our elderly patients, without showing differences between the two volume-replacement regimens. There is convincing evidence that cardiac surgery using CPB is associated with alterations in kidney integrity [6], especially in elderly patients. Kidney dysfunction can be either moderate or severe, requiring haemodialysis. Occult and moderate alterations in kidney integrity secondary to cardiopulmonary bypass have been identified by kidney-specific proteins [7,8]. As increase of kidney-specific proteins was only moderate in our study and gelatin-treated patients showed very similar changes, we concluded that the newest, third generation HES preparation (HES 130/0.4) is unlikely to change kidney integrity.

The influence of volume-replacement strategies on kidney function is a much-debated issue. However, no more reviews, meta-analyses, or overviews are necessary; instead, further well-performed research must be undertaken to fully evaluate the influence of specific volume-replacement strategies in specific patient populations. The information given by Dr Davidson does not help us much. Perhaps we should remember Winston Churchill: 'We are still confused – but on a much higher level'.

J. Boldt
Department of Anesthesiology and Intensive Care Medicine
Klinikum der Stadt Ludwigshafen
Ludwigshafen, Germany

References

1. Davidson IJ. Renal impact of fluid management with colloids: a comparative review. *Eur J Anaesthesiol* 2006; **23**: 721–738.
2. Schortgen F, Lacherade JC, Bruneel F *et al*. Effects of hydroxyethylstarch and gelatin on renal function in severe sepsis: a multicentre randomised study. *Lancet* 2001; **357**: 911–916.
3. Gosling P, Rittoo D, Manji M, Mahmood A, Vohra R. Hydroxyethylstarch as a risk factor for acute renal failure in severe sepsis. *Lancet* 2001; **358**: 581.
4. Godet G. Hydroxyethylstarch as a risk factor for acute renal failure in severe sepsis. *Lancet* 2001; **358**: 581.
5. Boldt J, Brenner T, Lehmann A, Lang J, Kumle B, Werling C. Influence of two different volume replacement regimens on renal function in elderly patients undergoing cardiac surgery: comparison of a new starch preparation with gelatin. *Intensive Care Med* 2003; **29**: 763–769.
6. Yallop KG, Smith D. The incidence and pathogenesis of acute renal failure following cardiac surgery, and strategies for its prevention. *Ann Cardiac Anaesth* 2004; **7**: 17–31.
7. Fauli A, Gomar C, Campistol JM, Alvarez L, Manig AM, Matute P. Pattern of renal dysfunction associated with myocardial revascularization surgery and cardiopulmonary bypass. *Eur J Anaesthesiol* 2003; **20**: 443–450.
8. Loef BG, Epema AH, Navis G, Ebels T, vanOeveren W, Henning RH. Off-pump coronary revascularization attenuates transient renal damage compared with on-pump coronary revascularization. *Chest* 2002; **121**: 1190–1194.

Deleterious renal effects of hydroxyethyl starch 130/0.4 and 200/0.5 solutions

doi: 10.1017/S0265021507000786

EDITOR:
My recent review of 92 studies, including 23 randomized clinical trials, focused on the renal impact of colloids [1]. One major conclusion from the review was that hydroxyethyl starch (HES) solutions across the full spectrum of clinically available molecular weights, substitutions and C2/C6 ratios can impair kidney function.

In comments on the review, Boldt [2] recapitulates several objections previously raised about the multicentre randomized clinical trial of 129 patients with severe sepsis or septic shock by Schortgen and colleagues [3], the largest randomized trial included in the review. Those investigators had earlier rebutted the objections [4] by noting that: (1) baseline differences affecting outcome would be unlikely due to random allocation; (2) the baseline difference in creatinine was not statistically significant; (3) the percentage of

Correspondence to: Ingemar J. Davidson, Division of Surgical Transplantation, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75390-9031, USA. E-mail: Ingemar.Davidson@Utsouthwestern.Edu; Tel: +1 214 648 4823; Fax: +1 214 648 4784

Accepted for publication 16 November 2006 EJA 4238A
First published online 20 June 2007

patients with renal dysfunction at baseline was actually higher in the gelatin (84%) than in the HES (75%) group, although again the difference was not statistically significant; (4) the criterion applied for acute renal failure (ARF) of a twofold serum creatinine increase might favour a group with higher baseline creatinine; and (5) ARF was the primary endpoint of the trial, which was neither designed nor powered to assess survival.

