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In Reply:—I thank Dr. Ben-David for his interest in our recently published paper on the risks associated with high injection pressure during lumbar plexus blockade.[1] Here is my brief reply:

1. Dr. Hadzic is a shareholder at Macosta-Medical USA (Houston, TX); none of the remaining authors have financial interest in the device used in the study. In hindsight, although we simply studied the effect of injection pressures on epidural spread during lumbar plexus block rather than the actual devices or means of monitoring, this probably would have been best disclosed *a priori*.
2. It would be logical to assume that a small volume of injectate is unlikely to lead to epidural/contralateral spread of the local anesthetic, regardless of the injection pressure. Our findings, however, specifically indicate that high injection pressure during a standard single-shot technique of lumbar plexus block using 35 ml carries a significant risk of this complication. Administration of local anesthetic through a small-gauge indwelling catheter may involve an entirely different process and/or injection pressure considerations. This was not the subject of our study, and I do not have data to comment on this objectively.
3. I appreciate Dr. Ben-David's description of an alternative technique consisting of paravertebral L1 to L2 low-volume injections for postoperative analgesia after hip arthroscopy.[2] In our study, a lumbar plexus block was used as anesthesia for knee surgery, rather than for postoperative analgesia as in Dr. Ben-David's publication.[1,2] Equating anesthesia with analgesia remains a common source of discussion bias when discussing regional techniques; techniques used for analgesia are not universally interchangeable with techniques used for anesthesia. Finally, an anecdotal publication of two successful patient management scenarios using a new technique does not support claims of greater safety, efficacy, and ease-of-use advantages.[2]

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References

1. Gadsden JC, Lindenmuth DM, Hadzic A, Xu D, Somasundarum L, Flisinski KA: Lumbar plexus block using high-pressure injection leads to contralateral and epidural spread. ANESTHESIOLOGY 2008; 109:683–8
2. Lee EM, Murphy KP, Ben-David B: Postoperative analgesia for hip arthroscopy: Combined L1 and L2 paravertebral blocks. J Clin Anesth 2008; 20:462–5

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What Happens with the Fluid Replacement in the Septic Surgical Patient?

To the Editor:—We have read the interesting review of Chappell *et al.*[1] about the rational approach to preoperative fluid management, and we would like to add several aspects related to the surgical patient with sepsis coming to the operation room.

In 2004, the first guidelines[2] of the management of the septic patient were published. In these guidelines, fluids were essentiality given to reach the objectives in terms of blood pressure. At the beginning of 2008 these guidelines were updated,[3] and one of the most important items was still fluid replacement. If you follow the guidelines, as you should, you will find yourself giving a huge amount of volume in the first 24 h.

These guidelines did not differentiate the surgical and the medical patient. As we all know, our surgical patient has many differences in terms of fluid management.

For example, if you are on duty and the surgeon calls us because he has a patient in septic shock because of peritonitis, then we follow the guidelines using different monitors that show us the fluids the patient needs (central venous saturation, systolic pressure variation, lifting the legs up, *etc.*); what we really obtain is a very liberal fluid strategy.

As Chappell *et al.*[1] analyze, there are many studies that show us that the liberal strategy increases the anastomotic leaks, pulmonary edema, and wound infection after colorectal surgery. So what do we do?

To try and answer this question, we have to first find studies that discuss this specific topic, but it is really difficult to find. So what we really do is extrapolate the studies of the surgical scheduled patient and the septic patient, and we put them all together.

In the majority of patients, the septic surgical patient reaches the operation room with a high negative fluid balance, hypoproteinemic (hypoalbuminemic), and hypotensive. At that moment we start to administer fluids, but what type of fluids? The septic patient guidelines indicate that there is no difference in terms of mortality in using colloids or crystalloids.

If we give only crystalloids it would provoke different complications,[4] but a big third space would be created in our patient, and this is related to higher morbidity,[5] including anastomotic leaks.[6] If we give only colloids, it could aggravate the septic kidney failure.[7]

In the end we try and balance the guidelines for the surgical and medical patient; colloid nephrotoxicity *versus* tissue edema of crystalloids, rapid fluid replacement *versus* slow fluid replacement with vasopressor.

The liberal strategy is beneficial for the septic patient but is deleterious for the surgical one. Trying to counterbalance the risks and benefits of the correct fluid replacement strategy is at times difficult because of the lack of studies and guidelines in the septic surgical patient.

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References

1. Chappell D, Jacob M, Hofmann-Kiefer K, Conzen P, Rehm M: A rational approach to perioperative fluid management. ANESTHESIOLOGY 2008; 109: 723–40
2. Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, Ramsay G, Zimmerman JL, Vincent JL, Levy MM: Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004; 32:858–73
3. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent JL; International Surviving Sepsis Campaign Guidelines Committee; American Association of Critical-Care Nurses; American College of Chest Physicians; American College of Emergency Physicians; Canadian Critical Care Society; European Society of Clinical Microbiology and Infectious Diseases; European Society of Intensive Care Medicine; European

Respiratory Society; International Sepsis Forum; Japanese Association for Acute Medicine; Japanese Society of Intensive Care Medicine; Society of Critical Care Medicine; Society of Hospital Medicine; Surgical Infection Society; World Federation of Societies of Intensive and Critical Care Medicine: Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008; 36:296–327

4. Dorje P, Adhikary G, Tempe DK: Avoiding iatrogenic hyperchloremic acidosis–call for a new crystalloid fluid. ANESTHESIOLOGY 2000; 92:625–6

