EXPERT REVIEWS

Transfusion medicine in trauma patients: an update

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In 2008, we reviewed the practical interface between transfusion medicine and the surgery and critical care of severely injured patients. Reviewed topics ranged from epidemiology of trauma, to patterns of resuscitation, to the problems of transfusion reactions. In the interim, trauma specialists have adopted damage control resuscitation and become much more knowledgeable and thoughtful about the use of blood products. This new understanding and the resulting changes in clinical practice have raised new concerns. In this update, we focus on which patients need damage control resuscitation, current views on the optimal form of damage control resuscitation with blood products, the roles of newer blood products, and appropriate transfusion triggers in the postinjury setting. We will also review the role of new technology in patient assessment, therapy and monitoring.

Keywords: blood bank protocols • clinical blood use • cryoprecipitate transfusion • injury • injury care • plasma transfusion • red cell transfusion • shock resuscitation • transfusion protocols • trauma center protocols

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In the first issue of *Expert Review of Hematology*, we reviewed the practical interface between transfusion medicine and the surgery and critical care of severely injured patients [1]. The article described the epidemiology of injury, the organization and extent of trauma systems, blood use in trauma resuscitation and subsequent care, the complications of blood use, and how new technology was changing the way we think about the treatment and control of hemorrhage and the need for blood products. The interim has seen progress and controversy on all of these issues. In this article, we will examine new thinking and evidence on the most rapidly evolving issues: the coagulopathy of trauma, damage control resuscitation, advances in monitoring, and evolving issues in blood safety.

Injury is still the most common cause of the loss of life in young people [101]. Traumatic injury leads approximately 9% of the population to seek medical care each year, consumes 5% of all medical costs and uses about 7% of the blood supply [2]. Furthermore, massively bleeding patients die quickly: trauma transfusion services must be able to respond to the special physiologic and logistic needs of these patients [3].

The coagulopathy of trauma

The human coagulation system can be rapidly overwhelmed by severe injury [4]. Direct loss and consumption of coagulation factors, dilution, hypothermia, acidosis and fibrinolysis all diminish hemostasis (Figure 1) [5]. Each of these mechanisms can occur independently, but all occur more frequently and severely with worsening degrees of injury, and their interaction can drive the coagulation system beyond functional and recuperative limits.

Blood loss is often a presenting symptom of injury but can be masked by internal bleeding or by evacuation of the patient from the site of injury and the visible signs of massive blood loss. Patients in stage IV shock may have lost up to 40% of their blood volume, with proportional loss of coagulation factors and platelets [6].

Dilution occurs both physiologically and iatrogenically. In physiologic hemodilution after injury via vascular refill, the loss of hydrodynamic blood pressure leaves the colloid osmotic activity of plasma unopposed, and water moves into the intravascular space, diluting plasma proteins until the forces are back in equilibrium. As mean blood pressure falls from 80 to 50 mmHg, water moves into the vascular space to dilute the plasma proteins. Each protein is diluted equivalently and their interactions, such as the assembly of factors IXa, VIIIa and X on platelet surfaces to form the intrinsic 'tenase' complex, is reduced in proportion to the product of the individual reductions in factor concentration. Thus, a 37% loss in the individual factor concentrations combines to cause a 75% reduction in overall complex activity [7]. Iatrogenic dilution of coagulation proteins with administered crystalloids or colloids has a similar effect.

Hypothermia contributes to coagulopathy by slowing plasma coagulation factor chemical reactions and, much more importantly, by reducing the activation of platelets [8]. Plasma coagulation factor enzyme activity decreases by approximately 5% with each 1°C fall in temperature, but anticoagulant activity also decreases. However, platelet activation by the von Willebrand factor–glycoprotein Ib (IX, V) interaction, is profoundly cold sensitive [9]. Measured in Couvé viscometers, this interaction is absent in 75% of individuals at 30°C and is compromised severely enough at 32°C that survival of severely injured hypothermic individuals is rare [10].

