In this issue of Clinical Science, Lobo et al. [1] report a direct comparison of changes in haemoglobin concentration ([Hb]), urinary output, serum albumin concentration ([Alb]) and electrolytes in 10 healthy young adult male volunteers receiving a 2 litre, 60 min infusion of 5% (w/v) dextrose in water or 0.9% (w/v) saline. Subjects were studied in the morning after an overnight fast. At the end of the infusion, plasma volume expansion, as estimated from the dilution of [Hb], was approx. 15% greater than preinfusion levels in both groups. (An 8% dilution of [Hb] equates to a 15% increase in plasma volume after correcting for a haematocrit averaging 45%.) Infusion of 5% (w/v) dextrose in water produced transient changes, resolving within 1 min after infusion in both [Hb] and [Alb], whereas 0.9% (w/v) saline produced a remarkably sustained reduction of [Hb] and expansion of plasma volume that diminished only slightly in the 5 h after infusion. [Alb] was reduced 20% after 0.9% (w/v) saline, and that reduction also persisted for 5 h after infusion.

These data represent an important addition to our understanding of the effects of bolus administration of crystalloid fluids, which is a mainstay of the treatment of hypovolaemia and a common pre-anesthetic intervention intended to reduce the magnitude of hypotension after induction of neuroaxial or general anaesthesia. Curiously, although considerable data describe changes in body composition after surgical or traumatic insults [2,3], little research defines the effects of fluid infusion alone in healthy conscious or anaesthetized volunteers. As a consequence, most clinicians assume that tissue trauma explains the reduction of [Alb] and the accumulation of interstitial fluid that accompany extensive surgery. In contrast, Lobo et al. [1] demonstrated that a substantial component of perioperative hypoalbuminaemia results directly from crystalloid fluid administration. These data confirm those of Svensen and Hahn [4] regarding the dilution of albumin after infusion of crystalloid. Of course, these data do not demonstrate that hypoalbuminaemia is harmful to patients in itself, or that colloid should be infused to avoid reduction of colloid osmotic pressure.

The merits of crystalloid and colloid fluids for perioperative fluid management continue to be debated. Although extensive research and systematic reviews of that research [5,6] have failed to resolve the debate, most surgeons and anaesthesiologists use sodium-containing crystalloids, such as lactate- or acetate-containing Ringer’s solutions or 0.9% (w/v) saline. Because the volume of distribution of solutions containing near-physiologic sodium concentrations is primarily the extracellular (sodium) space, they are retained intravascularly better than 5% (w/v) dextrose in water, which distributes throughout both the extracellular and intracellular spaces.

However, in the report by Lobo et al. [1], the persistence of intravascular retention, evidenced by the duration of the decline in [Hb] after infusion of 0.9% (w/v) saline, is provocative. Such persistence has not been as well documented in previous clinical studies, and contrasts strikingly with previous reports of the kinetics of [Hb] dilution after infusion of slightly hypotonic solutions, such as acetate-containing Ringer’s solution, in volunteers [4,7] and 0.9% (w/v) saline in experimental animals [8,9]. Using the calculation of Lobo et al. [1], peak blood volume expansion after infusion of 0.9% (w/v) saline was 8.1% of an estimated baseline blood volume of 4.35 litres (72.5 kg × 6%). Therefore the volume-expansion efficiency (estimated peak volume expansion of 342 ml divided by an infused volume of 2 litres) was 17.6%. This low efficiency of isotonic crystalloid is in keeping with other studies of crystalloid infusion [10], and is considerably less than the 33% efficiency often assumed for crystalloid infusion (i.e. the plasma volume expansion will equal one-third of the infused volume) [11]. After the infusion, [Hb] rapidly returned to baseline in the dextrose group but remained diluted after 0.9% (w/v) saline, increasing only from 92% of the preinfusion baseline immediately after infusion to 94% of baseline at 6 h. Over this time period, approx. 80% of the infused volume of 5% (w/v) dextrose was excreted in urine, whereas less than 30% of the infused saline volume was excreted over 6 h.

