

# Chapter 7

## DAMAGE CONTROL RESUSCITATION

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## INTRODUCTION

Damage control resuscitation (DCR) is defined as a systematic approach to major trauma, combining a series of clinical techniques from point of wounding to definitive treatment to minimize blood loss, maximize tissue oxygenation, and optimize outcome. The three major components of DCR are surgery to control bleeding, massive transfusion, and hemostatic resuscitation, instigated simultaneously (Figure 7-1).<sup>1,2</sup>

The term “damage control” originated in the United Kingdom (UK) Royal Navy as early as the 17th century and relates to doing whatever is required to bring a damaged ship home to port. DCR was introduced

into the UK Defence Medical Services (DMS) in 2005 with the publication of *Battlefield Advanced Trauma Life Support*<sup>3</sup> (BATLS) and later enhanced with hemostatic resuscitation and massive transfusion guidelines.<sup>4</sup> Further work in US military vascular trauma cases highlighted the value of implementing this important concept.<sup>5</sup> DCR represents a major step in the evolution of military trauma care. Since its inception, there has been a significant improvement in the number of unexpected survivors and a marked reduction in mortality from massive transfusion, despite increasing injury severity.<sup>6</sup>

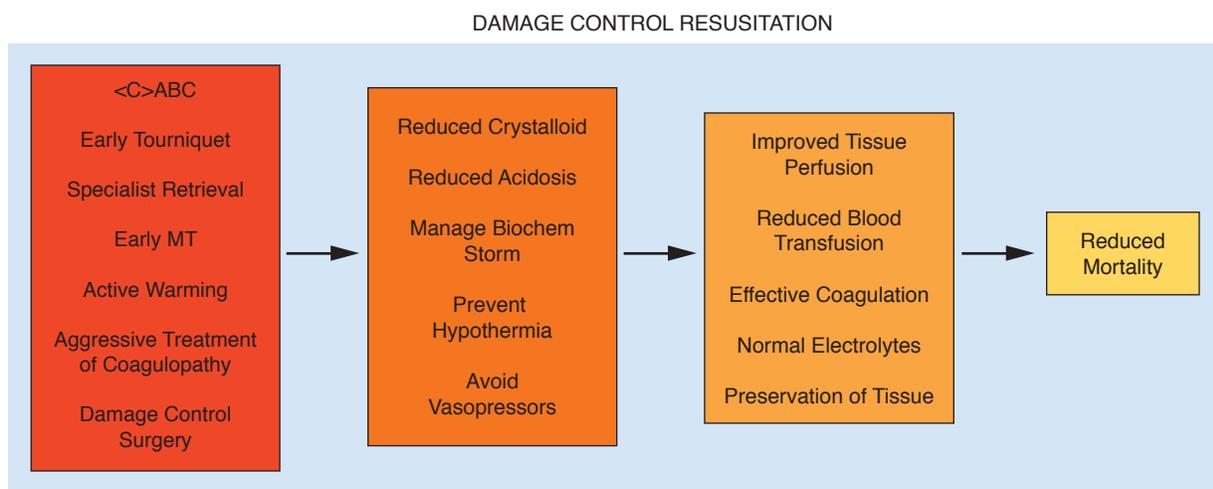
## THE EVOLUTION OF MILITARY TRAUMA CARE

Trauma care dates back to ancient Egypt, Greece, and Rome, inextricably linked to the wars these empires were built upon. The Edwin Smith Papyrus from the 17th century BCE details the clinical treatment of 48 cases of war wounds in ancient Egypt. Homer’s *Iliad* records 147 types of wound with an overall mortality rate of 77.6% during the Trojan War. The Romans probably created the first trauma center hospitals, called “valetudinaria,” during the 1st and 2nd centuries CE. Eleven such centers existed in Roman Britain.<sup>7</sup>

Trauma care did not advance greatly until the 14th century when, Guy de Chauliac (often termed the “father of surgery”) practiced the use of inhalational anesthesia, antisepsis, trephination, and thoracic surgery. From 1797 to 1812 Dominique Larrey acted as

Napoleon’s surgeon general and developed what was at the time a revolution in military trauma care: he introduced field hospitals located close to the front line and “flying ambulances” to quickly transport the wounded to the operating theatre, thereby reducing mortality in the perioperative period. Larrey understood the need for predeployment training for his ambulance teams (consisting of eight surgeons) and exercised them daily until their operations and application of bandages showed “the greatest degree of emulation and that the strictest discipline were prevalent among all the surgeons.”<sup>8</sup>