Acidosis is common in shock, and profoundly affects the plasma coagulation system. Plasma coagulation factors are slowly reactive in the plasma phase, but are much more reactive when assembled into complexes on negatively charged phospholipid rafts on the surfaces of subendothelial and inflammatory cells and platelets [11]. The increased activity that occurs with factors VIIa, IXa and Xa in their respective complexes is of the order of a million-fold and allows the coagulation system to achieve high local activity at the site of injury. The complexes are held together by binding of positively charged calcium ions against the negatively charged phospholipid rafts by the dicarboxylic acids of the vitamin K-dependent coagulation factors. In this process, the rafts stabilize the coagulation factor complexes, and the complexes stabilize the rafts. **Increasing hydrogen ion concentration destabilizes the complexes and the rafts, causing the net activity of all the coagulation factor complexes to fall.** A coagulation factor complex with normal activity at pH 7.4 has 50% of normal activity at pH 7.2, 30% at pH 7.0, and 20% of normal activity at pH 6.8 [12].

A conventional view is that coagulation factor substrates are consumed in clotting but the associated enzymes are not. However, in high-energy-transfer injury in which millions of endothelial microtears occur, each of the factors is continuously activated and consumed. Tissue injury releases tissue factor, phospholipids, histones and RNA, all of which either bind or activate coagulation factors. Shock-related hypoprofusion and injury-related inflammation increase the damage, and genetic or environmental factors that lead to hyperglycemia and hypercholesterolemia increase coagulation activity. Once activated, factors VIIa and Xa are inactivated by tissue factor pathway inhibitor, IIa, IXa, Xa, XIa and XIIa are irreversibly bound and cleared by antithrombin, and Va and VIIIa are inactivated by protein C [13]. The more severe the injury, the greater the degree of both activation and consumption.

Normally, clots are made and are stable for a period of time that allows control of bleeding and wound healing. High concentrations of thrombin lay down thick bundles of fibrin, activate the thrombin-activated fibrinolysis inhibitor, and activate plasminogen activator inhibitor, slowing the activation of plasmin [14]. When the thrombin burst is weak, the thrombin-activated fibrinolysis inhibitor is not activated, and when thrombin diffuses beyond the limits of the many endothelial microtears and encounters thrombomodulin on the surface of adjacent healthy endothelial cells, protein C is activated, which in turn inactivates plasminogen activator inhibitor. With severe injury, the balance between the extent of injury and the capacity of the coagulation system to modulate fibrinolysis can be exceeded.

The coagulopathy of trauma is the sum of all of these disturbances. **As blood becomes more dilute, cold and acidotic, activation slows and concentration-dependant regulation is lost.** The process begins when coagulation factor activities fall below 50% and becomes severe when they are below 20% [15,16]. The clinical drivers of the process can be seen in a classic study by Cosgriff and colleagues showing that moderate injury was associated with a 1% rate of coagulopathic bleeding [17]. However, the rate increased to 10% with severe injury, 40% with severe injury and hypotension requiring resuscitation, 50% with severe injury and hypothermia, 60% with severe injury and acidosis, and 98% when all of these elements were present.

