easily achieved if a fluid that is more normal than "normal" saline becomes commercially available.

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In Reply:—We are grateful to have the opportunity to respond to the thoughtful comments by Drs. Story *et al.*, Drummond, and Dorje *et al.* We entirely agree with Story *et al.* that the Stewart approach[1] provides a fundamental insight into acid-base equilibrium, and that in many cases this approach better explains the causes for metabolic pH changes than the Henderson-Hasselbalch[2] approach. Nevertheless, the Henderson-Hasselbalch equation is still correct, and most clinicians work well with this equation, despite the fact that the equation does not reflect the whole background of acid-base homeostasis. Consequently, it seemed appropriate to present a well-balanced discussion of our results in the light of the "traditional" Henderson-Hasselbalch approach and the "modern" Stewart approach.

We respond to the letter by Dr. Drummond by stating that we did not claim to be the first to evaluate acid-base changes under large saline infusions. However, probably because of unfortunately chosen key words, we did not come across the report by McFarlane and Lee while preparing our manuscript.[3]

The question asked by Dorje *et al.* whether artificial hyperchloremia has any important adverse effects cannot be answered with our data. Perioperative hyperchloremia seems to be benign in patients with normal renal function; however, we agree that for critically ill patients, especially those with acute or chronic renal failure, more "physiologic" crystalloid solutions would be advantageous. The proposal of Dorje *et al.* (Na^+ = 140 mM, Cl^- = 100 mM, and lactate or bicarbonate = 40 mM) would probably lead to an ongoing metabolic alkalosis in case of 40 mM bicarbonate content. Our experience with substitutes containing lactate suggests that these solutions will cause a slight but continuous increase in serum lactate concentration. Unfortunately, this artificial increase in serum lactate will lead to loss of an essential routine monitoring for inadequate tissue oxygenation. In summary, we conclude that the ideal electrolyte composition of crystalloids has not yet been found, and further investigations in this field are necessary.

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In Reply:—We appreciate the comments of Drummond[1] and Story *et al.*[2] Both letters address issues that clarify the report by Scheingraber *et al.*[3]

First, Drummond[1] appropriately calls additional attention to the important study by his colleagues at the Royal Infirmary in Edinburgh.[4] Both McFarlane and Lee[4] and Scheingraber *et al.*[3] conducted randomized clinical trials comparing 0.9% saline balanced salt solutions. The two studies differ in that McFarlane and Lee[4] enrolled patients under-

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going "major hepatobiliary or pancreatic surgery" averaging approximately 3.5 h in duration, whereas Scheingraber *et al.*[3] enrolled patients undergoing "lower abdominal gynecologic surgery" averaging approximately 2.25 h. Despite the somewhat shorter duration of surgery, the gynecologic patients randomized to the saline group received a slightly greater total volume[3] (71 ± 14 ml/kg during the first 120 min of infusion) than the patients receiving saline in the study by McFarlane *et al.*[4] (14.6 ± 41 ml · kg^{-1} · h^{-1} during an interval of 219 ± 77 min). As a consequence, the increase in plasma chloride and the decrease in plasma bicarbonate were greater in the gynecologic patients. Together, the reports suggest that hyperchloremic acidosis is a dose-dependent consequence of saline administration. Whether this acid-base abnormality is in fact harmful remains unclear, although we[5] were unable to cite any compelling evidence of adverse effects. We are skeptical that differences in outcome, if any, related to the choice of saline or balanced salt solution would justify the cost of a randomized clinical trial.

However, one noteworthy characteristic of Plasmalyte 148, the balanced salt solution used by McFarlane and Lee,[4] is that the sodium concentration is 140 mEq/l. Consequently, in contrast to lactated Ringer's solution, infusion of substantial volumes does not decrease serum sodium and serum osmolality, and does not raise the same theoretical concerns about increases in brain water.[5]

We agree with Story *et al.*[2] that the Stewart approach[6,7] offers interesting insights into acid-base chemistry; however, we disagree that the relative merits of the Stewart approach *versus* the conventional Henderson-Hasselbalch approach constitute a "central issue." Regardless of its attractive biochemical features, the Stewart approach has not yet become popular for routine clinical use, perhaps because it is less simple to quantify at the bedside and because it prompts no important differences in treatment.

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Dynamic Response to Volatile Anesthetics Has Been Examined Before

To the Editor:—Olsen and Dahan describe an analysis of the dynamic electroencephalographic (EEG) response to step changes in end-tidal concentration of isoflurane or sevoflurane. Understanding the dynamic and steady state responses of a system to a changing input is a prerequisite to designing a robust automatic control system. Unfortunately, the use of a single, fixed-size step change in concentration is suboptimal as a "forcing" function for several technical reasons, including (1) the absence within this function of many frequencies in the range of interest, and (2) the possible blinding to nonlinearities. The discipline of control systems engineering provides many better alternatives to the development of a dynamic response measurement of a complex "black box" system similar to an EEG response in a patient. We reported the use of one such technique (pseudorandom binary sequence testing) to measure the dynamic (impulse) response of canine EEG (spectral edge frequency) to volatile anesthetics.[1] This work was later reported in a Ph.D. thesis.[2] Historians of our specialty will also appreciate that Dr. N. T. Smith was administering sine-wave concentrations of agents at various frequencies to human volunteers and measuring EEG response in 1976.[3]

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