Importantly, the findings of Schortgen and colleagues [3] have now been fully confirmed by the new Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis (VISEP) multicentre randomized trial in 537 patients with severe sepsis or septic shock [5]. That trial compared morbidity and mortality in patients receiving an HES solution of 200 kDa molecular weight and 0.5 M substitution (HES 200/0.5) to a maximum of 20 mL kg^{-1} day^{-1} or Ringer's lactate control fluid. HES 200/0.5 increased both the incidence of ARF compared with that in the control group (34.9% vs. 23.2%; $P = 0.003$) and the frequency of renal replacement therapy (31.0% vs. 18.8%; $P = 0.001$). A trend towards higher mortality was also observed in the HES 200/0.5 group (41.0% vs. 33.9%; $P = 0.09$).

Boldt and colleagues [6] also recapitulate the interpretation they had placed on their randomized trial showing renal impairment after pump priming and volume expansion with HES 130/0.4 or gelatin in elderly cardiac-surgery patients. They argued that since both groups displayed renal impairment, and gelatin is devoid of adverse effects on the kidney, the observed deleterious renal effects may have been due to cardiopulmonary bypass itself rather than due to the fluid regimen. As detailed in my review, this argument proceeds from a flawed premise, because of randomized trial evidence that in fact gelatin does impair renal function compared with albumin [7,8]. Another commentator on this trial of Boldt and colleagues has also reached the conclusion that their data demonstrate renal impairment attributable to HES 130/0.4 [9].

Finally, Boldt contends that further reviews on volume replacement are not needed, even though he himself has been a prolific author of such reviews [10–12]. I disagree with this. Reviews serve the valuable aim of assembling and critically appraising evidence arising from a profuse and rapidly expanding clinical research literature. Reviews can also generate testable hypotheses. For example, the Cochrane albumin meta-analysis [13] motivated the Saline vs. Albumin Fluid Evaluation (SAFE) randomized trial [14]. Fluid-management strategies remain the subject of intensive investigation. Consequently, timely reviews will continue to play a key role in assimilating this growing body of evidence and in arriving at sound conclusions that can be incorporated into clinical practice.

I. J. Davidson
Division of Surgical Transplantation
The University of Texas Southwestern Medical Center at Dallas
Dallas, TX, USA

References

1. Davidson IJ. Renal impact of fluid management with colloids: a comparative review. *Eur J Anaesthesiol* 2006; **23**: 721–738.
2. Boldt J. Hydroxyethyl starch as a risk factor for acute renal failure in severe sepsis. *Lancet* 2001; **358**: 581–582.
3. Schortgen F, Lacherade JC, Bruneel F *et al*. Effects of hydroxyethyl starch and gelatin on renal function in severe sepsis: a multicentre randomised study. *Lancet* 2001; **357**: 911–916.
4. Schortgen F, Brochard L. Hydroxyethyl starch as a risk factor for acute renal failure in severe sepsis. *Lancet* 2001; **358**: 582.
5. Reinhart K, Bloos F, Engel C. Hydroxyethyl starch and Ringer's lactate for fluid resuscitation in patients with severe sepsis – results from the VISEP study. The German Competence Network Sepsis. *Intensive Care Med* 2006; **32**(Suppl 1): 213.
6. Boldt J, Brenner T, Lehmann A, Lang J, Kumle B, Werling C. Influence of two different volume replacement regimens on renal function in elderly patients undergoing cardiac surgery: comparison of a new starch preparation with gelatin. *Intensive Care Med* 2003; **29**: 763–769.
7. Himpe D, van Cauwelaert P, Neels H *et al*. Priming solutions for cardiopulmonary bypass: comparison of three colloids. *J Cardiothorac Vasc Anesth* 1991; **5**: 457–466.
8. Trull A, Hughes V, Cooper D *et al*. Influence of albumin supplementation on tacrolimus and cyclosporine therapy early after liver transplantation. *Liver Transpl* 2002; **8**: 224–232.
9. Wiedermann CJ. Renal impairment in cardiac surgery patients receiving hydroxyethyl starch. *Intensive Care Med* 2004; **30**: 519–520.
10. Boldt J. The Holy Grail of volume resuscitation in the septic patient is.... *Crit Care Med* 2006; **34**: 248–251.
11. Boldt J. Volume therapy in cardiac surgery: are Americans different from Europeans? *J Cardiothorac Vasc Anesth* 2006; **20**: 98–105.
12. Boldt J. Do plasma substitutes have additional properties beyond correcting volume deficits? *Shock* 2006; **25**: 103–116.
13. Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomised controlled trials. *BMJ* 1998; **317**: 235–240.
14. Finfer S, Bellomo R, Myburgh J, Norton R. Efficacy of albumin in critically ill patients. *BMJ* 2003; **326**: 559–560.