Published March 1, 2008 - articles remain available for CME credit for one year from time of publication

Thoughts on the Resuscitation of the Critically Ill Trauma Patient

Scott Weingart, M.D., RDMS
Director, Division of ED Critical Care
Department of Emergency Medicine
Mount Sinai School of Medicine
New York, NY

Chad M Meyers, M.D.
Surgical Critical Care
Department of Anesthesia
Brigham and Women's Hospital
Harvard Medical School
Boston, MA

Perhaps more than any other situation in the emergency department, the initial resuscitation of a critically ill trauma patient requires speed, integrated knowledge and teamwork. When our specialty first began, trauma resuscitation was the purview of the surgeons and our training came from members of that specialty. Today, trauma resuscitation is clearly our domain. If we are to excel in this role, we need the most current and evidence-based information on management strategies. This article reviews the most critical type of trauma resuscitation: the stabilization of the unstable bleeding patient.

> *Note: This article deals with the critically ill trauma patient; stable patients are treated very differently. Neither of the authors has any financial stakes in the medications, products, or devices mentioned in this article.*

Lethal Triad

In order to understand the complexities of the resuscitation in a bleeding trauma patient, we must become familiar with the "lethal triad". The lethal triad is the path the decompensating patient follows on the progression towards shock and death. The lethal triad consists of coagulopathy, hypothermia, and acidosis. These three factors all beget each other and contribute to a rapid and eventually irreversible spiral to death. There are a few additional features necessary to the lethal triad model, but these three factors are the most significant, so the triangle remains the chosen shape.

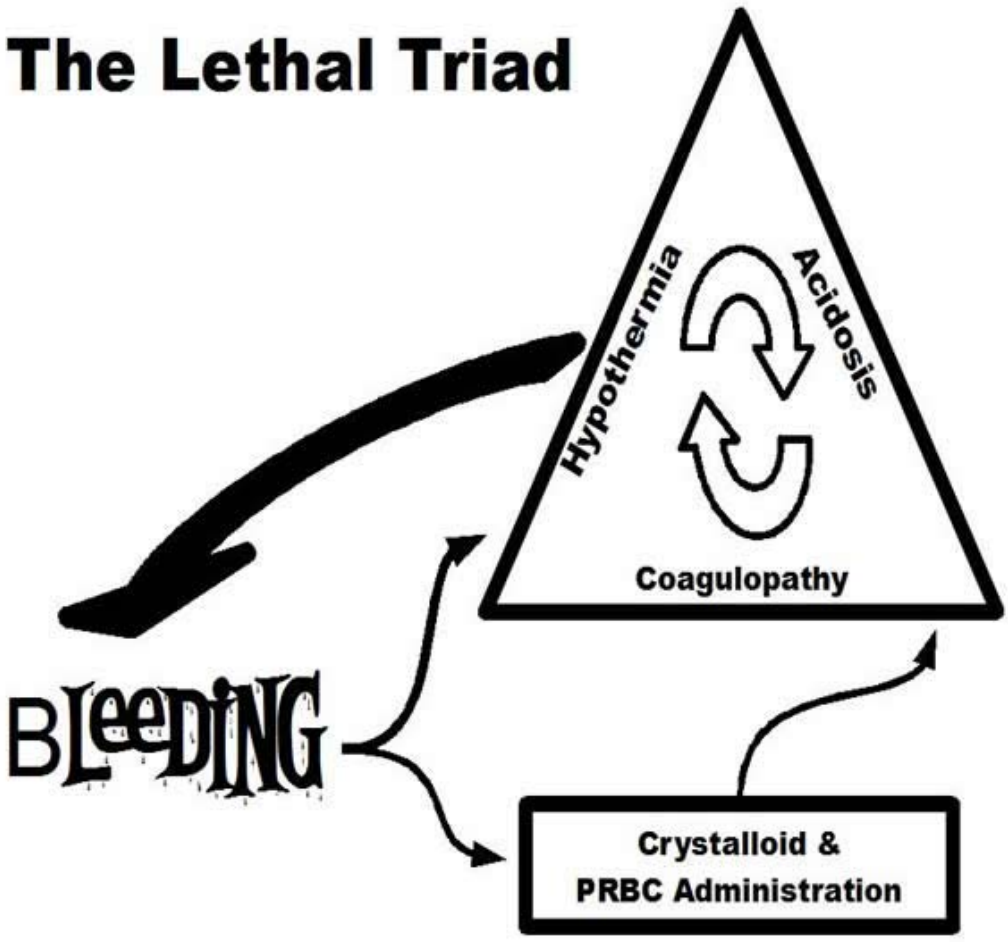


Figure 1: The Lethal Triad: Bleeding results in hypothermia, acidosis, and coagulopathy. Each of these leads to further bleeding and beget each other as well. ALL RIGHTS RESERVED SCOTT WEINGART, MD

