Italy
and
Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico
Milan, Italy

Thomas Langer, M.D.
University of Milano-Bicocca
Monza, Italy
and
Grande Ospedale Metropolitano Niguarda
Milan, Italy

Pietro Caironi, M.D.
Azienda Ospedaliero-Universitaria S. Luigi Gonzaga
Turin, Italy
and
University of Turin
Turin, Italy

Originally Published in Press as DOI: 10.1164/rccm.202005-1842LE on May 27, 2020

Luciano Gattinoni, M.D.
University of Göttingen
Göttingen, Germany

Antonio Pesenti, M.D.
University of Milan
Milan, Italy
and
Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico
Milan, Italy

On behalf of all the authors

ORCID IDs: 0000-0002-2967-2527 (A.Z.); 0000-0001-5380-2494 (L.G.).

*Corresponding author (e-mail: alberto.zanella1@unimi.it).

References

1. Zanella A, Caironi P, Castagna L, Rezoagli E, Salerno D, Scotti E, *et al*. Extracorporeal chloride removal by electrodialysis: a novel approach to correct acidemia. *Am J Respir Crit Care Med* 2020; 201:799–813.
2. Gattinoni L, Carlesso E, Cadringher P, Caironi P. Strong ion difference in urine: new perspectives in acid-base assessment. *Crit Care* 2006;10:137.
3. Kellum JA. Determinants of blood pH in health and disease. *Crit Care* 2000;4:6–14.
4. de Seigneux S, Malte H, Dimke H, Frøkiaer J, Nielsen S, Frische S. Renal compensation to chronic hypoxic hypercapnia: downregulation of pendrin and adaptation of the proximal tubule. *Am J Physiol Renal Physiol* 2007;292:F1256–F1266.
5. Bunker JP. The great trans-Atlantic acid-base debate. *Anesthesiology* 1965;26:591–594.
6. Fencl V, Leith DE. Stewart's quantitative acid-base chemistry: applications in biology and medicine. *Respir Physiol* 1993;91:1–16.
7. Langer T, Scotti E, Carlesso E, Protti A, Zani L, Chierichetti M, *et al*. Electrolyte shifts across the artificial lung in patients on extracorporeal membrane oxygenation: interdependence between partial pressure of carbon dioxide and strong ion difference. *J Crit Care* 2015;30:2–6.

Erratum: Lower Bacillus Calmette-Guérin Protection against *Mycobacterium tuberculosis* Infection after Exposure to Beijing Strains

There are errors in the research letter by Verrall and colleagues (1), published in the May 1, 2020, issue of the *Journal*. In Table 2, percentages should not have been listed in the bottom half of the first two columns (IGRA Negative and IGRA

Table 2. RR of IGRA Conversion at 14 Weeks, by *M. tuberculosis* Genotype and by BCG Vaccination Stratified by *M. tuberculosis* Genotype

	IGRA Negative (*n* = *275*) (*n*)	IGRA Positive (*n* = *108*) (*n*)	RR	95% CI	*P* Value	ARR	95% CI	*P* Value
RR of IGRA conversion in contacts by index case *M. tuberculosis* genotype*								
Other genotype	206	69	1.00	Ref.		1.00	Ref.	
Beijing genotype	69	39	1.44	0.98–2.10	0.06	1.39	1.00–1.93	0.048
RR of IGRA conversion by contact BCG vaccination status and index case *M. tuberculosis* genotype†								
Other genotype								
BCG: No	22	21	1.00	Ref.		1.00	Ref.	
BCG: Yes	184	48	0.42	0.28–0.63	<0.001	0.40	0.27–0.61	<0.001
Beijing genotype								
BCG: No	13	7	1.00	Ref.		1.00	Ref.	
BCG: Yes	56	32	1.04	0.54–2.01	0.9	1.02	0.56–1.85	0.9

Definition of abbreviations: ARR = adjusted relative risk; BCG = bacillus Calmette-Guérin; CI = confidence interval; IGRA = IFN-γ release assay; *M. tuberculosis* = *Mycobacterium tuberculosis*; Ref. = reference; RR = relative risk.
*Estimates obtained by multiple regression, adjusted for index case age, sex, smear grade, contact age, sex, hours spent with index case, smoking, BCG vaccination, and body mass index. Index case cough duration, cavities, extent of X-ray disease, drug resistance, and multidrug resistance were not retained in the model, nor was contact diabetes status.
†Estimates obtained by multiple regression, adjusted for index case age, sex, smear grade, contact age, sex, hours spent with index case, smoking, body mass index, and an interaction term for BCG and strain genotype. Index case cough duration, cavities, extent of X-ray disease, drug resistance, and multidrug resistance were not retained in the model, nor was contact diabetes status.