Damage Control Resuscitation: Directly Addressing the Early Coagulopathy of Trauma

John B. Holcomb, MD, FACS, Don Jenkins, MD, FACS, Peter Rhee, MD, FACS, Jay Johannigman, MD, FS, FACS, Peter Mahoney, FRCA, RAMC, Sumeru Mehta, MD, E. Darrin Cox, MD, FACS, Michael J. Gehrke, MD, Greg J. Beilman, MD, FACS, Martin Schreiber, MD, FACS, Stephen F. Flaherty, MD, FACS, Kurt W. Grathwohl, MD, Phillip C. Spinella, MD, Jeremy G. Perkins, MD, Alec C. Beekley, MD, FACS, Neil R. McMullin, MD, Myung S. Park, MD, FACS, Ernest A. Gonzalez, MD, FACS, Charles E. Wade, PhD, Michael A. Dubick, PhD, C. William Schwab, MD, FACS, Fred A. Moore, MD, FACS, Howard R. Champion, FRCS, FRCs, David B. Hoyt, MD, FACS, and John R. Hess, MD, MPH, FACP

Rapid progress in trauma care occurs when the results of translational research are promptly integrated into clinical practice. Experience with a high volume of severely injured casualties expedites the process. Historically, these conditions have converged during times of conflict, improving the care of combat casualties and subsequently that of civilian trauma patients.

In the most severely injured casualties, we know that when the lethal triad of hypothermia, acidosis, and coagulopathy are present, death is imminent. Current teaching is to avoid reaching these conditions by using “damage control surgery.” However, conventional resuscitation practice for damage control focuses on rapid reversal of acidosis and prevention of hypothermia, and surgical techniques focus on controlling hemorrhage and contamination. Direct treatment of coagulopathy has been relatively neglected, viewed as a byproduct of resuscitation, hemodilution, and hypothermia, and delayed by blood banking logistics. Damage control resuscitation addresses the entire lethal triad immediately upon admission to a combat hospital.

By demonstrating that in the severely injured the coagulopathy of trauma is present at admission, recent studies have brought back to light the importance of treating this disorder at an earlier stage. Reports of lactated Ringer’s solution and normal saline increasing reperfusion injury and leukocytic adhesion lead one to conclude that the standard crystalloid-based resuscitation guidelines in prehospital trauma life support (PHTLS) and advanced trauma life support (ATLS) may worsen the presenting acidosis and coagulopathy in severely injured trauma patients, and possibly increase ARDS, SIRS, and MOF. The safety of withholding PRBCs in hemodynamically stable patients has been demonstrated, and the risks associated with blood transfusion are well described. Further, massive transfusion in military and civilian casualties has been associated with an increased risk of death. Taken together, these observations suggest that the most severely injured may need a resuscitative approach tailored specifically to their needs. However, even in the largest civilian academic trauma centers, patients with injuries at the outer limits of survivability, such as those massively transfused with more than 10 units of RBCs in the first 24 hours, are uncommon and constitute only 1% to 2% of the patient population, making it difficult to develop and test new resuscitation concepts. Because 7% of combat casualties require massive transfusion, we have had just such an opportunity to observe the effects of new resuscitation strategies in the combat hospitals of Iraq and Afghanistan.

The military munitions used in Southwest Asia can inflict severe multisystem injuries on both combatants and civilians. These patients frequently present to American military medical personnel shortly after being wounded. Unlike civilian systems, where treatment of coagulopathy is often limited by standard blood bank logistics, in Iraq we frequently have immediate access to PRBCs and thawed AB or A plasma, and rapid access to apheresis platelets, prepoled cryoprecipitate, fresh whole blood, and rFVIIa, as indicated. Thus, the opportunity to formally evaluate the immediate and direct treatment of the coagulopathy of trauma is available.
## Title and Subtitle
Damage Control Resuscitation: Directly Addressing the Early Coagulopathy of Trauma

## Performing Organization Name(s) and Address(es)
U.S. Army Institute of Surgical Research (USAISR), 3400 Rawley E. Chambers Avenue, Fort Sam Houston, TX 78234-6315

## Abstract
Approved for public release; distribution unlimited
The trauma patients who are most severely injured (approximately 10%) also represent the majority of in-hospital trauma deaths. Considerable attention has been directed toward the technical details of damage control surgery and reversing the acidosis and hypothermia present at admission. Less attention has been directed toward reversing the coagulopathy related to blood loss that is present at the same time. Clinical experience in Operation Iraqi Freedom and Operation Enduring Freedom suggests that coagulopathy may be present at the time of admission before significant resuscitative fluid has been given, as a consequence of acidosis-induced coagulation factor dysfunction, coagulation factor consumption, and hypothermia-induced failure of platelet activation. Failure to recognize and immediately address the coagulopathy found in severely injured patients can be linked to several factors. Most studies of trauma-induced coagulopathy have measured the laboratory changes that happen in the OR after dilution with crystalloid and PRBCs, and have concluded that the coagulopathy could be fully explained by the resuscitation and/or hypothermia.30