Conflict continues to drive advances in military medicine. The sustained casualty rates since 2003 of UK military personnel in Operation Telic (Iraq)



**Figure 7-1.** Damage control resuscitation. Surgery to control bleeding, massive transfusion, and hemostatic resuscitation are encompassed within the the first (red) box. The positive sequelae from appropriate treatment are shown in subsequent boxes. <C>ABC: catastrophic hemorrhage, airway, breathing, and circulation; MT: massive transfusion

and Operation Herrick (Afghanistan) have allowed greater understanding of the pathophysiology of major trauma and stimulated the development of new paradigms of care and structured practice guidelines. The new practices, which evolved into DCR, are focused on a common team approach to ensure rapid restoration of physiology in preference to definitive surgical treatment.<sup>1,9</sup> To deliver effective DCR, this approach must be rehearsed in predeployment training so that each provider becomes familiar with new and often unfamiliar team dynamics. DCR principles include a horizontal trauma team in which all members (surgeons, anesthesiologists, nurses, and others) are encouraged to contribute to the trauma management discussion in order to solve problems and improve care. To this end, DCR training should train those who will be working together in future deployments. This training has been widely termed “crew resource management”; it aims to ensure all team members are familiar with the environment, equipment, and roles in future challenging DCR situations. All UK deploying clinicians attend a 5-day predeployment clinical

exercise practicing challenging medical scenarios in an exact copy of a Role 3 hospital.

During DCR it is possible that individuals, especially clinicians performing critical procedures, may become overly focused on immediate tasks and lose overall situation awareness (termed “reduced bandwidth”). Therefore, a designated leader of the resuscitation team must ensure effective communication among all key members. During the initial stages of resuscitation, the primary goal is restoring physiology, while surgery is limited to controlling hemorrhage and minimizing wound contamination (see Damage Control Surgery, below). It is incumbent on the resuscitation leader to ensure this aim is achieved. This may require a pause in surgery to focus on additional dressings, packs, clamps, or direct pressure to reduce bleeding while volume is restored by the anesthesia team. Once volume has been restored, surgeons should do the minimum surgery needed to save the patient’s life. Further debridement and definitive surgery can occur at a later stage in the evacuation process, hours or days after the initial resuscitation.

## PRINCIPLES OF DAMAGE CONTROL RESUSCITATION

### Pathophysiology

Major trauma is a generic term covering a wide range of injuries and injury mechanisms. The physical injury itself differs according to its etiology, for example blunt, penetrating, or blast, as well as the individual patient. Many factors, including presence of hemorrhage, head injury, coagulopathy, and hypothermia, as well as the care given, influence the initial physiologic insult sustained in the initial trauma.

DCR includes the accepted concepts of the “lethal triad” of hypothermia, acidosis, and coagulopathy; however, recent major advances in the understanding of coagulopathy have occurred.

“Trauma-induced coagulopathy” is a term encompassing the coagulopathy related to the traumatic insult and includes acidosis, hypothermia, platelet consumption, blood loss, and dilution. More recently a further subgroup of trauma-induced coagulopathy, termed “acute trauma coagulopathy” (ATC), has been described.<sup>2</sup> This is a primary pathological event whose cause remains uncertain, but increasing evidence points toward a mechanism that includes tissue hypoperfusion, hyperfibrinolysis, activation of protein C, and up-regulation of thrombomodulin. The driver of ATC appears to be related to poor tissue oxygen and results in activation of the vascular endothelium. The endothelium is a poorly understood structure that is implicated not only in ATC but also in the development of systemic

inflammatory response syndrome, which can ultimately lead to multiorgan dysfunction and increased mortality.<sup>10</sup> This process occurs independently of crystalloid administration, acidosis, and hypothermia.