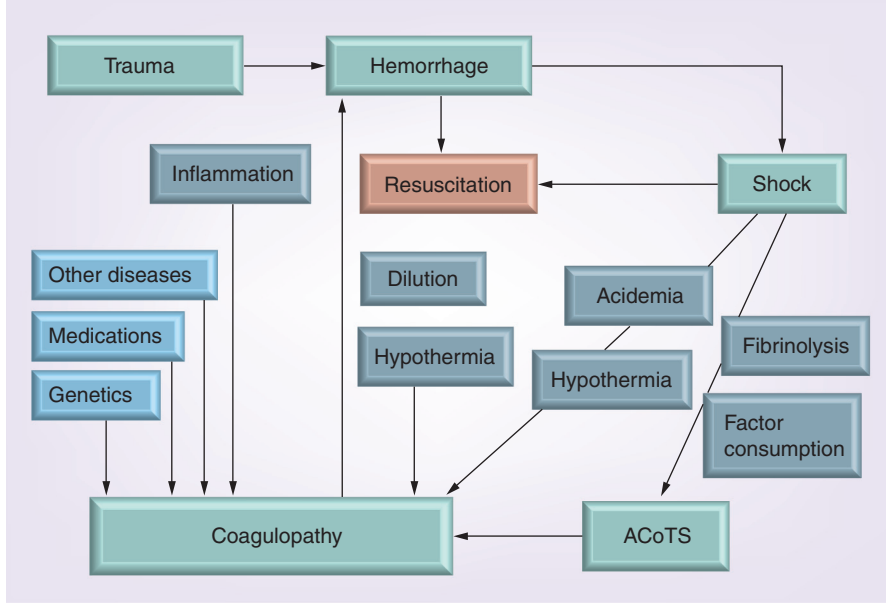

Figure 1. Trauma leads to bleeding that can lead to resuscitative blood dilution and hypothermia, which can lead to coagulopathy. Injury and hemorrhage can also lead to shock that can lead to acidosis and inflammation, which can cause coagulopathy. Tissue injury and shock can lead to factor consumption and fibrinolysis and ACoTS. In the face of severe injury and uncontrolled shock, coagulopathy occurs in a quarter of presenting trauma patients and develops in the course of treatment in 98% of patients treated with conventional resuscitation.
ACoTS: Acute coagulopathy of trauma and shock.
Reproduced from [6] with the permission of the *Journal of Trauma*.

Resuscitation with red cells in additive solution

All of the aforementioned effects were exacerbated by the historical shift from resuscitation with anticoagulated whole blood, which contained normal amounts of plasma, to the use of red cells in

additive solution with only 35 ml of plasma in each unit [18]. In the 1970s, whole blood was collected into citrate phosphate dextrose anticoagulant and stored for 3 weeks. Plasma coagulation factors, with the exception of factor VIII, generally tolerated this and the platelets, although rapidly cleared from the circulation after administration, may have provided an acute boost to hemostatic activity. Even when the platelets were removed in component production, some centers like the Puget Sound Blood Center in Seattle (WA, USA) made reconstituted whole blood by adding the plasma back to the packed red cells for local trauma center use. The classic article describing this technique by Counts and colleagues states: "It is not necessary to supplement transfusions of stored, modified whole blood with fresh blood or fresh frozen plasma" when resuscitation is performed with this distinctive product, not with the 'packed red cells' that were the available product elsewhere [19].

In 1979, citrate phosphate dextrose was superseded by citrate phosphate dextrose adenine as the standard storage solution for whole blood and was still used in the Seattle reconstituted whole blood. However, with the arrival of red cells in additive solution in 1981 concurrently with the AIDS epidemic, conventional wisdom evolved toward resuscitation with crystalloid fluids supplemented with enough red cells to maintain oxygen transport and plasma and platelets added only as necessary as directed by laboratory measures. This strategy was adequate for most patients and did limit blood exposure. However, for the sickest few patients, this strategy rapidly created dilutional coagulopathy, where hemorrhage begat resuscitation, resuscitation begat dilution, dilution begat coagulopathy and coagulopathy begat more hemorrhage, the so-called 'bloody vicious cycle.' Ever-improving surgical technique saved some patients, but for the most severely injured, evaporative cooling from open wounds led to heat loss at a rate of 1°C/40 min, hypothermia, operative failures and continued high mortality [20].

In response, a number of gifted trauma surgeons developed 'damage control' abdominal surgery, where short operations shunted injured named blood vessels, tied off other major vascular bleeding and sources of gut contamination, drained urinary contamination, packed oozing and then packed the wound open to prevent compartment syndromes [21]. With hemorrhage slowed to a manageable rate, the patient could be taken to interventional radiology for additional hemorrhage control and to the intensive care unit for warming and laboratory-driven correction of coagulation abnormalities. The change in strategy saved lives, but left large numbers of patients deeply anesthetized in intensive care units and susceptible to the complications of repeated operations and long-term mechanical ventilation. In this situation, drugs such as recombinant factor VIIa, which promised to stop bleeding quickly, were very attractive, but the sense persisted that coagulopathy was something that developed slowly as a result of dilution [22].