As an example of the evils of the lethal triad, consider an inebriated gentleman who decides his mood might be improved by thrusting his arm through the glass window of a drinking establishment. He lacerates his brachial artery and begins to bleed. His Mean Arterial Pressure is 40 and blood is slowly leaking through the EMS-placed pressure dressing on his arm. He has lost a large quantity of blood at the scene. Of course, we say he lost blood, but we often take this to mean red cells. What he really lost was not just RBCs, but plasma and platelets as well.

All of these losses and what we do to counter them can lead to acidosis, hypothermia, and coagulopathy. An appropriate resuscitation strategy will limit each of these factors. A less-than-appropriate management plan will not acknowledge their existence and lead to poor outcomes. We will return to our bleeding gentleman in a moment, but first let us discuss the components of the triad.

Acidosis

The major contributor to acidosis in a trauma patient is poor perfusion to the tissues. Decreased cardiac output, anemia, and hypoxemia all push cells towards anaerobic metabolism, causing the metabolism of glucose to lactic acid. Resuscitation with unbalanced crystalloids such as normal saline will also induce a hyperchloremic acidosis (1). Severe acidosis can further diminish cardiac output and make catecholamines less effective (2). Perhaps the most dangerous effect of acidosis in this patient population is the induction of coagulopathy (3, 4). Our body's coagulation system does not work in an acidic milieu. When the pH drops from 7.4 to 7.0, the activity of portions of the coagulation cascade decreases by 55-70% (5). Even potent procoagulant drugs such as activated factor VIIa cannot work when the blood pH is low (5).

Hypothermia

Strip ‘em and flip ‘em is the "E" step of the primary survey (though it is phrased more urbanely in the ATLS text). After cutting off all of the patients clothing, if we infuse room temperature crystalloid and near frozen packed cells, the patient’s core temperature begins to drop towards that of a well-stirred martini. The maintenance of normal temperature also requires ATP, a substance in short supply in the hypoxic cells of a hypoperfused patient. Hypothermia is a remarkable anticoagulant. The reactions of the coagulation cascade are all temperature dependent; as temperature drops, bleeding increases dramatically (6-8). Independent of its effects on coagulation, hypothermia can cause relative thrombocytopenia by inducing platelet sequestration and also causes qualitative platelet dysfunction.

Coagulopathy

In addition to the coagulopathy induced by acidosis, hypothermia, and the direct loss of clotting factors from bleeding, the ability to clot is further compromised by dilution and consumption.

Dilutional coagulopathy takes place any time we infuse fluid or products that do not contain clotting factors. Crystalloid, colloid, PRBCs, and platelets all dilute whatever clotting factors are remaining in the patient’s bloodstream. Plasma is one of the few things that we can infuse that will make the situation better instead of worse.

The ATLS-advocated treatment of trauma-induced bleeding and hypotension is to first give two liters of crystalloid. If the blood pressure does not stabilize, we then switch to packed red blood cells. In the critical trauma patient, this protocol may lead to a delay in transfusion and even this seemingly small amount of crystalloid may have deleterious effects.

Critically ill trauma patients also may consume their clotting factors in a manner similar to disseminated intravascular coagulation (DIC). Tissue trauma and the shock state can abnormally activate the clotting cascade and cause fibrinolysis out of proportion to the injury and in areas distant to the site of bleeding (9, 10).

Hypocalcemia may have a role in coagulopathy as well, but the evidence is not clear enough to say definitively. Hypocalcemia is caused by dilution and by the preservatives contained in blood products. Low ionized calcium will also adversely affect the patient’s cardiac output. If central access or a large antecubital IV is available, it is prudent to administer small aliquots of calcium chloride to bring the patient to the normocalcemic range.

> If we return to our patient with the brachial artery injury, he did not receive ideal management. He received 2 Liters of normal saline in addition to the 1 L administered in the field. The team stripped him down to look for any other injuries - none were found, but nobody covered the patient back up. Four units of type O blood were administered, but no other blood products were given. By the time the trauma surgeon arrives, 15 minutes into the resuscitation, the systolic BP was up to 130; the trauma team felt pretty good about their successful resuscitation. The surgeon appeared a bit dismayed by the thin, pale ooze still emerging from under the "pressure" dressing applied to the arm by EMS. She quickly rushed the patient to the operating room. The emergency trauma team was very surprised to find that the patient had a cardiac arrest on the table; it was after all, just an arm wound.