DCR aims to restore tissue oxygen delivery in order to reverse the pathological processes driven by the hypoxic endothelium and restore normal physiology. This approach is coupled with treatment and prevention of hypothermia, acidosis, and coagulopathy. The military approach is to target these pathologies as early and as aggressively as is practical from the point of wounding, along the evacuation chain, and into the Role 3 hospital. At the Role 3 hospital, the three major components of DCR, surgery to control bleeding, massive transfusion, and hemostatic resuscitation, are instigated simultaneously.<sup>1,2</sup>

### Point of Wounding

Hemorrhage remains the leading cause of death in military trauma.<sup>11</sup> Early treatment or temporary control at the point of wounding is essential for survival.<sup>11</sup> Much effort has gone into improving the care given at point of wounding.<sup>11</sup> This includes training in the use of the <C>ABC (catastrophic hemorrhage, airway, breathing, and circulation) paradigm, which is the core of the BATLS system and incorporates the use of the hemostatic agents and the timely application of tourniquets.

## Specialist Retrieval Teams

Care by appropriately trained prehospital doctors (with critical care and airway skills) has been shown to significantly improve survival from major trauma.<sup>12,13</sup> An integral part of the British military trauma system is the medical emergency response team (enhanced), or MERT(E), which consists of a prehospital-trained attending anesthesiologist or emergency physician, two paramedics, and an emergency department flight nurse. This specialist team is able to initiate DCR in flight by gaining rapid intravenous or intraosseous access and administering warm blood products with other specific therapies such as tranexamic acid. The ability to perform advanced airway maneuvers, diverting casualties to the appropriate medical facility, and senior decision-making have contributed to the success of this type of prehospital care. However, this model of prehospital care is very different from what is performed in the civilian setting or military medical systems of other nations. The MERT(E) model has been validated since its introduction and robust evidence of its effectiveness has been produced to guide other services.<sup>13-15</sup>

## Damage Control Surgery

Damage control surgery, the surgical component of DCR, is focused on control of major anatomical bleeding, removal of dead tissue, and gross decontamination.<sup>16</sup>

## Permissive Hypotension

Hypotensive resuscitation is a standard of practice in hemorrhaging patients without traumatic brain injury.<sup>17</sup> Numerous animal models of uncontrolled hemorrhagic shock have demonstrated improved outcomes when a lower than normal mean arterial pressure of 60 to 70 mm Hg is used as the target for fluid administration during active hemorrhage.<sup>18</sup> Two large human trials have demonstrated the safety of this approach (relative to the conventional target of greater than 100 mm Hg), suggesting various benefits including shorter duration of hemorrhage and reduced mortality.<sup>19,20</sup>

Animal models incorporating blast injury and hemorrhage, however, have demonstrated a high mortality if hypotensive resuscitation is used in blast injury patients. Follow-up studies using a prehospital blood pressure profile (termed "novel hybrid resuscitation") utilized a blood pressure of 90 mm Hg (palpable radial pulse) for 60 minutes, followed by volume boluses to a target blood pressure of 110 mm Hg. The study

concluded that more animals survived overall, and for longer, than those animals allowed 120 minutes of permissive hypotension. Using the results of this study's parameters with battlefield casualties may permit a longer survival timeline, allowing live casualties to reach a facility where DCR can be instigated.

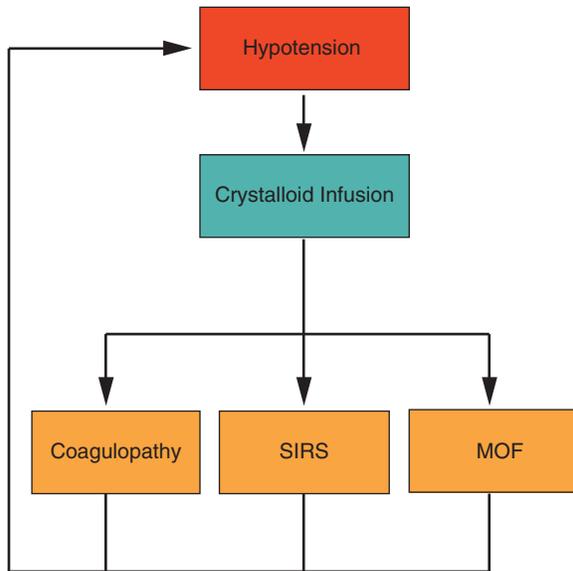
## Fluids

Crystalloid has been the mainstay of resuscitation since the Vietnam War, when it was first popularized.<sup>21</sup> In 1978 it was adapted by the American College of Surgeon's Advanced Trauma Life Support Group, who advocated using two large-bore cannulas and 2,000 mL of lactated Ringer solution for the hypotensive casualty.<sup>22</sup> With the introduction of the DCR protocol, however, the overall use of crystalloid has decreased dramatically.<sup>23</sup> This has helped reduce the major adverse effects of unchecked crystalloid administration: acute lung injury and acute abdominal compartment syndrome (diagnosed since the Vietnam War), together with acute renal failure, multiorgan dysfunction, and anastomotic leaks (termed the "vicious salt water cycle").<sup>21</sup>