The goal of shock resuscitation efforts in the past has been largely to support blood pressure and urine output and to reverse the metabolic derangements associated with the ischemia associated with acute blood loss.31,32 Although these goals are obviously important, the studies supporting this concept were based on controlled animal hemorrhage studies, and the results were not evaluated in randomized human trials.33–35 Additionally, the potential benefits of mitigating ischemia-induced reperfusion injury after standard crystalloid resuscitation were not fully recognized.14,36 Furthermore, recent resuscitation studies have overlooked the importance of an integrated and coherent prehospital, ED, OR, and ICU shock resuscitation plan that incorporates intravascular treatment of coagulopathy.32,37 Finally, the current generation of clinicians has been taught to not use plasma as a resuscitation fluid.38 We agree that current standard resuscitation methods are appropriate policy for the approximately 90% of trauma patients who are not in shock and are hypercoagulable after injury.39–42 However, for the approximately 10% of casualties who constitute the most seriously injured, are in shock and coagulopathic, and represent the potentially preventable hemorrhagic deaths, liquid plasma may be the optimal resuscitation fluid currently available.43–50

Based on (1) previous civilian clinical studies, (2) the recommendations of an international consensus conference on early massive transfusion for trauma,51 and (3) considerable experience in the current war, we think patients at high risk for coagulopathy can be readily identified at admission and prompt simultaneous treatment of hypothermia, acidosis, and coagulopathy initiated. Hypothermia, an independent factor for increased mortality in trauma patients, was an earlier focus for active prevention and treatment,52–54 but application of training and equipment recommendations of the Committee on Tactical Combat Casualty Care and the Joint Theater Trauma System has made it an uncommon finding.55 Acidosis significantly impairs the thrombin generation rates, critical to optimal coagulation function56 and is thus aggressively managed by use of THAM and volume loading with blood components once hemostasis is obtained, with restoration of a normal blood lactate, base deficit, or pH as the ultimate goal. Damage control resuscitation as a structured intervention begins immediately after rapid initial assessment in the ED and progresses through the OR into the ICU. All efforts are directed toward this goal by repeated point of care testing and the use of multiple blood products and drugs readily available in theater, albeit in new ratios and amounts. Compared with civilian practice, damage control resuscitation efforts are largely completed in the OR, with little resuscitation required in the ICU. Achieving this goal quickly in the OR may allow a shift from limited damage control surgery to earlier definitive surgical interventions, including sophisticated limb salvage techniques, and improved outcomes.

In the severely injured casualty, damage control resuscitation consists of two parts and is initiated within minutes of arrival in the ED. First, resuscitation is limited to keep blood pressure at approximately 90 mm Hg, preventing renewed bleeding from recently clotted vessels.15,17,39,57–62 Second, intravascular volume restoration is accomplished by using thawed plasma as a primary resuscitation fluid in at least a 1:1 or 1:2 ratio with PRBCs.8,10,48–50 Our initial clinical experience shows these ratios decrease mortality in similarly injured casualties (Borgman MA, et al. unpublished data). Recombinant FVIIa is occasionally used along with the early units of red cells and as required throughout the resuscitation. For casualties who will require continued resuscitation, the blood bank is notified to activate the massive transfusion protocol and deliver to the operating room 6 units of plasma, 6 units of PRBCs, 6 packs of platelets, and 10 units of cryoprecipitate stored in individual coolers.50 The most severely injured of this group also receive fresh warm whole blood as a resuscitative fluid.47,63 Additional coolers, containing the same mix of blood products, are provided as needed until the massive transfusion order is cancelled. Crystalloid use is minimized and serves mainly as a drug carrier and to keep lines open between the units of blood products.

In combat casualties requiring major resuscitation (10–40 units of blood products), we have found as little as 5 L to 8 L of crystalloid are utilized during the first 24 hours, representing a decrease of at least 50% when compared with current standard resuscitation practices. Using the damage control resuscitation approach, the lack of intraoperative coagulopathic bleeding has been remarkable, allowing surgeons to focus on surgical bleeding. Patients treated in this fashion almost always arrive in the ICU warm, euvoletic, and nonacidotic, with a normal INR and minimal edema. In the majority of patients the abnormalities of the lethal triad are absent. These patients appear to be easily ventilated and more quickly extubated than patients with similar blood loss treated with the standard crystalloid resuscitation volumes and blood component ratios. These admittedly anecdotal yet compelling...
observations cause us to question further the use of excessive crystalloid resuscitation and to begin to formulate hypotheses that can be tested to demonstrate beneficial effects of preemptive control of coagulopathy.14

For the first time in US warfare, data for all admitted trauma casualties in the current conflict in Southwest Asia are entered into a joint theater trauma registry (JTTR).64 A deployed combat research team is being sent into theater for the first time since Vietnam, operating under the same standards of IRB approval as practiced in the United States. Data collected by this team, along with outcome data from the JTTR, will allow an analysis of the effects of resuscitation with thawed plasma, fresh whole blood, administration of rFVIIa, and limited crystalloid. Additionally, focused effort will be required to describe the mechanisms causing the early coagulopathy of trauma present at admission. The clinical effects and consequences of damage control resuscitation will be measurable in patient outcomes. We will know if we are saving more severely injured soldiers, if reducing coagulopathy and edema leads to better outcomes, and, ultimately, whether we are creating more blood exposure or less. We will soon have sufficient data to assess the full benefits of damage control resuscitation in the population of critically injured for whom it matters most. As in the past, perceptive observation, thoughtful discussion, and insightful analysis concerning medical care during war from experienced military medics, surgeons, and scientists, in concert with our civilian colleagues, will generate recommendations for new and improved medical practice, with continuous modification as further experience, research, and development produce new and relevant information.1,2

REFERENCES