- ***Acidosis, hypothermia, and coagulopathy beget each other and the eventual demise of the patient***

It's Good to have a Goal

We have discussed the ways the lethal triad can lead to irreversible bleeding and death; now we need to discuss what we actually should be doing about it. The current practice of most ED's is to resuscitate based on blood pressure. Blood pressure is a poor representation of what we really care about: tissue perfusion. Better measures are on the horizon using devices that measure the tissue oxygen levels sublingually, in the central venous circulation, or at the thenar eminence (11, 12). Similarly, the Surviving Sepsis Campaign has moved to alternative measures of perfusion, because blood pressure alone is not sufficient. However, since most EDs do not yet have these or similar technologies, let us focus on the inferior - but universally available - parameter of blood pressure. If we use blood pressure, we might as well use the mean arterial pressure (MAP) as this parameter best represents actual organ perfusion and is less subject to artifact. MAPs are usually automatically calculated by vital sign monitoring machines. If you need to calculate a MAP from a manual blood pressure, the formula is:
MAP = Diastolic BP + 1/3(Systolic BP – Diastolic BP). Using MAP avoids the deception of a seemingly normal systolic blood pressure. A patient with a BP of 80/60 (MAP=66) is actually perfusing their organs better than a patient with a BP of 110/30 (MAP=56).

When measuring MAP, the method matters - cuff blood pressures can be inaccurate in patients in shock. A radial arterial line can be sterilely placed in seconds. Even this method can be foiled by the extreme vasoconstriction of endogenous catecholamines; at times, an accurate MAP can only be obtained by femoral artery catheterization. If there are adequate personnel to place this device without preventing more important resuscitative steps or operating room transfer, it is the gold standard. Once we have an accurate MAP, we require a target pressure to pursue and guide therapy. We have witnessed trauma resuscitations in which products and fluids are given to achieve normal or supranormal systolic BPs; this has no advantage and can cause great harm. The literature from septic shock shows that there is no perfusion advantage above MAPs of 65 mm Hg (13). Until further research emerges in traumatic/hemorrhagic shock, this short-term MAP endpoint seems a reasonable starting point. MAPs above this level may increase the pressure to bleeding vessels and dislodge clot without any perfusion benefit (14). Future work may bear out that even a lower MAP, i.e. 40 or 50, may be the ideal place to keep a trauma patient during the resuscitative phase (15). An even easier, but non-validated goal, may be to resuscitate until you can feel a radial pulse (*).

> ** It used to be thought that a radial pulse guaranteed an MAP of 80 mm Hg; we now know that there is no specific MAP correlation. However, resuscitating till a radial pulse can be palpated provides a goal that allows peripheral perfusion without flooding the patient.*

The caveat to this management strategy is the patient with increased intracranial pressure. In these patients cerebral perfusion must be maintained: a MAP of 80 may be the appropriate goal. Achieving a good balance between the need for cerebral perfusion vs. the risks of increased bleeding is one of the arts of trauma resuscitation.

- ***Use an MAP of 65 as your resuscitative goal, unless the patient has a head injury***
- ***In shock states, blood pressure cuff measurements can be inaccurate; if possible, place an arterial line***
- ***However, never delay transport to the operating room or resuscitation to place an arterial line***

Lab Tests

The only truly important lab test to order on a bleeding patient is the type and cross for blood products, but often we draw the full rainbow of lab tubes. If it is not immediately apparent that the patient is unstable, checking hematocrits, either single or serial, will add nothing to the picture. This test has never been shown to help predict the degree of illness or stability (16). The initial hematocrit is almost inevitably normal in even the sickest of acutely bleeding patients. Coagulation panels are fairly useless and will lag far behind the induced coagulopathy of bleeding and resuscitation. The thromboelastogram (TEG) is a far superior test, but unfortunately it is rarely available in the emergency department.