Reperfusion injury is marked in hemorrhaging trauma casualties.<sup>24</sup> There is evidence that crystalloid activates white cells, thereby stimulating systemic inflammatory response syndrome. This is probably potentiated by the "d" stereoisomer of lactate (present in Hartmann solution), which the body fails to metabolize.<sup>25</sup> Over-resuscitation with crystalloid may lead to uncontrolled hemorrhage due to dilution of clotting factors, causing a hypocoagulable state with the sequelae of reduced organ perfusion, and abdominal compartment syndrome (Figure 7-2).<sup>26</sup> These complications predispose casualties to multiple organ failure and increased mortality, compared with moderate resuscitation.<sup>21-26</sup>

## Hemostatic Resuscitation

Hemostatic resuscitation is defined as the rapid proactive treatment of coagulopathy associated with major trauma<sup>27</sup> and aims to gain physiological control of bleeding through the use of massive hemorrhage protocols with high ratios of packed red blood cells : fresh frozen plasma : and platelets (PRBC:FFP:PLT), as well as medical adjuncts guided by laboratory and point-of-care testing. This has been shown to improve outcomes.<sup>17</sup> Early in resuscitation, the patient is managed empirically using massive hemorrhage protocols with the emphasis on restoring lost blood volume, treating shock, and improving tissue oxygenation to avoid further development of ATC. Once bleeding has stopped and shock is reversed, a more goal-directed

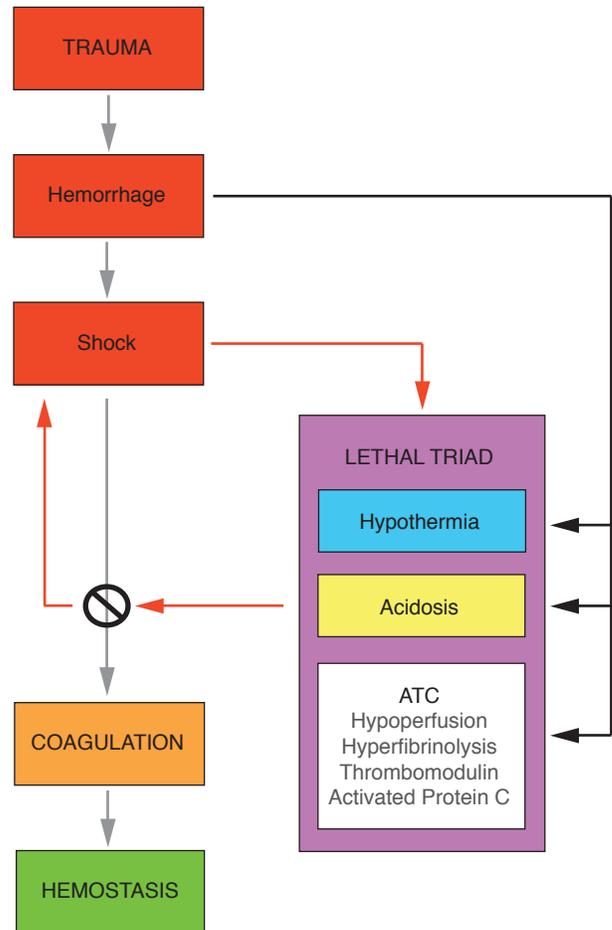


**Figure 7-2.** Perils of over-administration of crystalloid, which may lead to coagulopathy, systemic inflammatory response syndrome, and multiple organ failure.  
 MOF: multiple organ failure  
 SIRS: systemic inflammatory response syndrome

approach to managing coagulopathy is advocated; its aims are to prevent dilution, replace factors lost due to consumption and bleeding, and treat deficiencies caused by ATC through the administration of effective whole blood resuscitation using blood product components (Figure 7-3). This is done with the use of point-of-care coagulation testing such as ROTEM (TEM International GmbH, Munich, Germany) or TEG (Haemonetics Corp, Braintree, MA) and standard laboratory blood counts. To achieve effective whole blood replacement, PRBC:FFP:PLT ratios of approaching 1:1:1 have been advocated. Fresh whole blood is still available to the deployed clinician.