The acute coagulopathy of trauma & shock

In 2003, Brohi and colleagues reported a series of 1000 patients delivered by helicopter to the Royal London Hospital (London, UK) who had received less than a half a liter of crystalloid fluid in transport, 25% of whom were coagulopathic on admission as indicated by a prothrombin time (PT) ratio of 1.5 or greater [23]. Furthermore, the higher the injury severity score, the greater the incidence of coagulopathy, and the presence of coagulopathy predicted a four-times higher mortality. They have subsequently emphasized the importance of clinical hypoperfusion and shock in driving this syndrome [24]. Several months later, MacLeod and colleagues in Miami reported on a much larger series of 20,000 trauma center admissions, again with limited fluid administered before admission [25]. Among the 28% of patients with any prolongation of the PT time at admission, there was a 35% increase in the risk of hospital death. Among the 8% of patients with a prolonged partial thromboplastin time (PTT), the increased risk of death was 426%. Essentially all of these excess deaths occurred in the first 5 h of care and were related to uncontrolled primary hemorrhage.

At the University of Maryland Shock Trauma Center (MD, USA), Hess and colleagues reviewed the relationship between the admission laboratory coagulation tests and in-hospital mortality for more than 35,000 patients admitted directly from the scene of injury in calendar years 2000–2006 [26]. As in the Brohi study, increasing injury severity predicted a stepwise increasing fraction of patients with an increased PT on admission, rising to 45% of all patients with an injury severity score of >45. As in the MacLeod study, the PTT was less sensitive but far more specific, and for the small number of patients with a PTT ratio >1.5 and an injury severity score >25, mortality was 90%. Abnormalities of fibrinogen concentration and platelet count also showed the same stepwise increases in prevalence with increasing injury severity. Increased mortality was demonstrable with abnormalities in all the conventional coagulation tests from clearly abnormal values to the upper half of the normal range. In a separate study involving the same patients, Dutton and colleagues showed that, among patients admitted directly from the scene of injury who survived at least 15 min after admission but who then went on to die of hemorrhage, almost half were dead within 2 h and 80% were dead by 6 h after admission [3].

Damage control resuscitation

For calendar year 2000, Como and colleagues audited all blood products used by patients directly admitted to the Maryland Shock Trauma Center [27]. While only 8% of those admitted received red cells and only 6% received plasma, a total of 5219 units of red cells and 5226 units of plasma were given. In retrospect, this suggests that they were worsening coagulopathy by early resuscitation using crystalloid and red cells in additive solution and then rescuing them later, if possible, with plasma and platelets. On the basis of this insight, we began giving plasma sooner and in a more balanced proportion to the red cells administered. As the benefits of controlling coagulopathy sooner became clinically apparent, early use of platelets, cryoprecipitate and rVIIa also increased.

By the time the Como paper was published in 2004, Afghanistan and Iraq were active war zones, and the casualties from high-velocity munitions and improvised explosive devices were rapidly increasing. Combat support hospitals in

theater were seeing large numbers of multiply injured casualties who were being resuscitated with crystalloids and red cells in additive solution and dying of uncontrolled coagulopathic hemorrhage before type-specific plasma could be thawed. We encouraged the military trauma teams to convert to prethawed universal donor plasma, obtain prepooled cryoprecipitate and to use rVIIa. The results were dramatic. Not only did numbers of deaths from uncontrolled hemorrhage death appear to decrease, but earlier successful primary wound closures, earlier extubation and decreased ventilator days were also noted. In May 2005, the US Army Institute of Surgical Research hosted a conference on massive transfusion in trauma. A total of 45 North American and European experts in trauma surgery, anesthesia, hematology and transfusion medicine reviewed critical issues in the physiologic and clinical literature on massive transfusion [28]. The consensus opinion of this group was that resuscitation after massive hemorrhage should dramatically reduce dependence on crystalloid and focus on repletion of both red cells and plasma in roughly 1:1 proportions [29]. Shortly afterwards, the US Army Surgeon General issued a clinical guideline recommending resuscitation with 1:1 plasma to red cells [30]. As military physicians returned from deployment in the war zones, demands for change in resuscitation practice evolved rapidly into what was now being called 'damage control resuscitation' [31]. By April 2008, in a debate on plasma use in resuscitation before the elite American Surgical Association, Holcomb asked the audience how many were using more plasma in their resuscitations than they had several years earlier, and the response was universal [32]. Based on limited evidence, damage control resuscitation had become the standard of care in the USA.