The data are superficially similar to those of Grathwohl et al. [12], who infused 2.3±0.1 litres of 0.9% (w/v) saline over 30 min, followed by a continuous infusion of 0.9% (w/v) saline at a rate of 118±3.0 ml/h. At 3.5 h (and an additional 413 ml of maintenance fluid) after the original bolus, approx. 80% of the original [Hb] reduction remained, in comparison with persistence 5 h after the infusion of 75% of the original [Hb] reduction reported by Lobo et al. [1], who did not provide maintenance fluid infusion. The data contrast markedly with those of Svensen and Hahn [4], who studied a similar group of healthy young male adults, also subjected to an overnight fast, who received approx. 2 litres of acetate-containing Ringer’s solution over 30 min. They reported greater peak expansion (approx. 20%) of the plasma volume than Lobo et al. [1]; however, the
decreased [Hb] rapidly approached baseline within a few hours. Briefly, Lobo et al. [1] reported sustained volume expansion after 0.9% (w/v) saline, whereas Svensen and Hahn [4] reported transient expansion after acetate-containing Ringer’s solution.

What differences could account for rapid resolution of plasma expansion after crystalloid infusion in one study and persistent volume expansion in another? Despite a similar interval of fasting in both groups, it is possible that the pre-existing states of hydration were different, or that the experimental protocols induced different levels of stress and neurohumoral responses. Solutions containing sodium would be expected to induce diuresis in response to several well-established, volume-responsive mechanisms, such as increased atrial pressures, which release atrial natriuretic peptide [13], and increased cardiac output and reduced sympathetic tone, which increase renal blood flow [14]. However, if 0.9% (w/v) saline is rapidly infused, the associated increase in serum sodium and osmolality could reduce diuresis by causing release of antidiuretic hormone (ADH) [15]. Perhaps in fasted individuals, baseline osmolality might be slightly increased. Consequently, infusion of a slightly hypertonic solution (0.9% (w/v) saline) could stimulate, and infusion of a slightly hypotonic solution (acetate-containing Ringer’s solution) could inhibit ADH hormone release, owing to the steep slope of the relationship between ADH release and osmolality [16,17]. Diuresis after 5% (w/v) dextrose in water should exceed that after either balanced salt solutions or 0.9% (w/v) saline. Initially, rapid infusion of 5% (w/v) dextrose induces hyperglycaemia and osmotic diuresis. Subsequently, as serum glucose declines secondary to uptake by cells, the remaining sodium-free water should reduce serum osmolality and promote further diuresis secondary to reduced levels of ADH.

Therefore one would hypothesize that the magnitude and duration of volume expansion after infusion of 5% dextrose in water would be less than that after infusion of lactate- or acetate-containing Ringer’s solutions, which, in turn, should produce less sustained volume expansion than slightly hypertonic 0.9%. However, the effects secondary to changes in osmolality should be limited. Lobo et al. [1] demonstrated that 0.9% (w/v) saline produced acute, small increases of serum sodium and osmolality that dissipated within the first hour after infusion.

Another difference between the two studies that merits discussion is that the infusion rate was twice as rapid in the study by Svensen and Hahn [4]. Although physicians often administer substantial boluses of fluid over 15–30 min, one possibility is that slower infusions promote more sustained volume expansion. Indeed, in another study, Hahn and Svensen [18] used a volume kinetic model and data from infusions in volunteers to predict the effects of the rate and duration of infusion on [Hb] dilution. They concluded that slower infusions tended to increase the duration of [Hb] dilution in comparison with more rapid infusions. If this is true, it could explain the greater persistence of plasma volume expansion after the slower bolus administered by Lobo et al. [1].

We hypothesize that rapid crystalloid boluses may be an inherently inefficient method of expanding intravascular volume, and that hypotonic balanced salt solutions may be less effective crystalloids than 0.9% (w/v) saline. Additional studies, using identical protocols except for formulations and infusion times, are necessary to evaluate these hypotheses, both in normovolaemic volunteers and patients subjected to surgical stress and hypovolaemia. One study of particular value would be a direct comparison of acetate- or lactate-containing Ringer’s solution with 0.9% (w/v) saline in volunteers under otherwise identical conditions. Perhaps rapid boluses are effective in hypovolaemic states, but slower infusions are more appropriate in situations where it is considered desirable to increase plasma volume in normovolaemic patients, such as those about to undergo subarachnoid block or induction of general anaesthesia. There is no question that fluid therapy of perioperative and critically ill patients will benefit from a better understanding of how different crystalloids and infusion regimens affect both initial and sustained plasma volume expansion. Clinicians require better answers to the question: to b(olus) or not to b(olus)?

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REFERENCES