**Point-of-Care Testing**

Point-of-care testing is becoming increasing important and recognized as crucial to the treatment of the patient during DCR. It includes arterial blood gas analysis and coagulation monitoring using thromboelastometry (ROTEM or TEG). Either ROTEM or TEG can determine failure in each part of the clotting cas-



**Figure 7-3.** Hemostatic resuscitation.  
 ATC: acute trauma coagulopathy

cade from clot initiation to propagation, amplification, and stabilization. Recent clinical use of ROTEM with experimental use of platelet function analysis (multi-plate) has implied that platelet function is affected early in trauma, so some new guidelines now incorporate the early, empiric use of platelets rather than using the traditional trigger of a platelet count below 100.<sup>28</sup> Point-of-care testing gives results to clinicians in a clinically relevant time, allowing them to concentrate on delivering blood and blood products to the patient, and reduces the logistical delay and burden on laboratories. Ultimately it allows for more individualized patient treatment.

**MANAGING THE PHYSIOLOGY**

The evolution of DCR philosophy, coupled with increased training and experience in current conflicts, has resulted in very effective and aggressive administration of large amounts of blood products according

to massive hemorrhage protocols. Massive transfusion rapidly treats underlying hemorrhagic shock but, unless carefully monitored, has potentially lethal sequelae. Base deficit, calcium, and potassium levels

are all available in point-of-care blood gas analysis and should be performed at least every 30 minutes in the early stages of resuscitation.

### Acidosis

Virtually all coagulation stages are inhibited by acidosis. Platelets alter shape at a pH below 7.4, and  $\text{Ca}^{2+}$  binding sites are pH-dependent,<sup>29</sup> but the main process inhibited is thrombin generation.<sup>30</sup> Unsurprisingly, trauma nonsurvivors were more likely to have a lower pH than survivors.<sup>26</sup> Martini et al demonstrated that thrombin generation was inhibited by a pH of 7.1 by as much as 50% with an additional 35% reduction in fibrinogen. Platelet count was also reduced by 50%.<sup>30</sup>

In addition to pH, base deficit is a sensitive indicator of hypoperfusion and correlates with mortality.<sup>26</sup> At levels below -12.5, it has been demonstrated to directly inhibit coagulation.<sup>30-32</sup> Base deficit has also been used to predict transfusion requirements.<sup>33</sup> A recent review concluded that a notable impairment of hemostasis arises at a pH of 7.1 and below, with similar effects observed at base deficit of -12.5 or less.<sup>34</sup> Thus, when there is severe hemorrhage and acidemia, buffering toward physiologic pH values is advantageous, especially when massive transfusions of older PRBCs displaying exhausted red blood cell buffer systems are used.<sup>30</sup>

### Calcium

JR Green was the first to show that "calcium is instrumental in bringing about coagulation when added to plasma which shows little or no tendency to clot, and that coagulation in its absence is almost or quite prevented" (1887).<sup>31</sup> Hypocalcemia is common in critically ill trauma patients and is associated with increased mortality.<sup>32,33</sup> It has since been shown that calcium is required for several reactions in the coagulation cascade and in platelet activation.<sup>32-34</sup> Citrate (a chelating agent) is added to blood products (FFP in particular) to prevent clotting during storage. It follows that a patient receiving a massive transfusion will be hypocalcemic and coagulopathic regardless of other measures taken to improve coagulation. It is recommended that ionized calcium levels be maintained above 1.0 mmol/L for effective coagulation to occur.<sup>35</sup>

### Potassium

Hyperkalemia is common after PRBC transfusion, and often severe.<sup>36</sup> It appears to be more common after transfusion under pressure and with older units of PRBCs, most likely due to increased cell lysis. It is therefore essential to closely monitor potassium levels

throughout the resuscitation and maintain a concentration within the normal range. If hyperkalemia is detected, the myocardium should be protected by administering calcium and starting an insulin/dextrose infusion immediately to regain control.

