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TACTICAL COMBAT CASUALTY CARE: TRANSITIONING BATTLEFIELD LESSONS LEARNED TO OTHER AUSTERE ENVIRONMENTS

Fluid Resuscitation in Tactical Combat Casualty Care: Yesterday and Today

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The prevailing wisdom for the prehospital fluid resuscitation of trauma victims in hemorrhagic shock in 1992 was to administer 2 L of crystalloid solution as rapidly as possible. A review of the fluid resuscitation literature found that this recommendation was not well supported by the evidence at the time. Prehospital fluid resuscitation strategies were reevaluated in the 1993–1996 Tactical Combat Casualty Care (TCCC) research program. This article reviews the advances in prehospital fluid resuscitation as recommended by the original TCCC Guidelines and modified over the following 2 decades. These advances include hypotensive resuscitation, use of prehospital whole blood or blood components when feasible, and use of Hextend or selected crystalloids when logistical considerations make blood or blood component use not feasible.

Keywords: fluid resuscitation, Hextend, whole blood, dried plasma, hypotensive resuscitation

Prehospital fluid resuscitation strategy prior to Tactical Combat Casualty Care

The original Tactical Combat Casualty Care (TCCC) article in 1996 noted that, despite its widespread use, the benefit of fluid resuscitation using crystalloid solutions for trauma victims in hemorrhagic shock had not been well established.[1–13] The recommended regimen for fluid resuscitation in civilian trauma courses at the time was to administer 2 L of either lactated Ringer's (LR) or normal saline as rapidly as possible.

TCCC fluid resuscitation for hemorrhagic shock: 1996

Much of the presumed benefit of fluid resuscitation for hemorrhagic shock as practiced prior to 1996 was based on animal models of hemorrhage in which the animals were bled a specified fraction of their blood volume. The blood loss was then stopped and fluid resuscitation was accomplished—a so-called "controlled hemorrhage" model.[14,15] In other models, in which an injury was created and experimental animals were allowed to bleed freely from the injury site, aggressive fluid resuscitation was found to be of no benefit or to actually increase mortality.[16–22] Proposed reasons for the lack of benefit of fluid resuscitation in these uncontrolled hemorrhage models include vasodilation with increased blood flow to the site of bleeding, dilution of clotting factors, and increased intravascular pressure—all of which could interfere with attempted clot formation.

A large prospective, randomized, controlled trial performed by Bickell et al found that aggressive early resuscitation with crystalloid for hypotensive patients with penetrating wounds of the chest and/or abdomen resulted in increased mortality compared with patients in whom fluid resuscitation was delayed until after surgical control of bleeding had been accomplished.[7]

The original TCCC article also re-evaluated the recommendation of crystalloid for fluid resuscitation in hemorrhagic shock. Both LR and normal saline are crystalloids, which means that their primary osmotically active particle is sodium. Because the sodium ion distributes quickly throughout the entire extracellular fluid compartment and the water component of the solution follows, crystalloids redistribute rapidly from the intravascular space to the extravascular space. This means that a casualty in hemorrhagic shock who is

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administered 1000 mL of LR will have only 200 mL of that volume in his or her intravascular space 1 hour later.[23–25] This shift can both allow for a recurrence of hypotension and contribute to adverse secondary effects of fluid administration, such as pulmonary edema, cerebral edema, and abdominal compartment syndrome.[1,26]

Colloids, in contrast, contain larger molecules in solution that are retained within the intravascular space. Hespan, for example, contains the large hetastarch molecule, and the entire infused volume is retained in the intravascular space for 8 hours or longer.[27] In 1996, hetastarch was found to be a safe and effective alternative to LR in resuscitation of casualties with controlled hemorrhagic shock.[28,29]

Based on these considerations, the recommendations for fluid resuscitation in the original TCCC article were to

- delay starting intravenous (IV) lines and performing fluid resuscitation until the Tactical Field Care phase
- withhold IV fluids in casualties who are not in shock
- withhold IV fluids in casualties who are in shock as a result of uncontrolled hemorrhage
- resuscitate casualties in shock as a result of hemorrhage that has been effectively controlled with an initial volume of 1000 mL of Hespan
- limit Hespan to 1500 mL or less[1]

The 1999 TCCC Mogadishu Workshop

After the events of the Battle of Mogadishu were published in the book *Blackhawk Down*, the details of the casualties sustained in that combat action became known. In December 1999, at the annual meeting of the Special Operations Medical Association, the United States Special Operations Command funded a 1-day workshop to review the injuries sustained by the US casualties in Mogadishu, the treatment provided to them, and the casualty outcomes in order to determine whether there were lessons learned from that battle that should be incorporated into TCCC.