- ***In an unstable patient, the only test worth sending is the T+C***

Stop the Bleeding

It is the purview of the surgeons and interventional radiologists to stop internal bleeding, but we can do our part with external bleeding. Stopping the bleeding is the most important resuscitative step we can take, as it prevents further loss of RBCs, coagulation factors, and platelets. If a sick patient has extremity bleeding, apply a blood pressure cuff as soon as they roll through the door. Immediately inflate it to twice the systolic blood pressure. Perform your primary survey and initial resuscitation. As soon as the patient begins to stabilize, take down the cuff and assess the extremity; if there is any significant arterial bleeding which does not respond to direct pressure, re-inflate the tourniquet and leave it up.

Ten minutes of a properly applied tourniquet (or a couple of hours for that matter) will cause no ill effects. Most of the deleterious effects observed from tourniquets in the past were from improper application or narrow-banded tourniquets. A blood pressure cuff placed on the upper arm, well proximal to the elbow or on the upper thigh is safe for short periods of time. This paradigm shift emerged from the experience of combat medics during the recent overseas conflicts (24,25). If the patient leaves the trauma room with another service, make sure they are aware of the presence of the bp cuff tourniquet and the exact time of application. We have seen both brachial artery and popliteal artery injuries cause exsanguination and cardiac arrest while hidden under copious layers of "pressure" dressings.

On any blunt trauma patient, the pelvis should be assessed by one inward squeeze at the level of the greater trochanters. If there is inwards movement, **do not release your grip**. Keep inward pressure on the trochanters and have an assistant wrap a sheet around your hands and pull as tight as their strength will allow. Only when the sheet is about to be fully tightened, should you remove your hands. Reducing the volume of an open book pelvis injury will cut down on the venous bleeding.

Scalp wounds cannot be allowed to continue bleeding during the initial resuscitation. The moment you find a gushing scalp wound, throw in large hemostatic stitches with large gauge suture material. Be aware that when the patient is hypotensive, the wound may appear dry, only to start pumping out blood when the BP rises. After stabilization, these big, ugly stitches can be removed, the wound cleaned, and properly closed.

- ***Immediately place a tourniquet proximal to any arterial bleeding from the extremities***
- ***Bind open book pelvis injuries with a sheet***
- ***Close all scalp wounds with quickly-placed, hemostatic stitches***

Keep ‘em Toasty

All fluids infused into the sick trauma patient need to be warmed. The most effective way to accomplish this is by using a rapid infusion device with an integrated warmer. The Level I® fluid warmer (18) or other, similar devices can heat fluids and products to 40°C (104°F) as rapidly as they can be infused under pressure. If these devices are not available, fluids preheated in a fluid warming cabinet should be used, though this will not prevent the hypothermia from ice-cold blood products.

We must counter environmental losses as well by keeping the patient covered with blankets. The temperature of the trauma resuscitation area needs to be adjusted to the comfort of the patient and not the team: 80°F is ideal. If you’re not sweating, then you have the thermostat set incorrectly. In patients not immediately going to the OR or the trauma ICU, warming blanket machines or "French fry" lights can provide additional warming to achieve a normal core temperature.

- ***Administer all fluids and products through a fluid warmer***
- ***Keep the room warm enough to make you sweat***
- ***Keep the patient covered***

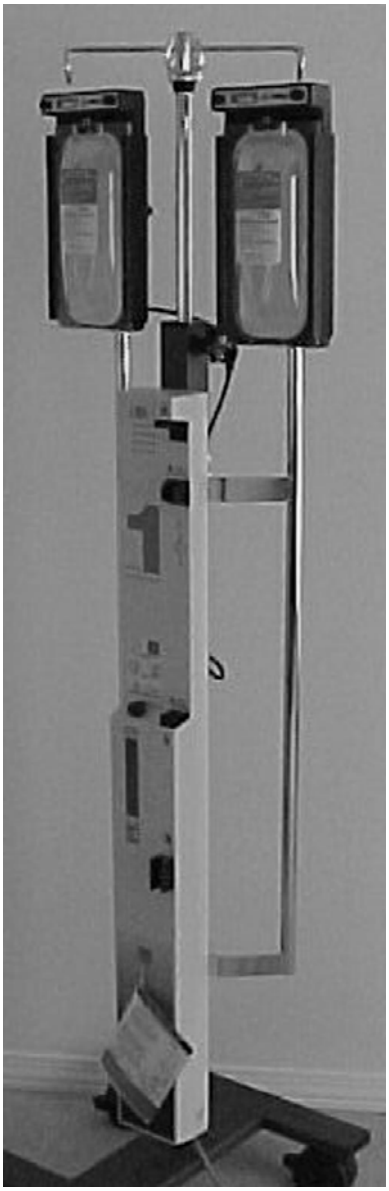


Figure 2: The Level I® rapid infusion device.