5. Nisanevich V, Felsenstein I, Almogy G, Weissman C, Einav S, Matot I: Effect of intraoperative fluid management on outcome after intraabdominal surgery. ANESTHESIOLOGY 2005; 103:25–32

6. Brandstrup B, Tønnesen H, Beier-Holgersen R, Hjortsø E, Ørding H, Lindorff-Larsen K, Rasmussen MS, Lanng C, Wallin L, Iversen LH, Gramkow CS, Okholm M, Blemmer T, Svendsen PE, Rottensten HH, Thage B, Riis J, Jeppesen IS, Teilum D, Christensen AM, Graungaard B, Pott F: Effects of intravenous fluid restriction on postoperative complications: Comparison of two perioperative fluid regimens: A randomized assessor-blinded multicenter trial. Ann Surg 2003; 238: 641–8

7. Davidson IJ. Renal impact of fluid management with colloids: A comparative review. Eur J Anaesthesiol 2006; 23:721–38

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In Reply:—We thank Dr. Navarro-Martinez and colleagues for their letter concerning our review on perioperative fluid management. In general, we would like to point out that our article was targeted on perioperative fluid therapy in patients who primarily have a steady state concerning their fluid compartments.[1] In these patients an intact vascular barrier function ensures that, despite a positive pressure within the circulatory space, plasma constituents are not distributed evenly across the whole extracellular compartment.[2,3] Rather, under normal physiologic conditions, they are predominantly retained where they are needed to maintain a sufficient cardiac preload. A small residual flow towards the interstitial space is managed by an intact lymphatic system.[1] In this situation, requirement-adapted fluid handling might limit tissue edema by considering physiologic and pathologic shifting, provided that the vascular barrier is primarily fully functioning.[1]

The septic patient, undergoing surgery or not, does not present such a steady state.[4] The normally accompanying capillary leakage syndrome, as a result of an insufficient vascular barrier, leads to a barely calculable shift of fluid and macromolecules (such as proteins and colloids) towards the interstitial space, representing a primary problem during sepsis.[5] Recent evidence suggested a deterioration of the endothelial glycocalyx by inflammatory mediators to be an important part of the underlying pathomechanism.[6,7] Therefore, a careful differential indication between crystalloids and colloids as suggested for the perioperative steady state might not only be insufficient in this context, but in vain.[1] Until today, we only know that we have to give enough, irrespective of the kind of fluid, to improve outcome of patients suffering from severe sepsis and septic shock.[8]

We support most of the interesting considerations by Dr. Navarro-Martinez and colleagues. However, septic patients were not the focus of our rational approach.

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References

1. Chappell D, Jacob M, Hofmann-Kiefer K, Conzen P, Rehm M: A rational approach to perioperative fluid management. ANESTHESIOLOGY 2008; 109:723–40

2. Jacob M, Bruegger D, Rehm M, Stoeckelhuber M, Welsch U, Conzen P, Becker BF: The endothelial glycocalyx affords compatibility of Starling's principle and high cardiac interstitial albumin levels. Cardiovasc Res 2007; 73:575–86

3. Rehm M, Zahler S, Lotsch M, Welsch U, Conzen P, Jacob M, Becker BF: Endothelial glycocalyx as an additional barrier determining extravasation of 6% hydroxyethyl starch or 5% albumin solutions in the coronary vascular bed. ANESTHESIOLOGY 2004; 100:1211–23

4. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent JL: Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med 2008; 34:17–60

5. Marx G: Fluid therapy in sepsis with capillary leakage. Eur J Anaesthesiol 2003; 20:429–42

6. Chappell D, Hofmann-Kiefer K, Jacob M, Rehm M, Briegel J, Welsch U, Conzen P, Becker BF: TNF-alpha induced shedding of the endothelial glycocalyx is prevented by hydrocortisone and antithrombin. Basic Res Cardiol 2009; 104: 78–89

7. Nelson A, Berkestedt I, Schmidtchen A, Ljunggren L, Bodelsson M: Increased levels of glycosaminoglycans during septic shock: Relation to mortality and the antibacterial actions of plasma. Shock 2008; 30:623–7

8. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M: Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001; 345:1368–77

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Nitric Oxide Metabolites, Platelet Activation, and Myocardial Ischemia Reperfusion Injury

To the Editor:—We read with great interest the research article by Nagasaka *et al.* demonstrating a role of nitric oxide and its metabolites in the systemic circulation.[1] As the authors impressively demonstrate, active nitric oxide metabolites are carried into the systemic circulation where they accumulate in the blood and in the heart, and as a result have significant impact on the extent of myocardial ischemia reperfusion injury.

Nitric oxide induces cyclic guanosine phosphatase activation and increases cyclic guanosine monophosphate levels in several tissues, including platelets. Several investigators have demonstrated that this is caused not only by endogenous nitric oxide with significant impact on platelet activity, but also by inhalative nitric oxide.[2,3] The crucial importance of platelets and the activity state of platelets on the extent of myocardial ischemia reperfusion injury was outlined by previous investigations.[3–5] A downstream target of cyclic guanosine phosphatase activation in platelets is vasodilator-stimulated phosphoprotein (VASP), a central cytoskeletal binding protein.[6] The intracellular increase in cyclic guanosine phosphatase results in a phosphorylation of VASP, which is a crucial step in the control of platelet activity. Clini-

The above letter was sent to the authors of the referenced report. The authors did not feel that a response was required. —James C. Eisenach, M.D., Editor-in-Chief.