While most of the emphasis on damage control resuscitation has been on the plasma-to-red-cell unit ratio, giving platelets can also be important. Cosgriff and colleagues reported that increased platelet use appeared to improve outcome [17]. Hess and colleagues showed that low admission platelet counts were strongly associated with mortality [26] and Holcomb and colleagues' data suggest that giving more platelets early is associated with lower mortality [32]. Spinella and colleagues suggest that most of the benefit occurs in patients with brain injury [33].

Resistance to damage control resuscitation

Resistance to damage control resuscitation has three not inconsiderable arguments. The first is that 1:1 plasma to red cell resuscitation is unproven; the second is that it is largely unnecessary; and the third is that the ratios are wrong. All three positions are at least partly true, and all three nonetheless miss overriding truths.

The original data from Baghdad used to justify the 1:1 plasma-to-red-cell ratio had a serious methodologic flaw [34]. This retrospective study looked at all patients who received more than 10 units of red cells (massive transfusion) in the first 24 h after admission, and compared survival among groups receiving low, intermediate and high ratios of units of plasma to units of red cells administered. However, uncross-matched group O red cells were available immediately while plasma was frozen and required blood typing before thawing, so many patients died before plasma was available. In addition, patients who survived were often given additional plasma to 'normalize' coagulation tests, elevating their plasma-to-red-cell unit ratio after hemorrhage had been controlled. These events created a 'survivor bias' that overestimated the size of the survival benefit of plasma treatment. The important secondary benefits of hemostatic resuscitation – early abdominal closure and shorter ventilator times, which are less susceptible to bias caused by early death because they occur later in care – were not included in the initial report.

All of the 22 subsequently published studies on the plasma-to-red-cell unit ratio have been retrospective and many suffer from survival bias [35]. Eliminating patients who died in the first hour reduces this bias but does not eliminate it. However, a large NIH-sponsored seven-center cohort study shows that massive transfusion itself has become less frequent as more plasma and platelets are given earlier, suggesting that coagulopathic hemorrhage is being controlled sooner in otherwise healthier patients [101]. Two other large series show improved survival in patients receiving 5–9 units of red cells [102,36]. Whether this improved survival represents improved speed to the operating room or a benefit of a high plasma ratio is not yet clear, but the relationship between massive hemorrhage and massive transfusion is affected by patterns of care. In the absence of a randomized study, which is several years away, the evidence for benefit of additional plasma remains Class III.

A second argument against resuscitation with plasma is that many patients do not need it and needlessly suffer the consequences of reactions to allogenic plasma [37]. Identifying patients early in care who need massive transfusion has turned out to be difficult. Several rapid clinical scoring systems have been proposed, and the simple ABC score performs well [38]. Administration of a unit of uncross-matched red cells in the first hour has only a 30–37% predictive value for subsequently receiving 10 units or more in the first 24 h, but clearly some of the patients who do not go on to massive transfusion are the ones who stopped bleeding because of early administration of plasma [39,40]. In the absence of prospective data, these issues cannot be definitively teased apart.

Third, there are those who argue that 1:1 is the wrong plasma-to-red-cell unit ratio for resuscitation. One can calculate that a ratio of six units of red cells to four units of plasma plus a unit of apheresis platelets in plasma would result in higher concentrations of all of the individual components. Giving one unit of each of the three components (1:1:1) addresses all blood component needs and is easy to administer in an emergency [39], although many patients clearly do fine with proportionately less plasma.