On the Administration of Fluids and Products

As important as the warming of fluids and products, is the need to administer them as rapidly as possible. When fluids/components are allowed to infuse by gravity through relatively small catheters, it is difficult to observe the response. While it may seem counterintuitive, the quicker the infusion, often the less we need to infuse. When you can infuse 250 cc in 30 seconds, you can immediately see the BP response, an increase in radial pulse strength, and an improvement in pulse oximetry waveform - you can then stop giving further fluids. When that same 250 cc takes 10 minutes, it is impossible to see a response to the therapy. Instead, the fluid is just left wide open and the fluid continues to pour in, while the team is distracted with other aspects of the resuscitation.

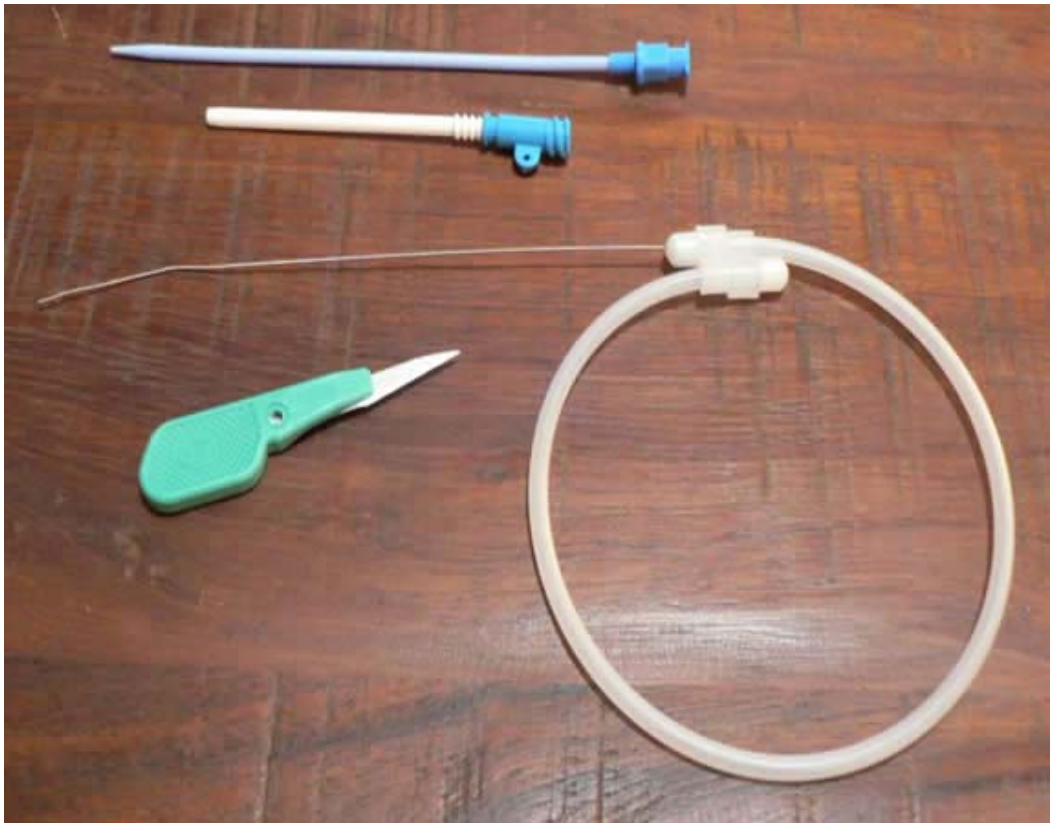
Example of the right way: A patient with pelvic trauma drops her MAP to 50; additional blood units have not yet arrived. Lactated ringers is placed in the rapid infusion device; after 15 seconds and 200 cc, the MAP on the arterial line is now 68, and the infusion is stopped. The trauma leader is able to see a beat to beat response of fluids and the entire fluid bolus can be observed within a one minute period.

Example of the wrong way: A patient with pelvic trauma drops her MAP to 50; additional blood units have not yet arrived. Lactated ringers is infused by gravity into an 18G placed in the forearm; after 1 minute, 60 cc has infused and the patient's MAP has increased to 53. The trauma leader steps to the phone to speak with the angiographer. By the time he again glances at the IV bag, 600 cc have been infused. When he recycles the arm blood pressure cuff, he finds the MAP is now 88.