### Hypothermia

The causes of hypothermia in the trauma patient are reduced heat production and increased heat loss. Hypovolemic shock results in an inadequate oxygen delivery to the tissues, which impairs cellular respiration and results in a decreased heat production. Hypotension and hypovolemia inhibit shivering, preventing this normal response to hypothermia. Increased heat loss occurs through environmental exposure and, during the resuscitation phase, is primarily caused by administering cold fluids. Heat loss is proportional to the volume given and the temperature difference between the patient and the fluid.<sup>37</sup> The energy needed by the body to warm 2,000 mL of fluid infused at 25°C within 1 hour exceeds the energy that can be delivered by conventional warming methods in the same time.<sup>38</sup>

Hypothermia has effects on all body systems, including reduced cardiac output and impaired respiratory and endocrine function. During DCR, its most significant effect is on coagulation, producing a reduction in platelet function and number, inhibition of the coagulation cascade, and increased fibrinolytic activity.<sup>39</sup> A significant effect on platelet function is observed even in mild hypothermia (34°C) through an inhibition of thromboxane  $\text{B}_2$  and reduced expression of surface molecules, leading to poor aggregation. At the same temperature the reduction in platelet numbers is due to sequestration in the liver and spleen.<sup>40</sup>

Coagulation cascade enzyme reactions are strongly suppressed by hypothermia. In one study, a temperature of 34°C was the critical point at which enzyme activity in trauma patients slowed significantly. At temperatures below 33°C, hypothermia produces a coagulopathy equivalent to 50% of activity at normothermia, despite the presence of normal clotting factor levels.<sup>41</sup> It is important to note that this effect on coagulation occurs even in isolated areas of the body, and superficial cooling of a limb with preserved core temperature results in a significantly prolonged bleeding time. It should also be noted that tests of coagulation are performed at 37°C, so a purely hypothermia-induced coagulopathy will not be demonstrated by laboratory tests.<sup>26</sup>

Avoiding and correcting hypothermia is critical in preventing or correcting coagulopathy in a patient receiving massive transfusion. The resuscitation and

operating rooms must be warmed. All fluids administered must pass through a warmer. Hot air convection should be used above the patient, and electric mattresses under the patient have been proven useful

when multiple body cavities are being operated on simultaneously. The patient should be insulated as much as possible, which can be difficult when large surgical exposure is required.

## MEDICAL ADJUNCTS

### Antifibrinolytics

The 2010 CRASH-2 trial showed that administering tranexamic acid to adult trauma patients with, or at risk of, significant hemorrhage within 8 hours of injury reduced all-cause mortality with no apparent increase in vascular occlusive events.<sup>42</sup> As a consequence of this trial, tranexamic acid has been incorporated into trauma treatment protocols worldwide. A further analysis of the CRASH-2 study demonstrated a 32% increased survival if the tranexamic acid is given within 3 hours to bleeding trauma patients, but beyond this time it is less effective and could be harmful. The trial protocol involved administering 1 g as soon as possible, followed by another 1 g administered over the subsequent 8 hours. This procedure rarely takes place in military medicine because the first dose is often administered near the point of wounding (eg, during the MERT(E) stage), and then further blood products and adjuncts are given when further laboratory or thromboelastometry results are known.

### Recombinant Activated Factor VII

Factor VII is a crucial component of coagulation, binding to tissue factor (a lipoprotein present in endothelial cells) exposed by injury, generating activated factor X and subsequently thrombin. Recombinant activated factor VII (rFVIIa) is licensed for use in

patients with hemophilia and inhibitory antibodies. Its enhancement of hemostasis directly at the site of injury has stimulated research into possible uses in trauma.<sup>43,44</sup> Two parallel, multi-center, randomized controlled trials have shown a statistically significant reduction in blood transfusion requirements in blunt (but not penetrating) trauma patients treated with rFVIIa.<sup>45</sup> Although the trial and statistics have been the subject of criticism, these studies remain some of the best evidence available. The effectiveness of rFVIIa (not limited to trauma) has also been assessed by a Cochrane review, which concluded that rFVIIa as a hemostatic adjunct in trauma remains unproven.<sup>46</sup>

The benefit of using rFVIIa must be balanced against its thrombogenic potential.<sup>47</sup> Although not licensed for the treatment of traumatic hemorrhage, rFVIIa use continues. Given its substantial cost, further research is warranted. Previously, it had been DMS policy to give rFVIIa to any salvageable patient with continuing hemorrhage that has failed surgical and nonsurgical treatments. However, with the advent of DCR, patients are now less coagulopathic, acidotic, and hypothermic, and consequently the use of rFVIIa has declined considerably. During mature operations such as Afghanistan the use of rFVIIa is now limited; however, in less well located and supported hospitals, there may be potential for the use of rFVIIa to help reduce blood usage and extend resuscitation timelines.

