impair cardiovascular function and lead to hemodynamic instability.[11] The clinical challenge that metabolic acidosis poses is more crucial as the dangers of $NaHCO_3$ treatment are appreciated.[12,13] We urge the anesthesia community to consider Stewart's new approach to acid-base management and consider the importance of changes in $[Cl^-]$ and in strong ion difference. Understanding of these concepts may lead to different practices of volume replacement during prolonged surgical procedures and an improved acid-base condition of our patients.

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Dilutional Acidosis: A Nonentity?

To the Editor:—I read with interest the case report by Mathes *et al.* on dilutional acidosis and wish to make some observations.

They administered in excess of 3100 mmol of chloride to their patient (mostly in the form of normal saline) causing the plasma chloride to increase from 90 to 128 mM. They noted a metabolic acidosis (pH, 7.16; HCO3, 13.2 mEq/l; base deficit, 14.5 mEq/l) and attributed this to dilution of the extracellular HCO3 pool by expansion of the extracellular space. This is incorrect. If this was the mechanism involved, then an acidosis should also occur with pure water expansion of the extracellular space such as in SIADH or psychogenic polydipsia. No acidosis is seen in these disorders. The actual mechanism involved is related to chloride-bicarbonate exchange.

Why is this so? The law of electrical neutrality of solutions requires that in extracellular fluid where Na is the predominant cation, giving CI in amounts equal to Na leaves no room for the second most common anion in serum, HCO3, which is then renally excreted (slow) or moved intracellularly (fast to slow). A decrease in HCO3 leads to *hyperchloremic acidosis,*[1] a term first coined by Black.[2]

Mathes *et al.* stated that hyperchloremic metabolic acidosis induced by the administration of large quantities of normal saline is likely to not be harmful. This as an unproven hypothesis. They also stated that despite a progressive severe metabolic acidosis they believed their patient had adequate end organ perfusion because of stable hemodynamics and a normal blood lactate. Firstly, it is worth noting that a metabolic acidosis not caused by end organ hypoperfusion is capable of impairing organ function. Secondly, abnormal hemodynamics and lactatemia have been shown to be variable and late signs of impaired organ perfusion and function.

In an acute hemorrhage swine model, resuscitation with normal saline lead to lower pHs and HCO3s and larger base deficits compared with other crystalloids.[3] Survival was higher in the group given Ringer's lactate, attributed to its lower Cl content not causing hyperchloremic acidosis.

Contrary to their case report, hyperchloremic acidosis has been described perioperatively. McFarlane and Lee reported on patients receiving an average of 3 l of normal saline intraoperatively and documented higher serum CI, lower HCO3, and larger base deficits compared with a group receiving Plasmalyte 148 (a balanced salt solution with a chloride content of 98 mM).[4]

Apart from the deleterious effects of inducing acidosis *per se,* hyperchloremia is not a benign condition either. Wilcox in a

series of studies has shown that renal blood flow and glomerular filtration rate are regulated by plasma chloride. Hyperchloremia induces renal vasoconstriction by inhibiting the intrarenal release of renin and angiotensin II, leading to a decreased urine output.[5,6] The cellular mechanism is unclear but may be related to adenosine, PGE_2, or thromboxane mediator release. Renal blood flow decreased by 36%, and GFR decreased by 29% with hyperchloremia.[7]

I submit that one should aim to not disturb electrolyte and acid-base physiology in the perioperative patient. This means not administering large volumes (*e.g.*, 20 l) of normal saline. To replace 1 l of blood loss, one could administer 3 l of normal saline, representing an excess chloride load of 165 mmol, or 3 l of Ringer's lactate, an excess of 27 mmol of chloride, or 1 l of normal serum albumen, an excess of 25 mmol of chloride. These latter two fluids with their lesser excess chloride load would be unlikely to produce hyperchloremic acidosis.

Management of a normal saline-induced acidemia should involve switching to Ringer's lactate and aiming for a pH above 7.2 where arrhythmias, myocardial depression, and decreased responsiveness to catecholamines are much reduced. This can be achieved by allowing the bicarbonate buffering system to be maximally effective by lowering the PCO_2 appropriately. This will minimize the titration of intracellular protein buffers.[8] Giving the chloruretic aciduretic agent furosemide will also be of use with functioning kidneys.[9] If fresh frozen plasma is indicated on transfusion criteria, then its administration may also be helpful because it has excellent buffering capabilities.[10,11]

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Dilutional Acidosis or Altered Strong Ion Difference

To the Editor: — Dilutional acidosis is an interesting concept but has not been clearly defined clinically. Mathes' *et al.*[1] and previous case reports[2,3] of metabolic acidosis secondary to the administration of large amount of normal saline have an additional feature in common, namely hyperchloremia. As a general rule, hyperchloremia is associated with metabolic acidosis and hypochloremia with metabolic alkalosis. In all these case reports, hyperchloremia may have caused the metabolic acidosis rather than by the dilution of serum bicarbonate. High chloride load as the cause of hyperchloremic metabolic acidosis has recently been suggested in anesthetic literature.[4]

How does a change in chloride concentration bring about such profound alteration in acid-base equilibrium? The answer to this question is not obvious when analyzed using the Henderson-Hasselbalch equation. However, it can be explained by Stewart's method of analysis of quantitative acid-base chemistry.[5] To understand and apply Stewart's approach to acid-base analysis and management requires a shift in the way we think and understand acid-base problems. Fencl and Leith[6] recently reviewed Stewart's quantitative approach to acid-base chemistry and summarized that "Stewart's approach shows the way to understanding and mathematical modeling of biological fluids as physico-chemical systems. It provides a basis for quantitative analysis and rational manipulation of acid-base state, *in vivo* and *in vitro*, and it challenges current interpretations of compartmentalized acid-base exchanges across biological membranes."

According to Stewart, in a solution containing strong electrolytes, the difference in the sum of the positive charges and that of the negative charges carried by the strong ions, referred to as strong ion difference (SID), is one of the major determinants of hydrogen ion concentration. It is the net unbalanced positive charge on the strong