When rapidity is truly important, the size of the catheter will often be the rate limiting step. While it is conventionally taught that two 14-18G catheters are acceptable as "large bore" access, these lines can be unreliable. In the heat of battle, these standard peripheral IVs can be dislodged or "blow". Two superior options exist for the critical trauma patient: the percutaneous introducer and the rapid infusion catheter (RIC®) (19).

An introducer placed in a subclavian vein is the ultimate access in the sick trauma patient. While you may be tempted by the seeming ease of a femoral vein placement, please resist! In the hypotensive, hypoxic multitrauma patient, venous and arterial blood appear identical both in color and in the spray out of the finder needle. In the heat of the moment, even with ultrasound-guidance, a line may be placed into the femoral artery. This is usually discovered only in the operating room when the blood pressure is restored. The internal jugular vein is often collapsed and inevitably covered by the patient's cervical collar. The subclavian is accessible, consistent in its anatomy, and remains patent even during hypotension. An 8.5 French introducer allows amazingly rapid fluid and product infusion. If additional access is needed for medications and drips, a specially designed catheter can easily be inserted through the introducer port. We cannot allow ultrasound to make the subclavian vein a dying art in the emergency department.

The second option is commonly used by our anesthesia colleagues, but has not yet reached most emergency departments. The RIC catheter is a 7 or 8.5 French introducer catheter placed in the antecubital veins. It is designed to up-convert an existing, standard 20 or 18 G IV catheter. A wire is thread through the IV catheter and the catheter is removed. A small nick is made and the RIC catheter with a dilator in its lumen is then threaded on to the wire. When the entire length of the RIC is in the vessel, the wire and internal dilator are removed in one motion. This placement by Seldinger technique is identical to the placement of a normal introducer catheter and familiar to all of us. Once in place, this wide-bore catheter can be sutured to the skin, making it far more reliable than the IV catheter it replaced.



Figures 3 and 4: The RIC infusion catheter. The wire will fit a 20 gauage or larger IV catheter. The existing IV catheter is removed over the wire and a scalpel nick is made. The RIC device with the dilator placed inside of it can be threaded over the wire into the vein. The wire and dilator is then removed.

Hence, the ideal setup is a subclavian introducer or antecubital RIC hooked up to a Level I fluid warmer/rapid infuser. This combination allows the infusion of 500 cc/minute of components and fluid. As we mentioned above, less is more: 250 cc aliquots are the preferred administration technique. It is absolutely essential that you **evacuate any air** in fluid or blood bags placed in a rapid infusion device or pressure bag. Bags of crystalloid commonly have 50-75 cc of air contained in them before spiking. If this air is infused under pressure, venous air embolism can result. If blood component bags are not spiked properly, air can also be present. The air filters of all but the newest rapid infusion devices cannot eliminate this quantity of air (20).

- ***Place an introducer catheter or RIC on critical trauma patients***
- ***Infuse products and fluids under pressure in order to get immediate feedback***
- ***Evacuate all air from fluid and product bags when infusing under pressure***

PRBCs

Red cells should be utilized early in critical hemorrhagic shock. As soon as you realize the patient is critical, call for blood. Use Type O blood until typed and eventually crossmatched blood is available. Though contradictory data are available, it is still recommended that PRBCs be infused in a line containing saline and not lactated ringers (21). Allowing 250 cc of warmed normal saline to run into the blood bag before infusing it will decrease the viscosity and increase the flow rate. If you are using a Level I®, this step is probably unnecessary.

Rather than infusing some unknown donor's blood, it is always better to infuse the patient's own. If the patient is bleeding from a chest wound, hook up an autotransfusion device to the chest tube. This whole blood can be immediately reinfused and it contains all the good stuff PRBCs lack: clotting factors and platelets.

- ***Give red cells early to achieve MAP goal***
- ***Autotransfuse any significant thoracic blood***

FFP

For all of the reasons we mentioned above, coagulation factors need to be added to any trauma resuscitation early on. Since many centers do not have thawed FFP available, an immediate call to blood bank to begin defrosting should be made upon patient arrival. Thawing may take between 20-40 minutes. As to when to administer FFP and how much to give, the debate continues in the journals and at the national meetings. Based on the most recent thoughts and literature, a ratio of 1 unit of FFP for every 2 units of PRBCs seems reasonable, though a slightly lower or higher ratio may eventually prove to be best (22). Ratios of greater than 1:4 contribute to dilutional coagulopathy and should be avoided. The need for FFP is unfortunately balanced by potential deleterious effects. In addition to the infection risks, it is the blood component most often associated with transfusion-related lung injury.