Resisted or not, critical changes in trauma transfusion in the last decade have been wrought by improved dialog between surgeons, anesthesiologists and transfusion medicine specialists. An important outcome of this improved communication has been the development and implementation of demonstrably useful massive transfusion protocols in many centers [40,41].

The future of resuscitation

Fresh frozen plasma is dilute and incurs unavoidable delays in thawing. Research into improving the availability and efficacy of plasma products for resuscitation has led to the development of single-donor freeze-dried plasma, which can be stored at room temperature close to patient care, and to resuscitation using plasma-derived coagulation factor concentrates [42].

Freeze-dried human plasma from donor pools was used in resuscitation in World War II but discredited because of high rates of associated hepatitis. Today, freeze-dried 600 ml units of apheresis-derived, pedigreed and quarantined single donor plasma are being prepared for clinical testing [42]. The combination of light weight, room-temperature storage and the possibility of reconstitution in less than full fluid volume to make concentrated plasma has made the material attractive to military planners. However, the presence of all of the plasma proteins in the lyophilized material means that the ability to concentrate the coagulation factors will be limited by the colloid osmotic activity of albumin and that all of the allergic risks of conventional plasma products will occur with this product [42].

European groups have shown that plasma-derived coagulation factor concentrates are both rapidly available in the operating room and highly active in the patients. [43] With fibrinogen concentrates, inactive six-factor prothrombin complex concentrates (PCCs; containing factors II, VII, IX and X, and proteins C and S) and blood bank platelets, reconstitution of the critical portions of the human extrinsic plasma coagulation system is possible. In this process, factors VII, IX, X and II come from the PCC, factor V from the platelet α granules, factors VIII, XI and XIII from the patient's residual plasma and fibrinogen is given as concentrate. Because these clotting factor concentrates are pharmaceuticals available in the operating room refrigerator, they are available quickly and without the volume-expanding effects of the extra albumin in plasma [43]. Use of these materials to resuscitate trauma patients has demonstrated rapid control of coagulopathy and reduced total blood use with reduced plasma complications, has become the standard of care in Austria, and is rapidly spreading in Europe where the new PCCs are available [43].

As noted previously, early clot stability can be overwhelmed by massive injury [43]. Preliminary investigation suggested that the use of the antifibrinolytic, tranexamic acid, in trauma resuscitation could reduce rebleeding without increasing the risk of vaso-occlusive events, and this led to implementation of the large, multinational, Clinical Randomization of an Antifibrinolytic in Significant Haemorrhage 2 (CRASH-2) trial [44]. Although controversial, the CRASH-2 trial, and especially the British military experience in the current war zones, suggests that early (though not late) use of tranexamic acid can limit rebleeding and save lives when widely used [45].

Hemorrhage-control methods are also improving. Early versions of fibrin bandages are available, and better ones are under development. Synthetic hemostatic bandages with excellent efficacy and safety have been developed and demonstrated in animal models [46].

Advances in therapy are being matched by advances in patient monitoring. Pulse oximetry-based continuous hemoglobin monitors, viscoelastic coagulation monitors, and ultrasound-based cardiac function measures are already available and being deployed widely. Continuous hemoglobinometry provides a real-time tool to manage red cell and volume administration [47]. Viscoelastic coagulation monitors provide near-real-time measures of clot formation and persistence by measuring plasma coagulation, platelet function and clot stability on small unprocessed blood samples [48,49]. Likewise, clinician utilization of point-of-care ultrasound techniques provides immediate critical visual information. Focused assessment sonography for trauma can demonstrate free fluid in the pericardium and abdomen, alerting the clinician to the possibility of occult bleeding, and focused rapid echocardiographic examination can demonstrate pericardial fluid, ventricular function and volume status [50,51]. High speed whole-body CT scanning can recognize sites of occult bleeding (Figure 2) [52].

