

Report Documentation Page				Form Approved OMB No. 0704-0188	
Public reporting burden for the collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to a penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.					
1. REPORT DATE 01 AUG 2013		2. REPORT TYPE N/A		3. DATES COVERED -	
4. TITLE AND SUBTITLE Re: Coagulation and fluid resuscitation by HyperHES in severe hemorrhage. Response to Letter-to-the-Editor.				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Martini W. Z., Dubick M. A.,				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release, distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 1	19a. NAME OF RESPONSIBLE PERSON
a. REPORT unclassified	b. ABSTRACT unclassified	c. THIS PAGE unclassified			

more quickly the hypovolemic shock (small-volume resuscitation concept).

More importantly, recent data have suggested that hypertonic saline would modify coagulation less than a colloid only would.⁴ In a model of hemorrhagic shock in pigs, resuscitation resulted in less impairment of clot formation when compared with administration of 6% HES or 4% gelatine.⁴

Contrary to isotonic crystalloids and colloids, which play only the ventricular preload, hypertonic saline also improves the other determinants of cardiac output, namely, ventricular afterload and inotropism.⁵

Finally, the volume of fluids needed to restore a good hemodynamics (mean arterial pressure, 65 mm Hg) is significantly different. By extrapolating the data by Martini et al., it would mean an average volume of 8,500 mL of lactated Ringer's solution for a man of medium weight (118 mL/kg). However, fluid resuscitation using HyperHES will start by an injection of 250 mL (recommended dose is 4 mL/kg).²

This last point seems not significant in a hospital context but is important in pre-hospital or war medicine. Indeed, in the setting of combat casualty care, the soldiers have to carry the first aid kit, and we cannot envisage to load them with so much weight.

In the context of trauma combat casualty care, fluid resuscitation by HyperHES, followed by normal saline infusion, seems to be an interesting option for both medical and tactical reasons.

*The authors declare no conflicts of interest.

Sylvain Vico, MD
Clément Dubost, MD
Stéphane Mérat, MD

Anesthesiology and Intensive Care Medicine
Hôpital d'Instruction des Armées Bégin
Saint Mandé, France

REFERENCES

1. Martini WZ, Dubick MA, Blackburn LH. Comparisons of lactated Ringer's and Hextend resuscitation on hemodynamics and coagulation following femur injury and severe hemorrhage in pigs. *J Trauma Acute Care Surg*. 2013; 74(3):732–740.
2. Dubick MA, Atkins JL. Small-volume fluid resuscitation for the far-forward combat environment: current concepts. *J Trauma*. 2003;54: S43–S45.
3. Sharma P, Benford B, Karaian JE, Keneally R. Effects of volume and composition of the resuscitative fluids in the treatment of hemorrhagic shock. *J Emerg Trauma Shock*. 2012;5: 309–315.
4. Haas T, Fries D, Holz C, Innerhofer P, Streif W, Klingler A, Hanke A, Velik-Salchner C. Less impairment of hemostasis and reduced

blood loss in pigs after resuscitation from hemorrhagic shock using the small-volume concept with hypertonic saline/hydroxyethyl starch as compared to administration of 4% gelatin or 6% hydroxyethyl starch solution. *Anesth Analg*. 2008;106:1078–1086, table of contents.

5. Kramer GC. Hypertonic resuscitation: physiologic mechanisms and recommendations for trauma care. *J Trauma*. 2003;54:S89–S99.

Re: Coagulation and fluid resuscitation by HyperHES in severe hemorrhage

In Reply:

We sincerely appreciate the interest in and comment from Drs. Vico, Dubost, and Merat regarding our article of “Comparisons of lactated Ringer's and Hextend resuscitation on hemodynamics and coagulation following femur injury and severe hemorrhage in pigs” published in the *Journal of Trauma and Acute Care Surgery*.

In our article, we reported that Hextend was effective in restoring hemodynamics and acid-base status with one-third volume of lactated Ringer's solution. However, this advantage was associated with undesired effects on coagulation possibly owing to greater and sustained hemodilution from Hextend resuscitation. Vico et al. reported that the French army uses HyperHES (a colloid and 7.5% saline) and suggested that HyperHES has the potential to be more effective in treating hypovolemic shock. We agree with their comments, since the effects on volume expansion have been reported in a large body of literature with 7.5% hypertonic saline as well as hypertonic saline with colloids such as dextran and hydroxyethyl starch.^{1–4} However, we are unaware of studies evaluating the effects of HyperHES on coagulation after hemorrhagic shock. With well-documented effects of large molecular weight hydroxyethyl starch on coagulation and the findings of prolonged compromise in coagulation function from Hextend resuscitation in our study and by others in our group,^{5,6} additional research effort is warranted to determine the effects of HyperHES on hemostasis under trauma and hemorrhagic shock. Perhaps, the lower molecular weight starch of HyperHES may have less effect on coagulation, but this will require confirmation. In addition, only 3% and 5% hypertonic saline solutions are approved by the US Food and Drug Administration, and HyperHES is not an approved product available in United States. Although the US military would like such a product

for resuscitation, the military's Tactical Combat Casualty Care Committee could only recommend Hextend as a lower-dose plasma volume expander for far-forward use.⁷ Thus, it is unlikely that a recommendation can be made for HyperHES for US combat casualty care in the near future, but we appreciate Dr. Vico and his colleagues bringing this product to our attention.

*The authors declare no conflicts of interest.

The opinions or assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

The study that this letter refers to has been conducted in compliance with the Animal Welfare Act, the implementing Animal Welfare Regulations, and the principles of the Guide for the Care and Use of Laboratory Animals.

Wenjun Z. Martini, PhD
Michael A. Dubick, PhD

US Army Institute of Surgical Research
JBSA Fort Sam Houston
San Antonio, Texas

REFERENCES

1. Dubick MA, Atkins JL. Small-volume fluid resuscitation for the far-forward combat environment: current concepts. *J Trauma*. 2003; 54(Suppl 5):S43–S45.
2. Sharma P, Benford B, Karaian JE, Keneally R. Effects of volume and composition of the resuscitative fluids in the treatment of hemorrhagic shock. *J Emerg Trauma Shock*. 2012; 5(4):309–315.
3. Robinson R, Schwendenwein I, Wacek S, Nell B, Mosing M. Plasma volume and electrolyte changes following intravenous infusion of hypertonic hydroxyethyl starch versus mannitol in healthy dogs. *Vet J*. 2011;190(2):268–272.
4. Kerbaul F, Rondelet B, Benas V, Grisoli D, De Waroquier A, Fesler P, Fusai T, Brimiouille S. Hypertonic saline hydroxyethylstarch restores right ventricular-arterial coupling after normovolemic hemodilution in piglets. *Anesthesiology*. 2011;115(1):136–143.
5. Sondeen JL, Prince MD, Kheirabadi BS, Wade CE, Polykratis IA, de Guzman R, Dubick MA. Initial resuscitation with plasma and other blood components reduced bleeding compared to hetastarch in anesthetized swine with uncontrolled splenic hemorrhage. *Transfusion*. 2011;51(4):779–792.
6. Kheirabadi BS, Crissey JM, Deguzman R, Perez MR, Cox AB, Dubick MA, Holcomb JB. Effects of synthetic versus natural colloid resuscitation on inducing dilutional coagulopathy and increasing hemorrhage in rabbits. *J Trauma*. 2008;64(5):1218–1228; discussion 1228–1229.
7. Butler FK Jr., Blackburn LH. Battlefield trauma care then and now: a decade of Tactical Combat Casualty Care. *J Trauma Acute Care Surg*. 2012;73(6 Suppl 5):S395–S402.