- ***For every two units of PRBC, administer one unit of FFP***

Platelets

While the emerging strategy of balanced product resuscitation includes infusion of platelets, the trauma community is even further from a consensus than on the issue of FFP. At this time, it seems safe to defer the decision to add platelets till after the first 6-8 units of PRBCs. By this point, most trauma patients should be in the OR or the SICU.

Massive Transfusion Protocols

In order to expedite the availability of blood products, many trauma centers have created interdisciplinary massive transfusion protocols. The protocols are implemented when a critical trauma patient arrives with the anticipation of large transfusion requirements. Activation of most protocols causes the automatic delivery of PRBCs, FFP, Platelets, and cryoprecipitate at set intervals and in predetermined combinations.

On the Need for Speed

In 1990s there was a paradigm shift in trauma surgery (23). Before this time, the critical multitrauma patient would be taken to the operating room for definitive repair of all of their injuries. Many patients died on the OR table; many of these deaths were the result of the lethal triad. A new strategy of staged operations began to show promise. Sick patients would be taken to the operating room for a temporizing procedure. Bleeding organs would be packed, vessels clamped, and bowel tied off. No definitive repairs would be attempted unless absolutely necessary; the abdomen or chest would be left open with a temporary dressing. The patient would be taken to the ICU for a full resuscitation of their hypothermia, coagulopathy, and acidosis. Only when fully corrected would the patient be returned to the OR for definitive repair. This staged strategy is known as **damage control surgery**. The operative surgeon will do only what is necessary to control the damage, not to fix it during the initial operation. This strategy has saved many lives.

The role we can play in this strategy is to get the patient out of the ED and to the OR as quickly as possible. Our treatments must not contribute to the lethal triad. We must adopt the plan of **damage limiting resuscitation**.

Predicting the Future

If you'll allow us to engage in a bit of soothsaying, we might see trauma resuscitation moving along the lines below. The following strategy is definitely not ready for use today, but in the near future, it may very well be the way it is done. Crystalloids require high volumes and contribute to edema later in the patient's course. Hypertonic saline (7.5%) can rapidly fill the intravascular space by the mobilization of interstitial fluids. Small volume aliquots of 50-100 cc can cause large amounts of intravascular filling. Obviously, these small volumes make rapid administration much easier, and limit the hypothermia of large volumes of unwarmed crystalloid. This therapy is already being used by the military, because much smaller volumes of fluid can be carried by frontline soldiers, but they still yield the same resuscitative results. Many trauma centers have moved to using hypertonic saline as a resuscitative fluid as well.

PRBCs will eventually be replaced by synthetic hemoglobin substitutes. Many products already exist, but currently all either have side effects or require further study. The emergence of a stable and safe product is very close. The infectious risks and transfusion reactions of standard PRBCs will thus be reduced.

Fresh frozen plasma is difficult to store, needs thawing, and can induce transfusion-related complications. An alternative already exists in the form of prothrombin complex concentrates (PCC). PCC can instantly replete many of the key components of the clotting cascade using just a 10 cc injection. It is supplied as a powder which can be reconstituted in the trauma room and is immediately ready for use. While factor VIIa is being used in similar circumstances, we believe PCC may be more useful for balanced resuscitation, with factor VIIa being reserved for intractable bleeding in the operating room. The major problems with its immediate adoption are its large cost and the need for more research on potential prothrombotic effects.

One therapy with huge potential is still very much in its nascent stages: induced suspended animation, also known as emergency preservation and resuscitation. A patient near death from traumatic injury can be cooled down to

profound levels of hypothermia and placed on crash cardiopulmonary bypass. After a trip to the operating room for the repair of life-threatening injuries, the patient can be rewarmed and removed from bypass. This has the potential to eliminate the progression of DIC, multi-organ failure, and ischemia. Trials have just begun on this exciting therapy.

When we put all of these together, a hypotensive, underperfused, multitrauma patients would be treated very differently than today. When they roll through the door with an absent radial pulse, they may receive 100 cc of hypertonic saline, 1 unit of synthetic hemoglobin, and a small volume of PCCs. Depending on response, additional rounds of this combination will be administered. Due to the small volume of each of these rounds, there will be less potential for hypothermia and dilutional coagulopathy.