One of the topics discussed at the Mogadishu workshop was the fluid resuscitation recommendations in TCCC. There was a clear consensus among trauma experts in the panel that casualties with mental status changes due to shock should be given enough fluid to resuscitate them to the point that mentation improves, even in cases in which the casualty's shock was the result of noncompressible (internal) hemorrhage. Panel members noted that the goal of resuscitation should not be to restore a "normal" blood pressure, but to produce improved mentation. Although little evidence was cited to support this recommendation, the opinions of the expert panelists were unanimous on this point.[30]

The US Army Medical Research and Materiel Command (MRMC) and Office of Naval Research Fluid Resuscitation Conferences 2001–2002

The interest generated in fluid resuscitation as a result of the 1996 TCCC paper and the 1999 Mogadishu Workshop spurred the United States Army Medical Research and Material Command (MRMC) and the Office of Naval Research (ONR) to sponsor a series of fluid resuscitation conferences in 2001 and 2002. These conferences were chaired by Dr John Holcomb and Dr Howard Champion and produced a hypotensive fluid resuscitation strategy to be used for casualties with either controlled or uncontrolled hemorrhage. This strategy also recommended the use of the synthetic hetastarch solution Hextend instead of the previously used Hespan because of the former's lesser adverse impact on coagulation status.[31,32]

Additional research by Sondeen et al[33] at the United States Army Institute of Surgical Research (USAISR) produced further insights into resuscitation and rebleeding in uncontrolled hemorrhage. Sondeen's team found that in 70 swine with aortotomies, 5 animals died before fluid resuscitation and 3 more died at onset of fluid resuscitation. For the remaining 62 animals, rebleeding occurred at a mean systolic blood pressure 94 mm Hg. This study documented that, in this animal model of severe bleeding, there was a blood pressure of threshold above which further resuscitation caused disruption of the body's attempt to establish hemostasis, effectively establishing an upper limit for resuscitation of casualties with noncompressible hemorrhage that has not yet been surgically controlled.[33]

TCCC fluid resuscitation for hemorrhagic shock: 2003

After the MRMC and ONR fluid resuscitation conferences and the work done by Sondeen et al, the newly formed Committee on Tactical Combat Casualty Care (CoTCCC) voted to modify the recommendations for fluid resuscitation in TCCC. The new guideline also incorporated a recommendation made at a CoTCCC meeting by Dr Peter Rhee that conscious casualties should be permitted to take water by mouth to prevent going to surgery dehydrated.[34] The updated fluid resuscitation guideline was as follows:

- Assess for hemorrhagic shock—altered mental status (in the absence of head injury) and weak or absent peripheral pulses are the best field indicators of shock

- For casualties who are not in shock
  - o no IV fluids are necessary
  - o fluids by mouth (PO) are permissible if the casualty is conscious and can swallow
- For casualties who are in shock:
  - o administer a 500 mL bolus of Hextend
  - o repeat once after 30 minutes if still the casualty is still in shock
  - o no more than 1000 mL of Hextend is to be given
- Continued efforts to resuscitate must be weighed against logistical and tactical considerations and the risk of incurring further casualties.
- If a casualty with an altered mental status due to known or suspected traumatic brain injury (TBI) has a weak or absent peripheral pulse, resuscitate as necessary to maintain a palpable radial pulse.