## END POINTS OF RESUSCITATION

DCR is a concept aimed at restoring physiology, and end points are critical in determining when aggressive protocols should cease and more measured approaches begun. Current end points are summarized in Figure 7-4. Critical to resuscitation is returning blood pressure to normal values when central circulation is filled. However, the patient still requires further resuscitation to ensure that peripheral circulation is also filled. To achieve this, targeted resuscitation must continue after blood pressure returns to normal. Many approaches to targeted resuscitation may be used, but most military proponents now administer a high-dose opioid anesthetic similar to cardiac anesthesia. This procedure causes a degree of vasodilatation allowing resuscitation of the peripheral compartment. It is fair

to say that end points of resuscitation remain uncertain; however, markers of tissue perfusion are likely to provide the most information about whole-body tissue oxygenation.

Future strategies are focusing on the treatment of coagulopathy with statins, with optimum ratios of FFP : PRBC : platelets, and earlier use of blood products, such as in the prehospital phase. Ongoing military research involves the use of prehospital recombinant erythropoietin and better use of blood products in the prehospital phase by using freeze dried plasma (Lypolas; DRK-Blutspendedienst West gGmbH, Hagen, Germany) and synthetic hemoglobin. Recent work with dogs cooled to below 18°C to ascertain whether surgery at this temperature would “suspend” further

tissue damage and allow trauma surgery to be undertaken with lower risk has moved into human trials. Also, work has recently begun at the UPMC Presbyterian Hospital in Pittsburgh, Pennsylvania, with deep hypothermia for trauma victims, termed emergency preservation and resuscitation. Lead researcher Dr Sam Tisherman and his team of surgeons are hoping to replicate animal research in this area. Probably the greatest advances in care will occur with earlier and more targeted treatment in the prehospital phase, particularly where long transport times are prevalent. Prehospital systems in Europe are already trialling the use of extracorporeal membrane oxygenation, and the first prehospital resuscitative endovascular balloon of the aorta (REBOA) has already been used successfully in London. Early use of synthetic blood products, better patient warming, intelligent tasking of doctor-led prehospital teams, and shortened on-scene times, together with early computed tomography scanning, will allow time to surgery to be reduced in those patients who require it. These efforts hold promise to improve outcomes and reduce morbidity.

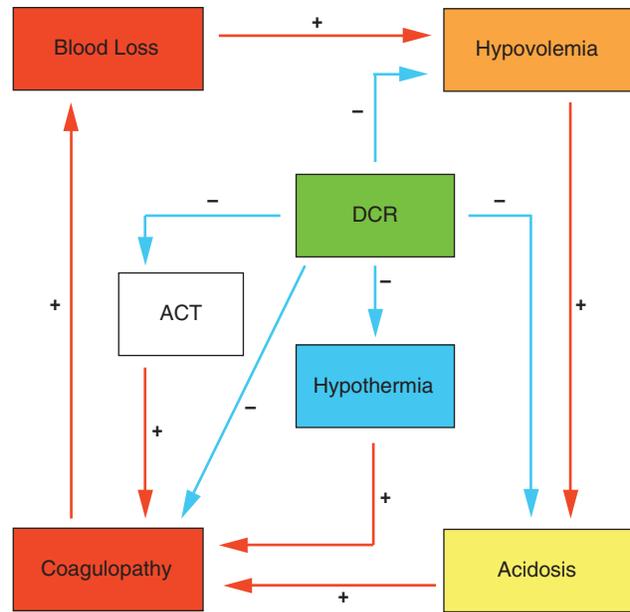


Figure 7-4. End points of damage control resuscitation.

### SUMMARY

DCR is a complex process that aims to restore physiology in order to save life. If practiced effectively by well-hearsed, experienced teams, life can be saved, physiology

rapidly restored, and surgical options increased. It is a technique that requires flexibility, a thorough understanding of the pitfalls of massive transfusion, and attention to detail.

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