In conclusion, the care we provide in the trauma resuscitation room can make an enormous difference in the patient's eventual outcome. The initial resuscitation of the bleeding trauma patient is clearly a job for an emergency physician. Understanding the lethal triad, allows us to choose therapies to counter the spiral rather than contributing to it. With rapid and aggressive care, damage limiting resuscitation can save lives.

References:

1. Ho, A.M., et al., Excessive use of normal saline in managing traumatized patients in shock: a preventable contributor to acidosis. J Trauma, 2001. 51(1): p. 173-7.
2. Adrogue, H.J. and N.E. Madias, Management of life-threatening acid-base disorders. Second of two parts. N Engl J Med, 1998. 338(2): p. 107-11.
3. Martini, W.Z., et al., Independent contributions of hypothermia and acidosis to coagulopathy in swine. J Trauma, 2005. 58(5): p. 1002-9; discussion 1009-10.
4. Hess, J.R. and J.H. Lawson, The coagulopathy of trauma versus disseminated intravascular coagulation. J Trauma, 2006. 60(6 Suppl): p. S12-9.
5. Meng, Z.H., et al., The effect of temperature and pH on the activity of factor VIIa: implications for the efficacy of high-dose factor VIIa in hypothermic and acidotic patients. J Trauma, 2003. 55(5): p. 886-91.
6. Ferrara, A., et al., Hypothermia and acidosis worsen coagulopathy in the patient requiring massive transfusion. Am J Surg, 1990. 160(5): p. 515-8.
7. Krause, K.R., et al., Hypothermia-induced coagulopathy during hemorrhagic shock. Am Surg, 2000. 66(4): p. 348-54.
8. Watts, D.D., et al., Hypothermic coagulopathy in trauma: effect of varying levels of hypothermia on enzyme speed, platelet function, and fibrinolytic activity. J Trauma, 1998. 44(5): p. 846-54.
9. Gando, S., et al., Posttrauma coagulation and fibrinolysis. Crit Care Med, 1992. 20(5): p. 594-600.
10. Kapsch, D.N., et al., Fibrinolytic response to trauma. Surgery, 1984. 95(4): p. 473-8.
11. Cohn, S.M., et al., Tissue oxygen saturation predicts the development of organ dysfunction during traumatic shock resuscitation. J Trauma, 2007. 62(1): p. 44-54; discussion 54-5.
12. Ikossi, D.G., et al., Continuous muscle tissue oxygenation in critically injured patients: a prospective observational study. J Trauma, 2006. 61(4): p. 780-8; discussion 788-90.
13. Bourgoin, A., et al., Increasing mean arterial pressure in patients with septic shock: effects on oxygen variables and renal function. Crit Care Med, 2005. 33(4): p. 780-6.
14. Bickell, W.H., et al., Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. N Engl J Med, 1994. 331(17): p. 1105-9.
15. Kwan, I., F. Bunn, and I. Roberts, Timing and volume of fluid administration for patients with bleeding. Cochrane Database Syst Rev, 2003(3): p. CD002245.
16. Zehtabchi, S., et al., Diagnostic performance of serial haematocrit measurements in identifying major injury in adult trauma patients. Injury, 2006. 37(1): p. 46-52.
17. Lavery, R.F., et al., The utility of venous lactate to triage injured patients in the trauma center. J Am Coll Surg, 2000. 190(6): p. 656-64.
18. Trademarked. Level I Sims Technologies. 2008 (cited.
19. Trademarked. Arrow International. 2008 (cited; Available from: http://www.arrowintl.com/products/boms/RC09700.asp?cat=9&item=RC-09700&xsec=.
20. Comunale, M.E., A laboratory evaluation of the level 1 rapid infuser (H1025) and the Belmont instrument fluid management system (FMS 2000) for rapid transfusion. Anesth Analg, 2003. 97(4): p. 1064-9, table of contents.
21. Lorenzo, M., et al., Can Ringer's lactate be used safely with blood transfusions? Am J Surg, 1998. 175(4): p. 308-10.

22. Borgman, M.A., et al., The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. J Trauma, 2007. 63(4): p. 805-13.
23. Schreiber, M.A., Damage control surgery. Crit Care Clin, 2004. 20(1): p. 101-18.
24. Welling D.R., et al., A Balanced Approach to Tourniquet Use: Lessons Learned and Relearned. J Am Coll Surg, 2006. 203(1):p. 106-115.
25. Lakstein, D., et al. Tourniquets for hemorrhage control on the battlefield: A 4-year accumulated experience. J Trauma. 2003. 54(5): p. S221-S225.