The recommendation to rely on mental status and the character of the radial pulse was based on the need to have a fast and battlefield-appropriate way of determining whether or not a casualty is in shock. Combat settings may entail high noise levels and very limited light conditions, thus making typical blood pressure measurement with a cuff and stethoscope impractical. Combat medical personnel need clinical indicators of hypovolemic shock that are more suitable for use on the battlefield. The tactically relevant definition of shock was therefore identified as: 1) unconsciousness or altered mental status (confused or drowsy) that is not due to TBI or drug therapy; and/or 2) abnormal (ie, weak or absent) radial pulse.[35] McManus et al found that radial pulse character was the best overall predictor of systolic blood pressure (SBP) among the 6 predictor variables. Weak pulse was associated with a mean SBP of 100 mm Hg, and normal pulse was associated with a mean SBP of 129 mm Hg.[36] The importance of maintaining cerebral perfusion pressure in TBI casualties was also emphasized in the updated wording for fluid resuscitation.[37] Other researchers using lower body negative pressure methodology have reported that both blood pressure and mental status were relatively well preserved until cardiac stroke volume had decreased by approximately 55%.[38] These observations have led the CoTCCC to recommend that other modalities to monitor casualties for shock (such as the cardiovascular reserve index, tissue oxygen saturation, or point-of-injury lactate measurements) be evaluated as alternatives to allow combat medical personnel to more precisely assess for shock on the battlefield and to guide fluid resuscitation.[39]

Tarpey published the first report of a combat unit employing TCCC fluid resuscitation in the *Army Medical Department Journal* in 2005.[40] The article noted that "We adhered throughout to the principle of hypotensive resuscitation, using IV fluids only when appropriate. Casualties not in shock were encouraged to take fluids orally. Those casualties in shock received 1000 cc of Hespan, the colloid available to us. It was very effective in resuscitating casualties without complications noted. Given our low supplies and little room to transport everything throughout the length of Iraq, we found colloids to be the better choice of fluid for resuscitation."[40]

TCCC fluid resuscitation for hemorrhagic shock: 2004

When a casualty in hemorrhagic shock arrives at a medical treatment facility, what fluid is he or she given? As soon as logistics allowed, the casualty was transfused with blood products, predominantly red blood cells (RBCs.) at the time. By 2004, there was a growing realization that, with the appropriate planning and logistic measures, RBCs could be administered to casualties before they arrive at medical treatment facilities. Although RBCs are beyond the logistic capabilities of most ground medics to carry, they could be carried and administered on evacuation platforms (eg, helicopters). In 2004, therefore, the fluid resuscitation guidelines in TCCC were modified to incorporate a recommendation that RBCs be given during the Tactical Evacuation phase of care when this is logistically feasible.[34]

TCCC fluid resuscitation for hemorrhagic shock: 2010

In 2010, a fluid resuscitation conference was again convened by the MRMC. In addition to reviewing the state of the science in fluid resuscitation at the time, a major focus of the conference was to evaluate whether the TCCC fluid resuscitation recommendation that still called for hypotensive resuscitation with Hextend at the time needed to be revised. Sixty-five resuscitation experts were invited to present, and the consensus document the group produced found that hypotensive resuscitation with Hextend was still a sound approach.[41]

That finding notwithstanding, Captain Jeff Timby conducted an extensive review of the fluid resuscitation recommendations in TCCC and found several opportunities for improvement. By this time, the use of plasma in addition to RBCs in a 1:1 ratio had been found to confer a significant survival benefit.[42–44] Timby's work was reflected in a Defense Health Board memo in 2010, and the major additions were that 1) the use of 1:1 RBCs and plasma was recommended over RBCs alone whenever feasible, and 2) target blood pressures were established for both TBI and non-TBI casualties.[45]

The fluid resuscitation guidelines in TCCC at the end of 2010 are shown in Table 1.

Table 1. TCCC fluid resuscitation for hemorrhagic shock: 2010

Tactical Field Care

6. Fluid Resuscitation: Assess for hemorrhagic shock; altered mental status (in the absence of head injury) and weak or absent peripheral pulses are the best field indicators of shock.

- If not in shock:
  - No IV fluids necessary
  - PO fluids permissible if conscious and can swallow
- If in shock:
  - Hextend, 500 mL IV bolus
  - Repeat once after 30 minutes if still in shock
  - No more than 1000 mL of Hextend
- Continued efforts to resuscitate must be weighed against logistical and tactical considerations and the risk of incurring further casualties.
- If a casualty with an altered mental status due to suspected TBI has a weak or absent peripheral pulse, resuscitate as necessary to maintain a palpable radial pulse.

Tactical Evacuation Care

5. Fluid Resuscitation: Reassess for hemorrhagic shock (altered mental status in the absence of brain injury and/or change in pulse character). If blood pressure (BP) monitoring is available, maintain target systolic BP 80−90 mm Hg.