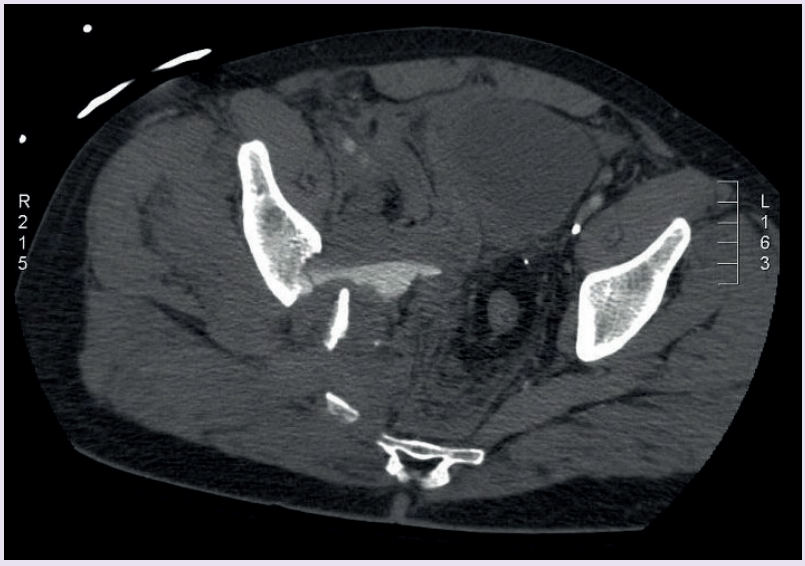

Figure 2. Pelvic CT scan of a trauma patient showing a complex pelvic fracture associated with vascular injury, an active plume of arterial bleeding, and a large, deep pelvic hematoma displacing the bladder and bowel. Emergent CT scanning in trauma centers is an important method for identifying sites of occult hemorrhage. See [55].

Blood safety

The most common causes of death from transfusion in the developed world are the immune and inflammatory complications of allogenic transfusion [53]. Efforts

to prevent mistransfusion due to mislabeled samples, mishandled units and misidentified patients have reduced acute hemolytic transfusion reactions, but 'never' events continue to occur even with 'fail-safe' electronic medical identification systems. Transfusion-related acute lung injury is recognized as the leading cause of transfusion-related death in developed countries [54]. It is the most clinically obvious reaction among a much larger number of patients with transfusion-associated organ injury. Estimates of the frequency of transfusion-related acute lung injury remain at approximately 1:6000 transfusions, but excess mortality following transfusion in hemodynamically stable patients was 1:25 in the prospective, but underpowered, Transfusion Requirements in Critical Care (TRICC) trial [55] and 1:20 in a larger retrospective study by Vlaar and colleagues [56]. The importance of leukoreduction in limiting acute lung injury is becoming increasingly obvious [57].

Concern about 'old blood' was heightened after a widely publicized article by Koch and colleagues in the *New England Journal of Medicine* in February 2008 suggested increased mortality in cardiac surgery patients transfused with red cells stored for longer than 14 days [58]. The excess mortality in this study is more directly explained by the higher numbers of patients receiving 7 or more units of red blood cells in the longer storage group and their previously reported high mortality [59]. Concern about stored red cells is more appropriately directed to the known accumulation of lysophospholipids in stored products, to the loss of microvascular density and flow seen after administration of stored red blood cells in supravital microscopy and the burden of noncirculating cells [60]. These effects are potentially reducible with better storage solutions and leukoreduction [61,62]. Whether the storage-dependent reduced concentrations of red cell 2,3-diphosphoglycerate are clinically important remains unclear [60]. Plasma stored in liquid form for more than a few hours can be associated with kinin generation, but coagulation factor concentrations are well preserved. Storage of platelets remains problematic.

Expert commentary

Resuscitation of the severely injured has changed radically in the last 8 years from a paradigm based on early administration of red cells and crystalloids, associated with iatrogenic coagulopathy that was linked to high mortality and long intensive care unit stays, to a plan of giving more plasma and platelets early in the hope of limiting coagulopathy. It will change further to the use of coagulation factor concentrates given in response to very rapid bedside testing with the goal of immediate correction of coagulopathy in actively bleeding patients. Blood products will still be necessary, so efforts to improve their safety and efficacy are still important. As these changes come, surgeons and transfusion medicine specialists will need to plan for the optimal care of patients under the unique conditions of each hospital.

