that the removal rate could not exceed the production rate of inflammatory cytokines. Taken together, we think that individualized dosing regimens according to the metabolic needs of patients, rather than fixed dosing, should be considered. Lower-dose CRRT combined with alternative therapy such as hemoperfusion also could be considered. Finally, the exclusion of patients with extremely severe sepsis or stratified randomization according to the severity of sepsis could be recommended for future clinical trials.

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Sodium-Chloride Difference as a Simple Parameter for Acid-Base Status Assessment

To the Editor:
We read with great interest the recent article by Adrogue and Madias and agree with all its conclusions. However, the article did not comment on a simple and useful parameter for assessing acid-base status; namely, the difference between 2 major serum ions, sodium and chloride.2,3

The relationship between serum bicarbonate, sodium-chloride difference, and the anion gap (AG) can be expressed by the equation: AG = Na+ – Cl– – HCO3-. AG corrected for albumin (mEq/L) = AG + [0.25 × (44 – albumin [g/L])].

Figure 1. The relationship between serum bicarbonate and sodium-chloride difference in patients with chronic kidney disease with anion gap (AG) corrected for albumin within the reference range of 8 to 16 mEq/L. AG = Na+ – Cl– – HCO3-. AG corrected for albumin (mEq/L) = AG + [0.25 × (44 – albumin [g/L])].

In our opinion, the evaluation of sodium-chloride difference as a surrogate of strong ion difference is appropriate for both physiologic and physicochemical approaches and should be used in daily practice for 2 reasons. First, its decline can indicate acidosis with normal anion gap even before analyzing acid-base parameters, as shown in Fig 1 in patients with chronic kidney disease; it is especially useful in unexpected renal tubular acidosis with normal glomerular filtration rate or dilution acidosis. Second, in cases of high anion gap acidosis, a decrease or increase in sodium-chloride difference can detect coexisting metabolic acidosis or alkalosis, although the isolated sodium and chloride concentrations are still within the wide normal limits.

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In Reply to ‘Sodium-Chloride Difference as a Simple Parameter for Acid-Base Status Assessment’

We are pleased that Drs Havlin, Matousovic, and Schück1 are in agreement with the conclusions of our recent article.2 However, we would disagree with their assertion that serum sodium-chloride difference is a useful parameter for assessing acid-base status. Quite the contrary, when used as proposed, this parameter can be misleading and therefore can cause errors in diagnosis and management. Whereas the authors would interpret the narrowing of the serum sodium-chloride difference as indicative of normal anion gap (hyperchloremic) metabolic acidosis, it might well evidence respiratory alkalosis or a mixed acid-base disorder. Similarly, widening of the serum sodium-chloride difference is not diagnostic of metabolic alkalosis, but might well be associated with respiratory acidosis or a mixed disorder.

We would strongly discourage sole use of the serum sodium-chloride difference in assessing acid-base status. There are no shortcuts to applying the physiologic approach, which remains the optimal approach to assessing the acid-base composition of the blood.2,3

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Vitamins E and C May Differ in Their Effect on Contrast-Induced Acute Kidney Injury

To the Editor:

A recent meta-analysis by Su et al1 compared 12 different prophylactic interventions against contrast medium–induced acute kidney injury (CIAKI). In their meta-analysis, Su et al pooled different vitamins into a single group of “vitamins and analogues,” but in so doing, did not take into account that vitamin C is water soluble whereas vitamin E is fat soluble, and therefore their relative effects might be different. Su et al calculated an odds ratio of 0.64 (with a 95% credible interval of 0.41-0.95) for the effect of “vitamins and analogues,” but they did not calculate the specific

![Figure 1](image-url)

**Figure 1.** Effect of vitamin E in preventing contrast medium–induced acute kidney injury. This meta-analysis pools the vitamin E trials identified by Su et al.1 There is no heterogeneity among the 3 trials, with I² = 0%; P = 0.7 for the test of heterogeneity. In the forest plot on the right side, the vertical line indicates the placebo group level (risk ratio [RR] = 1). The horizontal lines indicate the 95% confidence intervals (CIs) for the effect, and the square in the middle of the horizontal line indicates the point estimate of the effect in the particular trial. The diamond shape indicates the pooled effect and its 95% CIs. Abbreviation: RR, risk ratio.