- If not in shock:
  - No IV fluids necessary
  - PO fluids permissible if conscious and can swallow
- If in shock and blood products are not available:
  - Hextend 500 mL IV bolus
  - Repeat after 30 minutes if still in shock
  - Continue resuscitation with Hextend or crystalloid solution as needed to maintain target BP or clinical improvement
- If in shock and blood products are available under an approved command or theater protocol:
  - Resuscitate with two units of plasma followed by packed red blood cells (PRBCs) in a 1:1 ratio.
  - If blood component therapy is not available, transfuse fresh whole blood.
  - Continue resuscitation as needed to maintain target BP or clinical improvement.
- If a casualty with an altered mental status due to suspected TBI has a weak or absent peripheral pulse, resuscitate as necessary to maintain a palpable radial pulse. If BP monitoring is available, maintain target systolic BP of at least 90 mm Hg.[45]

IV, intravenous; PO, by mouth; TBI, traumatic brain injury.

Fluid resuscitation in TCCC—2014

By 2014, there was an increasing awareness that, when a casualty loses blood, the ideal resuscitation fluid is one that approximates as closely as possible that which has been lost—whole blood. This is especially true when the loss of blood is severe and the transfusion is massive. A workshop held at the USAISR in 2008 helped to lay the groundwork for the significant advances made by the US military in this area.[46–50] In situations in which whole blood is not logistically practical, "Numerous recent retrospective single and multicenter studies have associated improved outcomes with earlier and increased use of plasma and platelets."[51,52]

In contrast, a number of publications reported adverse effects from large-volume resuscitation with both crystalloids and colloids.[7,26,53–56] Upon reflection, these reports should pose no great surprise. As an eloquent quote from Lieutenant Colonel Andre Cap notes, "The historic role of crystalloid and colloid solutions in trauma resuscitation represents the triumph of hope and wishful thinking over physiology and experience."[57]

Furthermore, studies from the conflict in Afghanistan described the increased use of blood products by coalition forces in Afghanistan during Tactical Evacuation (TACEVAC) care and even in Tactical Field Care (TFC).[46,58] Resuscitation with RBCs and plasma in a 1:1 ratio during TACEVAC care was pioneered by the British Medical Emergency Response Team and was associated with improved casualty survival, even with the relatively short evacuation times seen in Afghanistan in recent years.[59,60] There was also the realization that prehospital blood products might convey an even more important survival benefit when used in theaters of conflict that do not have the advanced combat casualty care system present in Afghanistan at the end of the United States involvement with the conflict in that country.[46] Prehospital blood component therapy with 1:1 plasma and RBCs is now routinely provided to trauma patients in shock at both the Mayo Clinic in Rochester, Minnesota, and Memorial Hermann Hospital in Houston, Texas.[61,62]

For combat medical personnel caring for casualties at the point of injury, training and logistic requirements typically limit the availability of blood products. In this setting, the best option available is widely considered to be dried plasma. Plasma restores fibrinogen and other hemostatic factors, as well as volume, in contrast to crystalloids and colloids, which restore volume without any hemostatic factors and thus contribute an iatrogenic component to trauma-associated coagulopathy.[39,46,63] Dried plasma is used by the United Kingdom, France, Germany, the Netherlands, and Israel,[39,64,65] but no Food and Drug Administration

(FDA)-approved dried plasma product is currently available to US forces, although some select US special operations combat medical personnel carry the French dried plasma product and use it under a treatment protocol.[46]

Lacking to date are studies that show a survival advantage when plasma alone is used in prehospital fluid resuscitation, as well as studies and that document the optimal volume and timing for plasma-only fluid resuscitation in the prehospital setting. That said, "combat casualties often have a coagulopathy; coagulopathy increases mortality, and plasma administration reduces the coagulopathy."[46]

Drawing on both the combat trauma experience with damage control resuscitation as reported by the US, UK, and French militaries from the recent conflicts and incorporating published reports from the US and European civilian sectors as well, the CoTCCC again undertook to revise its fluid resuscitation guidelines in 2014. The 2014 revision stressed the importance of resuscitation with blood products as soon as they can be made available for casualties, even before the TACEVAC phase of care. The updated guidelines were published in the *Journal of Special Operations Medicine*[46] and are still in use at the time of this writing. The current TCCC recommendations for fluid resuscitation from hemorrhagic shock are as shown in Table 2.