Five-year view

The safest transfusion remains the one not given. Once hemorrhage is controlled, the low red cell transfusion triggers associated with safe outcomes in the TRICC trial and recommended in the Eastern Association for the Surgery of Trauma–Society of Critical Care Medicine guidelines are appropriate and improve safety by limiting unnecessary transfusions [63]. Similarly, avoidance of transfusion at PT and PTT ratios less than 1.5 and platelet counts above 30 K are ways of reducing exposure in selected patients. The importance of increased platelet counts in patients with neurologic injury is an important exception.

The nature of resuscitation will continue to change as the tools available for monitoring the cause and extent of bleeding, for achieving early control of hemorrhage and for monitoring response to therapy continue to improve. New blood products – better red cell storage solutions, platelets in additive solution, PCCs and fibrinogen concentrates, freeze-dried plasma and frozen platelets – will be incorporated into resuscitation practice, driven by a combination of availability, efficacy, safety and cost concerns. Secondary and tertiary prevention of hemorrhagic death will improve with better local hemostatic agents and the use of tranexamic acid.

Key issues

- Traumatic injuries are the leading cause of death in young people.
- Coagulopathy in trauma is multifactorial.
- Damage control resuscitation with red blood cells, plasma and platelet units given in equal numbers has become the standard of care for severely injured patients.
- Resuscitation with plasma-derived coagulation factor concentrates is developing rapidly and will replace damage control resuscitation as soon as the materials become available in quantity. Tranexamic acid use will increase.
- Continuous hemoglobin monitors, bedside ultrasound and rapid viscoelastic coagulation monitors can guide resuscitation and allow better blood management.
- Once hemorrhage control is obtained, lower transfusion triggers are desirable to reduce blood exposure and its inflammatory consequences.
- Low transfusion triggers and massive transfusion protocols depend on the rapid availability of rescue blood products.
- Communication between the transfusion service and the trauma service remains critical.

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Activity Evaluation
Where 1 is strongly disagree and 5 is strongly agree

	1	2	3	4	5
1. The activity supported the learning objectives.					
2. The material was organized clearly for learning to occur.					
3. The content learned from this activity will impact my practice.					
4. The activity was presented objectively and free of commercial bias.					

1. You are called to the emergency department to see a 24-year-old man who received three gunshot wounds to the abdomen and chest. He has lost a significant amount of blood.
What should you consider regarding blood loss during severe trauma as you initiate your evaluation of the patient?

- ☐ **A** Factor X is diluted to a greater degree than other proteins in severe shock
- ☐ **B** Hypothermia improves the aggregation of platelets
- ☐ **C** Lower serum pH values promote more effective blood clotting
- ☐ **D** The rate of coagulopathic bleeding increases with the severity of injury

2. You consider ordering damage control resuscitation for this patient. Traditionally, what has this treatment included?

- ☐ **A** Red blood cells: plasma in a 1:3 ratio; no platelets
- ☐ **B** Red blood cells: plasma in a 3:1 ratio; no platelets
- ☐ **C** Red blood cells: plasma in a 1:1 ratio plus platelets
- ☐ **D** Red blood cells: plasma in a 1:3 ratio plus platelets

3. What else should you consider in making a decision regarding damage control resuscitation?

- ☐ **A** 'Survivor bias' may lead to overestimation of the efficacy of damage control resuscitation
- ☐ **B** Multiple randomized trials now support the use of damage control resuscitation
- ☐ **C** New algorithms accurately predict which trauma patients will require massive transfusion
- ☐ **D** The 1:1 red cell:plasma ratio is well established as being superior to other regimens

4. Transfusion-related injury to which of the following organs is the leading cause of transfusion-related mortality in advanced countries?

- ☐ **A** Brain
- ☐ **B** Kidney
- ☐ **C** Liver
- ☐ **D** Lung