Fluid resuscitation in TCCC—the way ahead

To oversimplify a complex series of research efforts underway in the US military Combat Casualty Care Research Program, the most promising avenues for further improvements in fluid resuscitation in battlefield trauma care at present are

1. Development of techniques and technologies to make type O, low anti-A, low anti-B titer (universal donor) whole blood available as early in the continuum of care as possible for combat casualties. Better preservation methods and improved refrigeration capabilities in mounted military convoys may eventually allow FDA-compliant whole blood to be available at the point of injury.[39]
2. Advanced battlefield trauma care training and technologies may allow combat units to identify individuals with type O, low anti-A, low anti-B titer (universal donor) blood as potential donors and subsequently perform whole-blood transfusions using this universal donor whole blood in situations in which that option is deemed to be potentially lifesaving.[57,66–70]
3. In combat circumstances in which there is no capability to make whole blood or RBCs available,

Table 2. TCCC fluid resuscitation for hemorrhagic shock: 2014

Tactical Field Care and TACEVAC Care

7. Fluid resuscitation

a. The resuscitation fluids of choice for casualties in hemorrhagic shock, listed from most to least preferred, are whole blood[a]; plasma, RBCs, and platelets in 1:1:1 ratio[a]; plasma and RBCs in 1:1 ratio; plasma or RBCs alone; Hextend; and crystalloid (lactated Ringers or Plasma-Lyte A).

b. Assess for hemorrhagic shock (altered mental status in the absence of brain injury and/or weak or absent radial pulse).

1. If not in shock:

- No IV fluids are immediately necessary
- Fluids by mouth are permissible if the casualty is conscious and can swallow

2. If in shock and blood products are available under an approved command or theater blood product administration protocol:

- Resuscitate with whole blood[a]; or, if not available,
- Plasma, RBCs and platelets in a 1:1:1 ratio[a]; or if not available,
- Plasma and RBCs in 1:1 ratio; or if not available,
- Reconstituted dried plasma, liquid plasma, or thawed plasma alone or RBCs alone;
- Reassess the casualty after each unit. Continue resuscitation until a palpable radial pulse, improved mental status or systolic BP of 80−90 mm Hg is present.

3. If in shock and blood products are not available under an approved command or theater blood product administration protocol due to tactical or logistical constraints:

- Resuscitate with Hextend; or, if not available,
- Lactated ringers or Plasma-Lyte A;
- Reassess the casualty after each 500 mL IV bolus;
- Continue resuscitation until a palpable radial pulse, improved mental status, or systolic BP of 80−90 mm Hg is present.
- Discontinue fluid administration when one or more of the above end points has been achieved.

4. If a casualty with an altered mental status due to suspected TBI has a weak or absent peripheral pulse, resuscitate as necessary to restore and maintain a normal radial pulse. If BP monitoring is available, maintain a target systolic BP of at least 90 mm Hg.
5. Reassess the casualty frequently to check for recurrence of shock. If shock recurs, recheck all external hemorrhage control measures to ensure that they are still effective and repeat the fluid resuscitation as outlined above.

Table 2 (*continued*)

- If a casualty with an altered mental status due to suspected TBI has a weak or absent peripheral pulse, resuscitate as necessary to maintain a palpable radial pulse. If BP monitoring is available, maintain target systolic BP of at least 90 mm Hg.[45]

[a] Neither whole blood nor apheresis platelets are FDA-compliant as currently collected in theater. Consequently, whole blood and 1:1:1 resuscitation using apheresis platelets should be used only if all of the FDA-compliant blood products needed to support 1:1:1 resuscitation are not available, or if 1:1:1 resuscitation is not producing the desired clinical effect.

RBC, red blood cells; TBI, traumatic brain injury; BP, blood pressure.

plasma is a better option than crystalloids or colloids. Dried plasma requires no refrigeration and can be carried in the field by combat medics for extended periods. The CoTCCC identified the development of an FDA-approved dried plasma product as the number 1 research priority in battlefield trauma care in 2015.[39,71]

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